Project on-

‘Guideline for acute therapy and management of Anaphylaxis’

Submitted by-

ID: 173-29-1124

18th Batch

This project report was presented in order to meet the requirements for the Bachelor of Pharmacy degree in the Department of Pharmacy

Department of Pharmacy

Daffodil International University

Declaration

I, hereby humbly declare that, the dissertation work titled "**Guideline for acute therapy & Management of Anaphylaxis** " a requirement for the degree **Bachelor of Pharmacy (B. Pharm**) program under the faculty of Allied Health Sciences **Daffodil International University**, Bangladesh was carried out by me under the guidance of my supervisor during the study period of ----------

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APPROVAL

'Guideline for acute therapy and management of Anaphylaxis' is submitted by **Md. Jewel Rana . ID: 173-29-1124** ; to the **Department of Pharmacy, Daffodil International University** has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of B.Pharm in the Pharmacy Department, and its style and contents have been authorized.

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Dedication

Dedicated to my beloved parents , teachers and my elder adorable sister for their amicable support and help .

Guideline for acute therapy and management of Anaphylaxis

Abstract: Anaphylaxis is the most severe form of an immediate-type allergy that can be fatal. Because of the often dramatic start and clinical course of these responses, clinicians and patients must have practical understanding of how to manage them. There must be a distinction made between acute therapy modalities and general management suggestions for patients who have experienced an allergic reaction. Acute care includes general procedures such as positioning, inserting an intravenous catheter, calling for assistance, ensuring the patient's comfort, and administering medication. Depending on the severity of the clinical symptomatology, the acute therapy modalities are chosen. First and foremost, anaphylaxis must be diagnosed early and a variety of differential diagnoses must be considered. The diagnosis is entirely clinical, and laboratory testing are of no use in an emergency. In pharmacologic treatment, epinephrine is the most important anti-anaphylactic medication. It should be administered intramuscularly first, with intravenous administration being attempted only in the most severe cases or in the case of surgical operations. Furthermore, glucocorticosteroids are used to avoid long-term or biphasic anaphylaxis; nevertheless, they are ineffective in the acute scenario. Auto injectors for epinephrine can be used by the patient. In mild anaphylactic reactions, histamine H1-antagonists are useful; if possible, they should be given intravenously. In anaphylactic treatment, volume replenishment is critical. In the beginning, crystalloids can be utilized, but in cases of severe shock, colloid volume replacements must be employed. Patients experiencing an anaphylactic reaction should be monitored for 4-10 hours, depending on the severity of their symptoms. It is critical to be aware of or recognize high-risk patients, such as those with severe uncontrolled asthma or those who are on -adrenergic blockade. Inhaled under-agonists can also be used for laryngeal edema when bronchial symptoms are the focus. Prior to the administration of potentially anaphylaxis-inducing medications (e.g. radiographic contrast media), the use of combination H1- and H2-antagonists has been advocated for prophylaxis. Patients who have survived an anaphylactic reaction must be extensively investigated, and an allergy diagnosis must be made based on the eliciting agent and pathogenic mechanism. In the case of IgE-mediated anaphylaxis, allergen-specific immunotherapy is available for some allergens and can be beneficial, as in the instance of insect venom anaphylaxis. Patients should also be educated on the nature of anaphylaxis, the main eliciting agents, and the principles of behavior and coping with the condition, including how to use epinephrine autoinjectors and antianaphylactic medications. There have been produced educational programs for anaphylaxis.

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Chapter -1

Introduction: Anaphylaxis is a life-threatening acute hypersensitivity reaction that is a common medical emergency. It's a widespread, multi-system allergic reaction that's continuously evolving. Anaphylaxis is often fatal if not treated, as it quickly progresses to respiratory collapse. Anaphylactic reactions have traditionally been classified as IgE-mediated events, whereas anaphylaxis reactions have been classified as IgE-independent events. These words have recently been merged into a single anaphylactic diagnosis. Because the clinical condition and treatment for each reaction are identical regardless of causality, this unified nomenclature is now the standard vernacular. [1-3]

Because the number of meaningful studies on anaphylaxis treatment is so limited, many fields still rely on empirical management, which is frequently based on pathophysiological thoughts. Anaphylactic responses can come to a halt at any stage of symptomatology, but they can also develop despite effective treatment. Because of this unpredictability, evaluating the efficacy of therapeutic interventions is difficult. The effectiveness of specific measures cannot be determined based on observations of a single case. However, it is clear that patients who developed anaphylaxis as a result of an insect sting did not receive proper follow-up care [4, 5]. The fact that basic patient care is inadequate emphasizes the necessity for additional study as well as the significance of the current guideline.

This guideline is for all doctors and other medical professionals who are involved in the immediate care, diagnosis, and counseling of anaphylactic patients.

Objectives :

Discuss the most recent definition of anaphylaxis .To figure out how common anaphylaxis is .The goal of this paper is to discuss the clinical aspects of anaphylaxis. Recognize the most common inciting sources in anaphylaxis etiology. Explain the role of IgE-mediated immunity in the pathophysiology of anaphylaxis. Write a summary of the clinical criteria used to assess anaphylaxis. Emphasize the need of strengthening care coordination among members of the inter professional team to enhance anaphylactic patient outcomes. Review biphasic anaphylactic events Compile a list of relevant ED discharge materials. Plan for effective anaphylactic therapy. Understand the symptoms and indications of anaphylaxis. Identify gaps in anaphylaxis diagnosis and management. Learn about food allergy testing and how to use them. Understand and be able to show how to use an epipen. Plan for effective anaphylaxis therapy. Explain how to manage and follow up on anaphylaxis in outpatient settings. Identify anaphylaxis patients who should be monitored after their symptoms have subsided. I got a chance to browse inside the shock box and practice drawing up adrenaline. List seven drugs used to treat anaphylaxis and their dosages in Anaphylaxis. Anaphylaxis is suspected based on the identity discovery. Learn about the causes, symptoms, and clinical manifestations of anaphylaxis. Demonstrate a safe response to a patient who has anaphylaxis. Understand how to diagnose and treat a patient who is experiencing life-threatening Anaphylaxis. Understand the decisive management and referral choices for an Anaphylaxis patient.

Chapter -2

Epidemiology of Anaphylaxis

The non-uniform ICD-10 coding terms of anaphylaxis are a limitation of data on the epidemiology of anaphylaxis. Anaphylaxis is included in a number of ICD-10 code phrases. Furthermore, anaphylaxis is defined in a variety of ways around the world [6].

The actual prevalence and incidence of anaphylaxis in the general population and across various age groups is unknown. Anaphylaxis caused by insect stings is estimated to affect 1 to 3 percent of people. [7-8]

According to retrospective research, up to 1% of patients who present to a maximum-care hospital's emergency department have an anaphylactic reaction [9]. Anaphylaxis-related deaths are estimated to be one to three per million people each year [10].

On the epidemiology of anaphylaxis, there are recent research from the United States, the United Kingdom, and Australia. They report anaphylaxis rates ranging from 7 to 50 per 100,000 per year [11–13]. Foods are the most common triggers of anaphylaxis in children, according to data from various countries throughout the world (Tab-1) [14]. Insect poison and medications are the most common triggers in adults around the world. Boys are more likely than girls to develop anaphylaxis throughout childhood, with gender distribution adaptation occurring after puberty [15].

Table -1

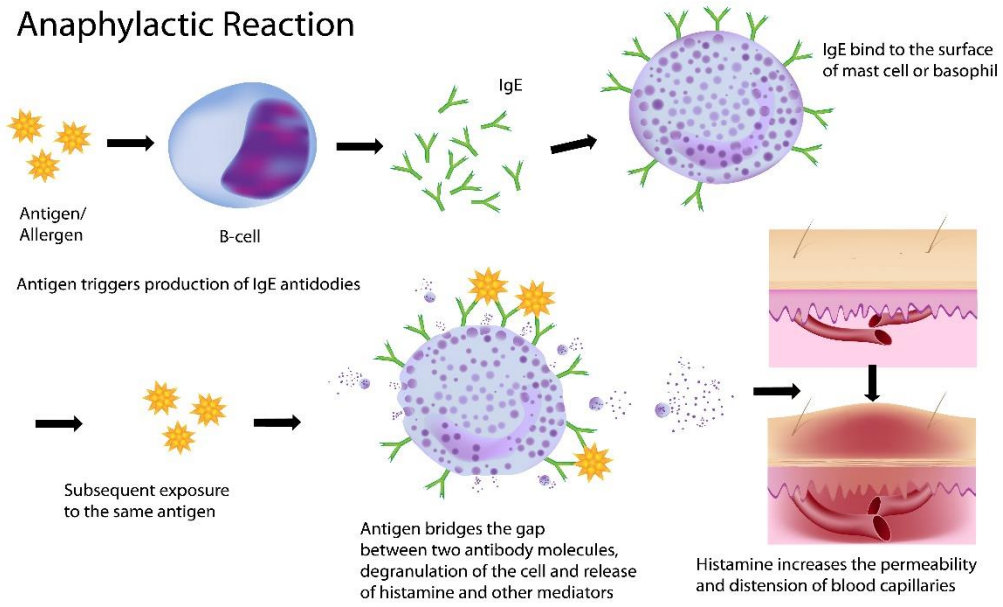
Elicitor	Children	Adults
Food	58%	16%
Insect Venoms	24%	55%
Drug	8%	21%

Pathophysiology of Anaphylaxis

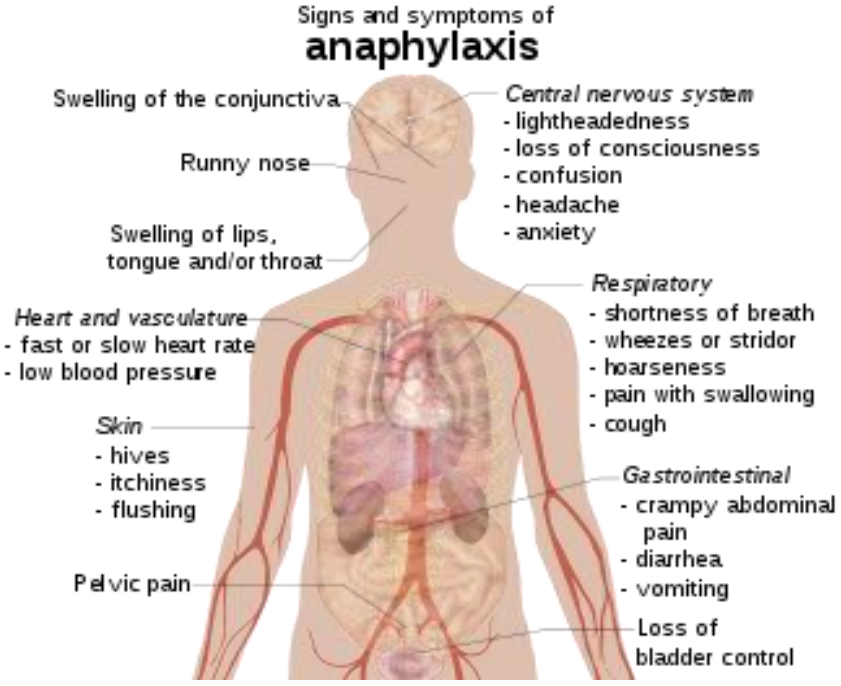
The symptoms of anaphylactic reactions are caused by the release of various mediators from mast cells and basophil granulocytes (e.g. histamine, prostaglandins, leukotrienes, tryptase, platelet-activating factor, cytokines, chemokines) [16–18], but the individual significance of each of these is not assessed in detail. Histamine, on the other hand, is widely believed to have a key role in anaphylactic reactions.

Many of these mediators are thought to be involved in anaphylactic pathophysiology. Histamine enhances vascular permeability, heart rate, cardiac contraction, and glandular secretion through stimulating vasodilation. Bronchoconstrictor, pulmonary and coronary vasoconstrictor, and peripheral vasodilator, prostaglandin D2 Bronchoconstriction, increased vascular permeability, and airway remodeling are all caused by leukotrienes. PAF is a bronchoconstrictor that also increases vascular permeability. TNF- stimulates neutrophils, attracts other effector cells, and boosts the production of chemokines [19].

These overlapping and synergistic physiological effects contribute to the overall pathophysiology of anaphylaxis, which can manifest as urticaria, angioedema, bronchospasm, and other respiratory symptoms, hypotension, syncope, and other cardiovascular symptoms, as well as nausea, cramping, and other gastrointestinal symptoms. Anaphylaxis can be biphasic or last for a long time"[20]



Sign & Symptoms of Anaphylaxis



All of these symptoms aren't always present at the same time in a patient.

There are numerous types of reactions that could happen:

Uniphasic - these appear suddenly and the symptoms quickly worsen, but once treated, the symptoms disappear and do not reappear.[21]

Bi-phasic reactions are characterized by mild or severe symptoms at first, followed by a period of no symptoms, followed by an increase in symptoms such as breathing and blood pressure difficulties. The majority of biphasic reactions take place within hours of the initial reaction, however they might occasionally take longer . A biphasic reaction has been documented to occur up to 72 hours following the initial reaction on very rare occasions.[21]

Prolonged anaphylaxis might linger for many days and necessitate hospitalization for a period of time.[21]

The severity of anaphylaxis is graded from I to IV, depending on the severity of the clinical symptoms (Tab.2) [22-23]

Table-2

Grade	Skin	Abdomen	Airways	Cardiovascular System
I.	Urticaria Angioedema Itch Flush	–	–	–
II.	Urticaria Angioedema Itch Flush	Cramps of Nausea	Hoarseness Dyspnea Rhinorrhea	>20 beats per minute tachycardia (> 20 mm Hg syst.) hypertension Arrhythmia
III.	Urticaria Angioedema Itch Flush	Defecation Vomiting	Edema of the larynx Cyanosis of the Bronchospasm	Schock
IV.	Urticaria Angioedema Itch Flush	Defecation Vomiting	Respiratory failure	Arrest of the heart

Chapter -3

Allergens & triggers

Anaphylaxis can be triggered by nearly any foreign material. [29] Venom from insect bites or stings, meals, and medications are all common causes. [18] In children and young people, food is the most prevalent trigger, although in older adults, drugs and insect bites and stings are more common. [24] Physical factors, biological substances such as semen and latex, hormonal changes, dietary additives such as monosodium glutamate and food colors, and topical drugs are some of the less common reasons. [28] Physical variables like exercise (also known as exercise-induced anaphylaxis) and temperature (hot or cold) can operate as triggers by directly affecting mast cells. [24] Exercise-related events are typically linked to cofactors such as the consumption of certain meals. [26][30] or by taking a nonsteroidal anti-inflammatory drug (NSAID). Neuromuscular blocking drugs, antibiotics, and latex are the most common causes of anesthetic complications. [31] In 32–50 percent of instances, the etiology is unknown, which is referred to as "idiopathic anaphylaxis." [23] Six vaccines are known to cause anaphylaxis (MMR, varicella, influenza, hepatitis B, tetanus, and meningococcal), and HPV may also cause anaphylaxis. [33]

Food

Many foods can cause anaphylaxis, which can happen even after the first known ingestion. [18] The most common triggering meals differ from country to country. In Western cultures, the most common causes are ingestion or exposure to peanuts, wheat, nuts, certain types of seafood such as shellfish, milk, and eggs. [24] [27] Sesame seeds are common in the Middle East, while rice and chickpeas are prominent allergy triggers in Asia. [24] Although severe cases are primarily triggered by eating the allergen,[8] some persons have a strong reaction simply by coming into contact with it. Allergies can be overcome by children. By the age of 16, 80 percent of children with anaphylactic reactions to milk or eggs, and 20% of children with isolated anaphylactic reactions to peanuts, can tolerate these foods. [29]

Medicine

Anaphylaxis can be triggered by any medicine. -lactam antibiotics (such as penicillin) are the most common, followed by aspirin and NSAIDs. [27] [34] Other drugs have been linked to fewer cases. Anaphylactic reactions to NSAIDs are either agent specific or occur among those that are structurally related, which means that people who are allergic to one NSAID can usually tolerate another or a combination of NSAIDs. [35] Chemotherapy, vaccinations, protamine, and herbal treatments are some of the most common causes. [3] Some drugs, such as vancomycin, morphine, and x-ray contrast, cause anaphylaxis by causing mast cell degranulation. [18]

The frequency of a reaction to an agent is determined in part by the frequency with which it is used and in part by its intrinsic qualities. [36] Anaphylaxis to penicillin or cephalosporins develops only after the antibiotic binds to proteins inside the body, with some agents adhering more readily than others. Anaphylaxis to penicillin occurs in per 2,000 to 10,000 courses of treatment, with fewer than one in every 50,000 courses resulting in death. Anaphylaxis to aspirin and NSAIDs affects roughly one person out of every 50,000. If someone has had a penicillin reaction, the chance of having a reaction to cephalosporins is higher, but still less than one in 1,000. [26] The older radiocontrast agents caused reactions in 1% of cases, while the current reduced osmolar agents induce reactions in 0.04 percent. [36]

Venom

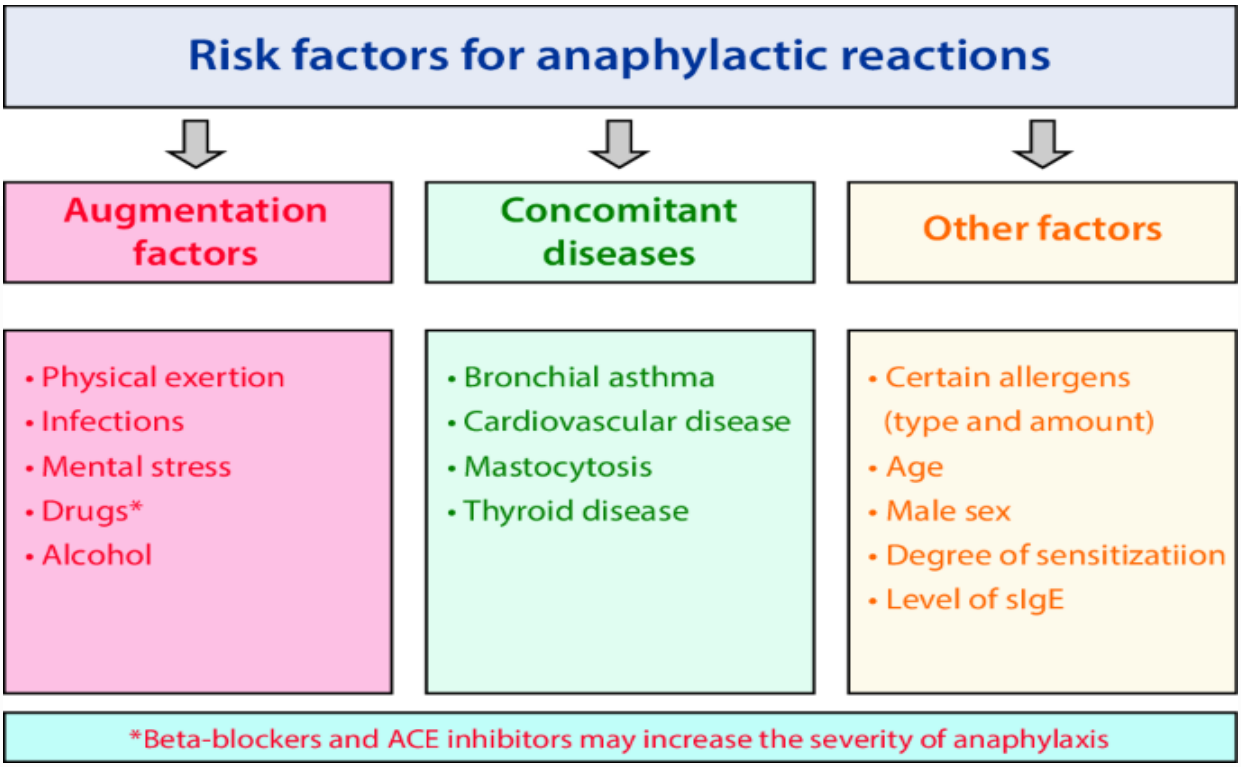
Hymenoptera (ants, bees, and wasps) and Triatominae (kissing bugs) venom can trigger anaphylaxis in persons who are allergic to it. [25] [37-38] Previous systemic reactions that are more than a local reaction near the sting site are a risk factor for future anaphylaxis; nevertheless, half of fatalities have never had a systemic reaction. [39]

Risk factors of Anaphylaxis

The risk of severe anaphylaxis might be increased by certain endogenous or external variables. Advanced age, significant cardiovascular disease, (inadequately treated) bronchial asthma, use of

certain medicines that enhance mast cell activation or leukotriene secretion (such as NSAID), and mastocytosis are all risk factors of this type (Fig. 1), which are independent of the elicitor. [40-41].

Figure-1



A number of case reports and case series [42-44], as well as two case control studies on anaphylaxis frequency and severity after administration of radiographic contrast media [45,46], support the theory that taking beta-adrenoceptor antagonists (beta-blockers) increases the risk of severe anaphylaxis.The use of beta-adrenoceptor antagonists is linked to a higher incidence of severe anaphylaxis [40]

There have been reports of food-induced anaphylaxis, with allergic bronchial asthma being a key risk factor [47]. Finally, the elicitor may be a risk factor in and of itself—primary sensitization to peanut or fish, both highly potent allergens, has been shown to be a risk factor for severe reactions [48]

Chapter -4

Diagnosis and important differential diagnosis

Anaphylaxis can be difficult to diagnose since the clinical symptoms are not always consistent. Various acute reactions, such as other forms of isolated urticaria, bronchial obstruction, vomiting, nausea, diarrhea, agitation, loss of consciousness, cardiac arrhythmia, and/or cardiac arrest, must be distinguished from anaphylactic symptoms. Bellow lists relevant differential diagnoses. Following adequate initial treatment, measuring mediators in the blood, particularly serum tryptase, is beneficial—ideally 1–3 hours after the onset of anaphylaxis and, if possible, in comparison to basal serum tryptase. Tryptase can be measured retrospectively, even after death, but it is not always increased [41, 49, 50].

Cardiovascular Diseases –

- Cardiogenic shock
- Cardiac arrhythmia
- Vasovagal syncope
- Hypertensive emergency
- A pulmonary embolism is a type of blood clot that forms in the lungs
- Myocardial infarction (myocardial infarction) is a type of heart attack that occurs

Endocrinological diseases –

- Pheochromocytoma
- Thyrotoxi crisis
- Carcinoid syndrome
- Hypoglycemia (low blood sugar)

Psychiatric disorders –

- Anxiety/panic attacks
- Dissociative disturbances and conversion disorders
- Hyperventilation syndrome
- Mental illnesses
- Mental illnesses (Münchhausen syndrome)
- Somatoform abnormalities (for example, psychogenic dyspnea and "voice cord dysfunction")
- Epilepsy is a condition that affects people.

Respiratory Diseases –

- Status asthmaticus (acute severe asthma with no other organ involvement)
- Acute obstructive tracheitis

- Obstruction of the trachea/bronchi (e.g. foreign objects)

Skin Diseases –

- Urticaria and angioedema, both hereditary and acquired

Medicinal Substances –

- Ethanol
- Histaminosis is a type of histaminosis that occurs
- Opioids are a type of opioid (morphine)
- Histaminosis (e.g., scombroid poisoning)
- Hoigné-Syndrome is a kind of Hoigné-Syndrome.

The following symptoms were identified as being particularly important for the diagnosis of anaphylaxis at a consensus meeting [6]:

- Rapid onset respiratory symptoms (e.g. dyspnea, wheeze, cough, stridor) or a sudden blood pressure drop or clinical manifestations thereof (e.g. collapse, tachycardia, incontinence) or a sudden blood pressure drop or clinical manifestations thereof (e.g. collapse, tachycardia, incontinence) or a sudden blood pressure drop or clinical manifestations thereof (e.g. collapse, tachy cardia, incontinence)
- Hypotension after coming into contact with a known allergy or another anaphylactic trigger.

The pharmacology of the most major medications used to treat anaphylaxis

The following drugs have been shown to be useful in particular pharmacotherapy:

Vasoactive substances

Adrenaline: The most significant medicine in the acute treatment of anaphylaxis (epinephrine). [51-52] .Adrenaline antagonizes all of the key pathomechanisms of allergy by vasoconstriction, vascular permeability reduction, bronchodilation, edema reduction, and positive inotropy in the heart by activating - and -adrenergic receptors. It has the quickest onset of effect of all anaphylactic medications when given intravenously.

Immediate intramuscular administration of 0.3 to 0.5 mg adrenaline (body weight range 30 to 50 kg) to the outer upper thigh is the medication therapy of choice in a patient who does not require resuscitation. The risk of serious cardiac side effects is significantly decreased when compared to intravenous administration. In the event that there is no response, the injection can be repeated every 5–10 minutes, depending on the side effects.

Because of poor absorption, which results in a delayed beginning of effect, subcutaneous injection of adrenaline is no longer indicated.

If the patient is unstable or during resuscitation, i.e. in case of respiratory and/or circulatory arrest, adrenaline should be applied intravenously [53]. For this, a dilution of 1 mg adrenaline in 10 ml NaCl 0.9 %, i.e. a solution of 0.1 mg/ml is administered, depending on effects and side effects, under continuous control of circulatory parameters. A continuous infusion of approx. 0.05–1 µg/kg/minute is equally effective. Control of pulse and blood pressure is mandatory. In patients receiving treatment with β-adrenoreceptor antagonists and not responding to the repeated injection of adrenaline or other vasoactive substances (see below), administration of glucagon is recommended [54]. Glucagon, however, only has an effect on cardiac symptoms. Glucagon, on the other hand, solely affects heart symptoms.

In the case of laryngeal edema and bronchospasm, further inhalation of adrenaline following intramuscular administration is useful. Adrenaline (e.g. 2 ml of 1 mg/ml) delivered with oxygen through a nebulizer and breathing mask is recommended for this purpose. Inhaled adrenaline cannot take the place of parenteral administration.[55]

Additional administration of an inhalative -adreno-receptor agonist, such as salbutamol or terbutaline, at a dose of 2–4 puffs, is beneficial in the case of predominantly bronchial blockage. When employing an aerosol spray, a spacer device should be employed to optimize the efficacy of inhalation.[57]

Treatment failure or negative effects might occur even when adrenaline is used properly. Because an increase in cardiac output leads to increased oxygen consumption and can be arrhythmogenic, intravenous adrenaline can trigger angina pectoris or a myocardial infarction in people with coronary heart disease. Adrenaline has no absolute contraindication in the case of severe life-threatening anaphylaxis. In individuals with pre-existing heart disease, however, the indication should be carefully examined.[56,58]

Other vasoactive substances

In the emergency room, emergency physicians employ dopamine, noradrenaline, and vasopressin, as well as cardiopulmonary motoring in intensive care patients.

Dopamine

Dopamine, which acts on alpha- and beta-adrenoceptors and has a short half-life [59, 60], is no longer used in emergency and intensive care medicine since it can elicit undesired tachycardia and is markedly less effective in stabilizing blood pressure than adrenaline or noradrenaline, which can be well titrated with syringe drivers.

Noradrenaline

Noradrenaline has a lesser stimulatory potency at the beta2-adrenoceptor than adrenaline and so has a poorer bronchodilatory action at therapeutic levels. As a result, it has the primary effect of increasing peripheral resistance and systolic blood pressure. It has a minor effect on the lungs. When volume replacement and adrenaline are insufficient, noradrenaline is employed [52, 62,63]. It should only be used as a continuous intravenous infusion under strict blood pressure and pulse monitoring because of its significant vasoconstrictive effects. The dosage ranges from 0.02–0.15 g/kg every minute.

Vasopressin

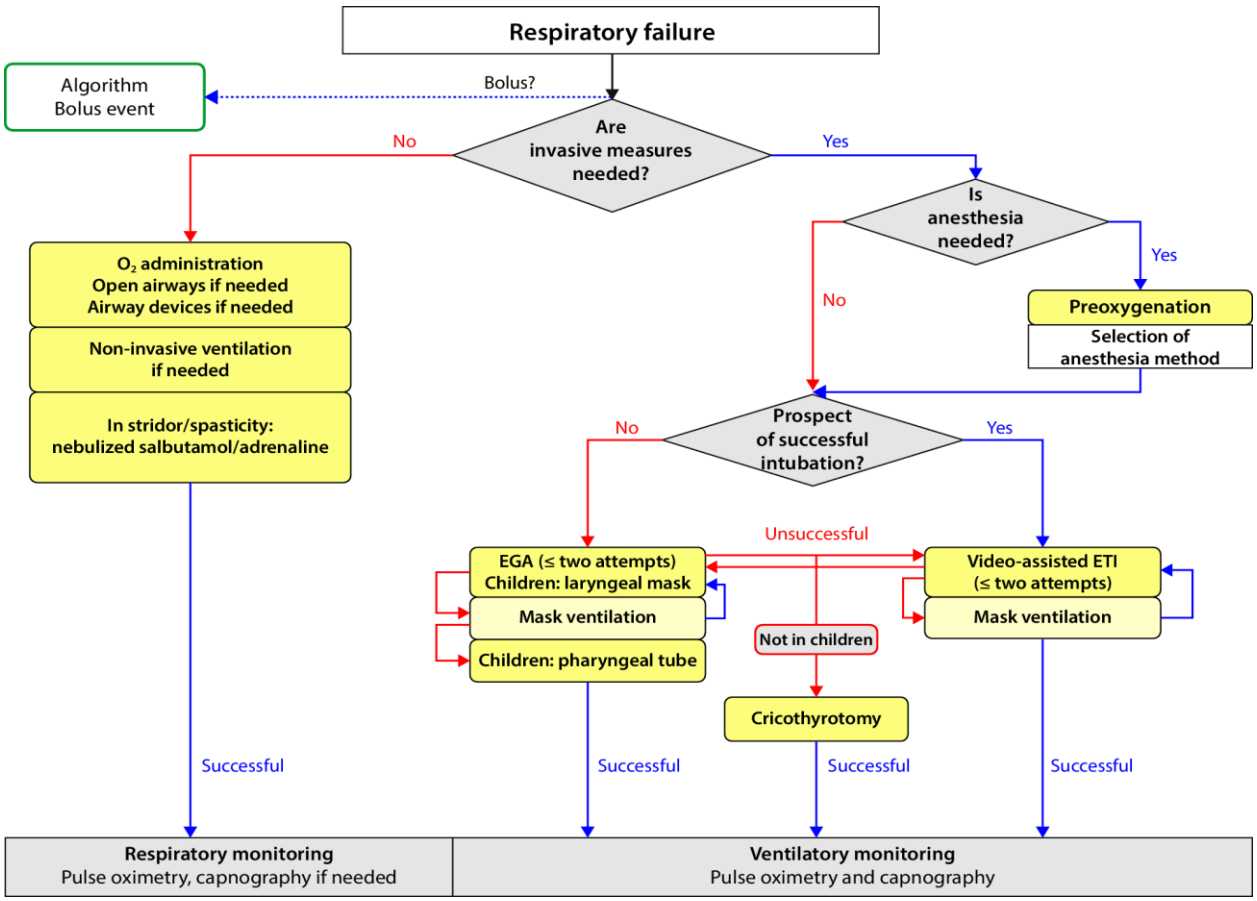
Anesthesiologists [62] have described the use of vasopressin in the treatment of severe hypotension.Vasopressin has been used successfully in volume- and catecholamine-refractory

shock, according to individual accounts. This is not an evidence-based treatment; it is used only in the most severe cases of chronic shock when volume and other catecholamines have failed to relieve the symptoms. For children, there was no evidence of an influence on mortality or the length of time spent in critical care. The dosage ranges from 0.01 and 0.03 international units (IU) per minute .

Oxygen

When there are obvious cardiovascular or pulmonary symptoms, oxygen should be administered through a breathing mask, preferably a non-rebreather mask. It is recommended that high-flow oxygen (100 percent) be administered. It may be beneficial to use a laryngeal mask or tube. Tracheal intubation by an experienced physician (typically an emergency physician or anesthetist) is only required in rare cases. The reader is directed to the S1 prehospital airway management guidelines, which provide an algorithm that explains both the indication for and the execution of invasive prehospital airway care (Fig. 2; [55]).

Figure-2



The resultant relative hypovolemia caused by vasodilation and capillary leakage [64] is a fundamental pathophysiologic component of anaphylaxis. As a result, volume therapy can only be employed in conjunction with adrenaline therapy's important mast cell stabilizing and vasoconstrictor effects [65-67]. A large-lumen intravenous catheter is the only way to achieve this. Intraosseous access should be acquired if an intravenous injection is not possible. In adults, anaphylactic shock necessitates the fast delivery of a large volume: 1–3 liters of balanced electrolyte solution, depending on the reaction. In children, 20 ml/kg BW is first given by hand as quickly as feasible. Following re-evaluation, repeated 20 ml/kg boluses are given until hemodynamic stabilization is achieved.

Despite their beneficial hemodynamic effects, gelatin and dextran solutions should not be utilized in anaphylaxis due to their histamine-releasing potency and risk of triggering anaphylaxis (e.g., dextran without pretreatment with lo w molecular hapten-dextran) [69].

The European Medicines Agency (EMA) recently concluded that hydroxyethyl starch (HES) preparations are contraindicated in critically unwell patients [69-71]. The guideline group is hesitant to issue recommendations because of a paucity of relevant material.

Antihistamines (histamine H1-receptor antagonists)

Histamine's central role as a mediator of allergic reactions, as well as the effect of histamine H1-receptor antagonists in acute urticaria or rhinoconjunctivitis, is undeniable; nevertheless, their effects on circulation and bronchoconstriction have yet to be established [72]. Antihistamines take longer to take effect than adrenaline, but they have a strong benefit–risk ratio and a broad therapeutic window. It's reasonable to expect that there will be an effect on allergic reactions. Antihistamines should be provided in all anaphylactic reactions to counteract the effects of histamine as soon as possible once essential functions have been stabilized.

Only the first-generation histamine H1-receptor antagonists dimetindene (0.1 mg/kg BW) and clemastine (0.05 mg/kg BW), with their well-known sedative side effects, are available for intravenous administration in the immediate treatment of anaphylaxis. Antihistamines can cause antimuscarinic effects such as tachycardia, mouth dryness, intestinal atony, urine retention, elevated intraocular pressure, glaucoma attack, and paradoxical states of arousal at larger doses [73]. As a result, these signs and symptoms must be considered.

Second-generation histamine H1-antagonists are not yet approved for the treatment of anaphylaxis and are not available for intravenous injection; however, the newer, more selective histamine H1-antagonists are frequently recommended as an oral treatment because they have shown rapid onset of action in placebo-controlled skin test studies [72]. When it comes to oral antihistamines, the maximum permitted dose is usually the best option. Higher doses (up to four times the allowed single dose) can be administered in particular situations, according to the expert panel, as indicated in the treatment of chronic urticaria [74]. More research with novel H1-receptor antagonists for

anaphylaxis treatment is urgently needed. Intravenous formulations of contemporary non-sedating H1-antihistamines, in particular, would be desired.

There isn't much evidence that histamine H2-receptor antagonists help in acute anaphylactic events. In one trial, the addition of ranitidine to histamine H1-receptor antagonists alone in the treatment of allergic reactions resulted in a reduction in cutaneous symptoms [75]. Although the effect was not tested independently from other treatments, there is more evidence for the avoidance of allergic events by adding histamine H2-receptor antagonists [76-78]. It is possible to utilize histamine H1- and H2-receptor antagonists together [79].

Glucocorticoids

Because of their late start of action, glucocorticoids have a secondary role in the acute phase of anaphylaxis [82].

For this indication, there have been no systematic clinical trials. In the treatment of asthma, however, glucocorticoids are useful. Review publications [81-82] suggest that very large dosages of glucocorticoids (in humans, 500–1000 mg, regardless of potency) have a non-specific membrane-stabilizing impact within 10–30 minutes of administration. Glucocorticoids can be given orally in syrup form or rectally in suppository form in the absence of intravenous access, especially in small children (e.g., prednisolone suppositories or rectal enemas) at a dose of 2 mg/kg.

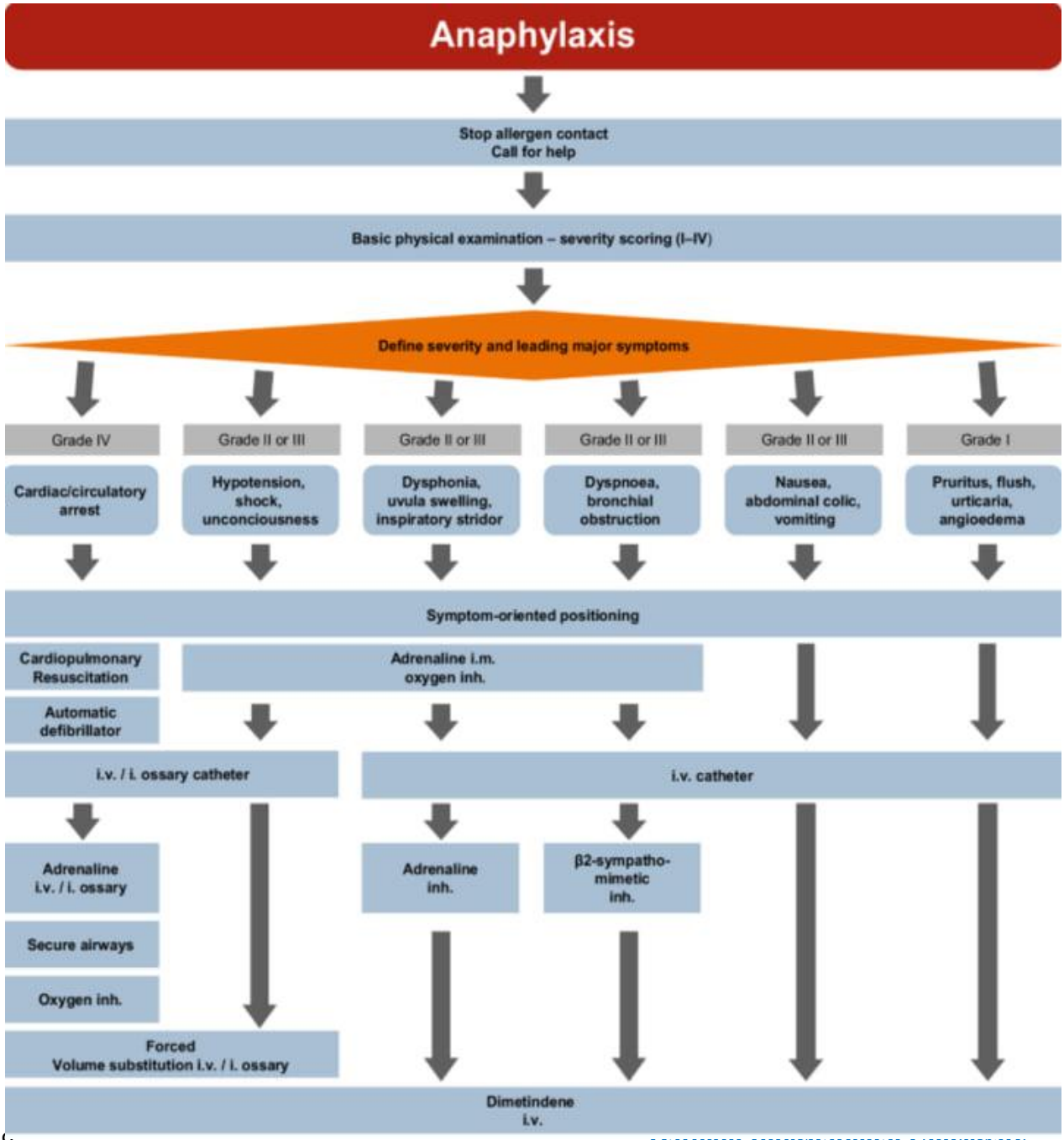
Treatment with glucocorticoids should be used only after essential functions have been stabilized and emergency life-saving measures have been taken, such as oxygen, intramuscular adrenaline, or volume substitution!

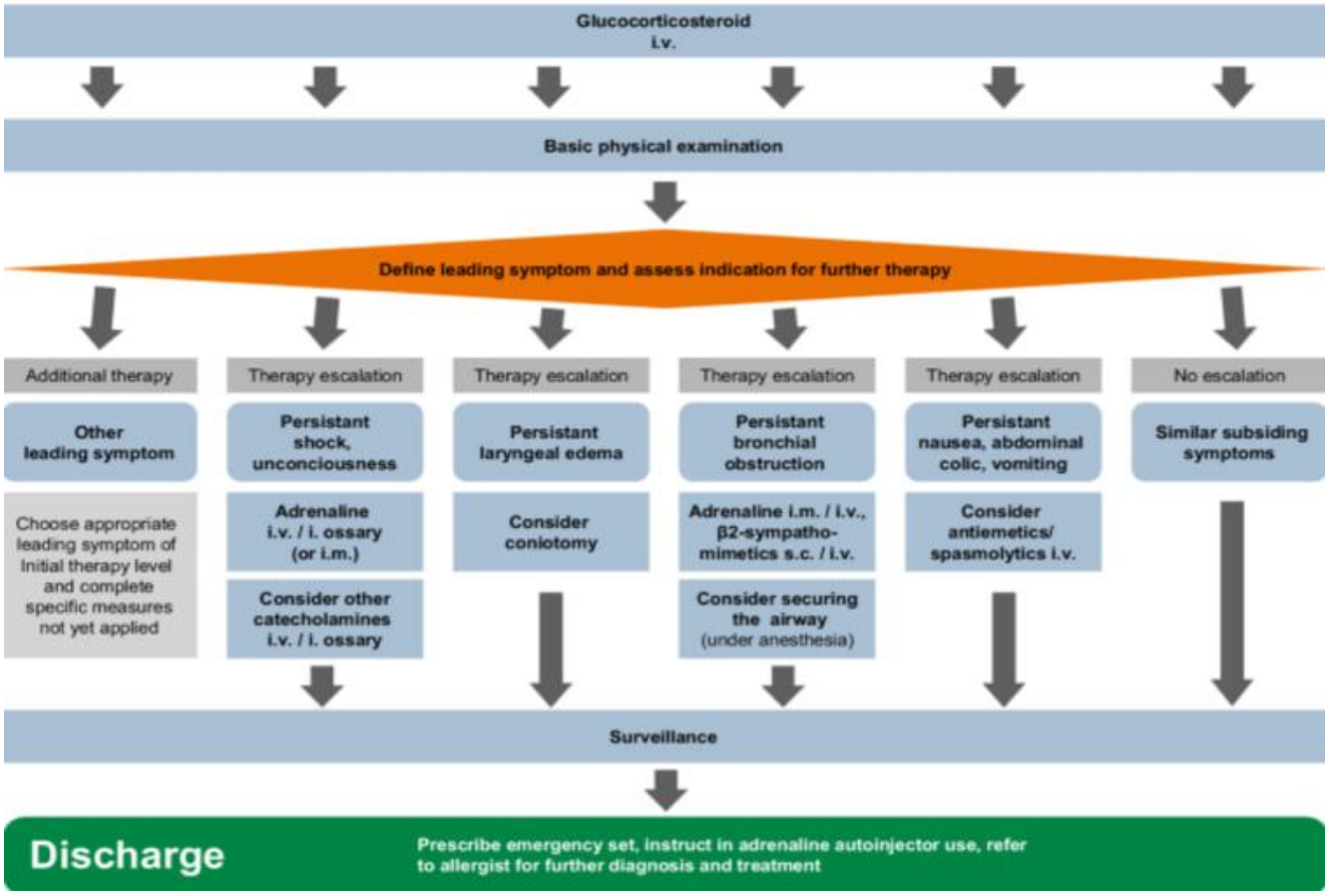
Chapter -5

Treatment

Anaphylaxis must be treated quickly and symptomatically. A schematic depicting the treatment stages for physicians and the emergency team has been published and is being updated in the development of this guideline (Fig.3) [83].

Figure-3





If feasible, further allergen exposure should be avoided at first. In some cases (such as intravenous infusion), this can be accomplished quickly. Due to the minimal therapeutic efficacy and risk of losing time for more crucial measures, applying a tourniquet and/or injecting epinephrine subcutaneously around a local allergen depot (e.g., a wasp sting or injection site of particular immunotherapy) is no longer suggested. To ensure sufficient medical care, more aid should be requested. In his or her practice, every physician should have emergency equipment for the treatment of anaphylactic responses (Tab.3). It's best to take a collaborative strategy that allows you to delegate procedures.

Table -3

Emergency equipment for treatment of anaphylactic reactions [85]
Blood pressure monitor and stethoscope
Mask/nasal cannula for oxygen
Intubation equipment, Guedel-tube, bag valve mask, suction unit
Adrenaline is a substance that can be injected.
Intravenous infusion of H1 antihistamines
Infusion solutions (0.9 percent NaCl solution, electrolytes/colloids in a balanced ratio)
Intravenous injections of glucocorticoids
Bronchiodilator (adrenoreceptor agonist for inhalation or intravenous injection that acts quickly)
External automatic defibrillator (optional)
Pulse oximeter is a device that measures the amount of oxygen in the blood (optional)

First, take a fast history and perform a basic physical examination (Fig.3). This includes the following [84]:

- Vital signs examination (spontaneous movements and breathing)
- Pulse and blood pressure readings (strength, frequency, regularity)
- Breathing assessment (dyspnea on speaking, inspiratory or expiratory stridor, wheezing, optional: auscultation, measurement of the peak flow using a mechanical peak flow meter, pulse oximetry),

- Visible skin and mucous membranes are examined.
- Questioning for further problems (e.g. nausea, need to vomit, headache, sternal pressure, visual disruption, pruritus, etc.).
- Trying to figure out if there are any allergies.

Possible alert values for vital parameters are described in (Tab.4) In the course of acute management, these examinations should be done on a frequent basis. [85]

Table -4

Age-related alarm thresholds	**1year maximum**	**1 to 5 years**	**6 to 14 years**	**> 14 years old**
Pulse rate (per minute)	>160	>130	>120	>110
Blood pressure is a measurement of the amount of pressure (systolic, mmHg)	<50	<60	<60	<70
(min) Respiratory rate	>40	>35	>30	>25
Saturation of Oxygen (percent)	<92	<92	<92	<92

Smaller youngsters can be inspected first in their parents' arms. To enable for proper inspection and treatment, it is necessary to calm both the youngster and the parents. Inspection of the mouth or auscultation of the heart may be difficult or impossible when the youngster is fidgety. The use of a spatula can irritate the airway, which should be avoided. Prolonged expiration, in- or expiratory stridor, wheezing, salivation, thoracic wall retraction, and nasal alae constriction should all be checked for as symptoms of airway blockage.

Severity assessment

The severity of the anaphylaxis should be assessed based on the examination, and the most dangerous anaphylactic symptom should be determined (Fig.3)[83] Anaphylaxis' most life-threatening symptom should be addressed first. This could result in one of six scenarios:

- Anaphylaxis in the presence of cardiac or circulatory arrest (anaphylaxis grade IV)
- Anaphylaxis with a prominent cardiac and circulatory reaction (grade II/III anaphylaxis)
- Anaphylaxis with upper airway obstruction (anaphylaxis grade II/III)
- Anaphylaxis with lower airway obstruction (anaphylaxis grade II/III)
- Anaphylaxis with gastrointestinal involvement is the most common type of anaphylaxis (anaphylaxis grade II)
- Anaphylaxis with broad systemic cutaneous signs and subjective symptoms (anaphylaxis grade I).

Positioning

The patient should be positioned according to their symptoms right after the evaluation. The fundamental strategies are horizontal positioning and avoiding further physical activity (walking or attempting to sit up). The location can be changed depending on the situation. Getting up and doing strenuous activity should be avoided due to the risk of anaphylaxis worsening (as with co-factors). The recovery position is preferred when consciousness is disturbed, particularly in a preclinical scenario. The patient may be placed in the Trendelenburg position to improve their hemodynamic status (elevated legs). A (half) sitting position is better in cases where respiratory symptoms are prominent. Actions should not be forced in the handling of children in order to prevent worsening their anguish.

With cardiac or circulatory arrest, anaphylaxis can occur

Adults should begin cardiopulmonary resuscitation with chest compressions and mouth-to-mouth breathing at a ratio of 30:2 (compressions:breaths). In children, resuscitation is started according to the current European Resuscitation Council (ERC) recommendations, which include five initial breaths followed by two breaths every 15 chest compressions. In the instance of ventricular fibrillation, an automatic defibrillator should be employed, and early defibrillation should be administered. Further pharmacological treatment will necessitate the use of an intravenous or intraosseous catheter. The medicine of choice is adrenaline (intravenous or intraosseous) at a dose of 1 mg in adults or 0.01 mg/kg in children, which is given in 3–5 minute intervals until spontaneous circulation is stabilized [56,58]. Bag-valve-mask ventilation with 100% oxygen is sufficient for sufficient oxygenation in emergency treatment. Supraglottic airway devices are utilized if optimization measures (head positioning, Guedel tube, two-person technique) are unsuccessful in the case of mask ventilation issues. Laryngeal masks and tubes can be used by people of all ages. In tiny children, a pharyngeal tube can be used instead; breathing is induced by a nasal tube (tube length = tip of nose–ear tragus) while the mouth and other nostrils are kept closed. The ultimate approach of airway management is endotracheal intubation. In the case of sufficient knowledge, this can also be done as a first step. Endotracheal intubation should only be conducted by experienced personnel [55,86], regardless of age group.

According to the pathophysiology of anaphylaxis, it is critical to correct for the underlying volume shortage by using forced volume replacement. It is suggested that you be transferred to an intensive care unit as soon as possible and treated there (Table 5).

Table-5

Pediatric, adolescent, and adult pharmacotherapy in intensive care settings

Substance	Application Procedure	15 kg (body weight)	15-30 kg body weight	30-60 kg body weight	> 60 kg body weight
Adrenaline	1 bolus intravenous	(from 1 mg/10 ml) 0.1 ml/kg bw 1	(from 1 mg/10 ml) 0.1 ml/kg bw 1	0.05–0.1 ml/kg bw (from 1 mg/10 ml) 1	0.05–0.1 ml/kg bw (from 1 mg/10 ml) 1
Adrenaline	Infusions on a continuous basis	0.05–1.0 g/kg per minute	0.05–1.0 g/kg per minute	0.05–1.0 g/kg per minute	0.05–1.0 g/kg per minute
Adrenaline	Using a nebulizer, inhaled	two milliliters	two milliliters	two milliliters	two milliliters
Dimetindene	Intravenous	one milliliter	3–2 ml	Four milliliter	1 ml/10 kg bw = 8 ml3
Prednisolone	Intravenous	50 milligrams	100 milligrams	250 milligrams	Between 250 and 1000 mg
Terbutalin Salbutamol	Inhaled	Per spacer,2 puffs DA	Per spacer,2 puffs DA	2-4 puffs per spacer of DA	2-4 puffs per spacer of DA

Repoterol	Infusions on a continuous basis	0,1 micro gram /kg/min	0,1 micro gram /kg/min	0,1 micro gram /kg/min	0,1 micro gram /kg/min
Volume	bolus (0.9 percent NaCl	20 ml/kg body weight	20 ml/kg body weight	10-20 ml/kg body weight	10-20 ml/kg body weight
Volume	Infusion	1-2 ml per kilogram per minute	1-2 ml per kilogram per minute	1-2 ml per kilogram per minute	1-2 ml per kilogram per minute
Oxygen	Inhaled	2 l/min – 10 l/min	5-12 liters per minute	5-12 liters per minute	5-12 liters per minute

Anaphylaxis with a cardiovascular response as the main symptom

An intramuscular (body weight-adjusted) injection of adrenaline is indicated as an emergency measure, especially if an intravenous catheter is not available (Fig 3; Table 5). In this case, the usage of adrenaline auto-injectors for layman administration may be useful due to their ease of use. Auto-injectors with standardized doses of 0.15 mg, 0.3 mg, or 0.5 mg are realistic single doses for delivery. The intramuscular injection might be repeated after 5–10 minutes if the reaction is insufficient.

The goal of oxygen delivery is to increase the inspired oxygen fraction (FiO2) to >0.5. With a non-rebreather oxygen mask, this is conceivable. Nasal tubes do not substantially raise FiO2.

Vomiting should be predicted in all cases of diminished consciousness. This must be taken into account when situating the patient. The Esmarch (jaw thrust) maneuver should be used to open the mouth and check for vomited material or foreign things (e.g., dental prostheses). It's beneficial to have a working suction device.

Further treatment will necessitate the use of an intravenous catheter (Table 5). In the event that this is not achievable, an intraosseous catheter is recommended. The main goal of treatment is to compensate for the loss of relative volume. A volume bolus of a crystalloid solution (balanced electrolyte solution) over 5 minutes is necessary for forced volume replacement. Adults receive 500–1000 ml, whereas children receive a volume bolus of 20 ml/kg at first. A large-lumen indwelling venous catheter (at least 18 gauge) or numerous catheters are required for a flow rate of this size.

In cases of prolonged or life-threatening shock, fractionated intravenous/intraosseous or intramuscular adrenaline injection or a continuous drip of adrenaline is recommended. After vital functions have been stabilized and i.m. adrenaline has been administered, antiallergic medicines such as histamine H1-receptor antagonists (note: antimuscarinic side effects of sedating anthistamines!) or glucocorticoids should be utilized (Table 5). In these circumstances, continuous blood pressure and pulse monitoring is recommended. Other sympathomimetic medications, such as noradrenaline, or a continuous infusion starting with pumps under continuous monitoring, may be utilized with enough knowledge.

Anaphylaxis with upper airway obstruction

This condition is marked by clinically noticeable enlargement in the area of the upper airways. Swelling of the tongue or uvula, dysphonia, or inspiratory stridor are all symptoms of this. If the laryngeal entry is occluded, these conditions might become life-threatening. Adrenaline injections intramuscularly and oxygen delivery are indicated as a quick fix (Fig. 3). In such cases, further adrenaline inhalation is often recommended (Tables 5 and 6). If the therapeutic response is insufficient, prehospital airway management should be performed using the algorithm in the S1 guideline (Fig. 2; [55]).

Table -6

Under non-intensive conditions, pharmacotherapy for children, adolescents, and adults (e.g., outpatient setting)

Substance	Application Procedure	15 kg (body weight)	15-30 kg body weight	30-60 kg body weight	> 60 kg body weight
Adrenaline	Intramuscular	1 mg/1 ml (0.01 ml/kg bw)	1 mg/1 ml (0.01 ml/kg bw)	1 mg/1 ml (0.01 ml/kg bw)	1 mg/1 ml (0.01 ml/kg bw) 1
Adrenaline	Auto injector IM	See i.m .	150 micro gram	300 micro gram	300-600 micro gram
Adrenaline	1 Intravenous bolus	0.1 ml/kg bw (equivalent to 1 mg/10 ml) 1	0.1 ml/kg bw (equivalent to 1 mg/10 ml) 1	(of 1 mg/10 ml) 0,05–0,1 ml/kg bw 2	(of 1 mg/10 ml) 0,05–0,1 ml/kg bw 2
Adrenaline	Using a nebulizer, inhaled	two milliliters	two milliliters	two milliliters	two milliliters
Dimetindene	Intravenous	one milliliter	1 mL per 10 kg of body weight (max. 4 ml)	4 ml Equals 1 ampule	1–2 ampule = 4–8 ml3 (1 ml/10 kg body weight)
Prednisolone	Intravenous	50 milligrams	100 milligrams	250 milligrams	Between 500 and 1000 mg

Terbutalin Salbutamol	Inhaled	Per spacer,2 hubs DA	Per spacer,2 hubs DA	2-4 hubs per spacer of DA	2-4 hubs per spacer of DA
Volume	bolus (0.9 percent NaCl	20 ml/kg body weight	20 ml/kg body weight	10-20 ml/kg body weight	10-20 ml/kg body weight
Volume	Infusion	1-2 ml per kilogram per minute	1-2 ml per kilogram per minute	1-2 ml per kilogram per minute	1-2 ml per kilogram per minute
Oxygen	Inhaled	2 l/min – 10 l/min	5-12 liters per minute	5-12 liters per minute	5-12 liters per minute

Anaphylaxis with bronchial obstruction as the primary symptom

This is one of the most typical symptoms of anaphylaxis. Adrenaline should be administered intramuscularly in all potentially life-threatening conditions. The use of topical bronchodilators is critical ([87]; Fig. 3). For the treatment of bronchial obstruction, a number of short-acting beta-adrenoceptor agonists (e.g., salbutamol, terbutaline) have been licensed (Tables 5 and 6). Patients with anaphylaxis frequently have limited experience with inhalation therapy, therefore spacers for metered dosage inhalers or techniques with continuous aerosol administration (such as pressure/oxygen connection masks and electric nebulizers) are more easily used. This is equally true for young children and youngsters who have never used inhalation therapy before. Compact battery-powered nebulizers are now available and can be utilized in preclinical emergency scenarios as well. Repeated i.m. adrenaline is given if therapy needs to be intensified. If resuscitation is required quickly, adrenaline can be given intravenously. An injectable beta2-adrenoceptor agonist (e.g., terbutaline s.c. or reproterole i.v.) is another option for treatment (Table 5).

Emergency anesthesia with invasive ventilation may be required in acute severe asthma cases with muscular exhaustion and failure of non-invasive ventilation [88]. Current anesthesia with esketamine and midazolam guidelines and recommendations should be followed [86].

Anaphylaxis with abdominal symptoms as the primary symptom

Anaphylaxis characterized by mostly stomach symptoms is treated similarly to anaphylaxis characterized by broad cutaneous symptoms (Fig.3). Only if systemically administered antiallergic medications fail to provide a satisfactory response will gastrointestinal symptoms be addressed separately. Symptoms such as nausea, vomiting, or stomach cramping may be present. Treatment options include antiemetics like metoclopramide, antihistamines like dimenhydrinate, and serotonin-[5-HT3] antagonists like ondansetron. Intravenous injection of a muscarinic receptor antagonist (butylscopolamine) may be considered for abdominal cramps.

Skin symptoms of anaphylaxis

The initial step is to insert an intravenous catheter. To keep this open, a crystalloid solution drip (e.g., balanced electrolyte solution) is recommended. Antiallergic medications such as dimetindene or glucocorticoids are used in standard doses (Fig. 3; Table 6).

Chapter -6

Hospitalization has certain unique elements

Drugs that should be kept at the emergency room or on the ward in case of an emergency

Up to two adrenaline auto-injectors in the doses of 300 g or 500 g should be maintained on hand in emergency rooms and wards where provocation testing or allergy procedures with a higher risk of anaphylaxis are done. If minors are to be treated, two more 150-g adrenaline auto-injectors must be kept on hand. A nebulizer should be provided for administering adrenaline. Salbutamol for inhalation with appropriate devices (spacer or wet inhalation) as well as injectable histamine H1-receptor antagonists and glucocorticoids should also be on hand.

The process of treating patients with acute anaphylaxis at the emergency room

Individuals who present to the emergency department with anaphylaxis should be treated very away. Clinical criteria must be applied in order to obtain the diagnosis of "anaphylaxis". Continuous circulation monitoring, including pulse, blood pressure, and peripheral oxygen by pulse oximetry, must be established in addition to an initial examination of clinical signs and symptoms (Fig.3). Due to the likelihood of a biphasic (bimodal) reaction, patients with severe anaphylactic reactions (e.g., requiring an adrenaline auto-injector) should be hospitalized and observed for 24 hours.

The process of treating anaphylaxis on the ward

On the ward, anaphylaxis elicitors are frequently utilized as treatment. Parenterally delivered drugs cause quick reactions after use. Delayed symptoms are also conceivable with drugs for enteral administration. The first step is to stop exposing patient to allergens and notify the emergency team, depending on the severity of the situation.

Planned provocation testing in anaphylaxis has several unique issues

When a procedure with a risk of anaphylaxis is planned (allergy provocation test, allergen-specific immunotherapy with hymenoptera venom), meticulous planning is required, which includes:

- Emergency medication and an emergency plan are listed on the monitoring sheet
- Near the patient, emergency medications are produced in weight-adjusted doses
- If you experience allergy symptoms, get medical attention right away.
- Intravenous catheters are used to administer intravenous medications and fluids quickly.
- According to the flow diagram, the indication to administer medication is determined (Fig. 3).

In order to prepare for administration at home, it is recommended that affected patients or, in the case of small children, their parents learn to use the auto-injector under the supervision of medical personnel. If at all possible, training should be done using the same sort of auto-injector that the patient will use. This method allows patients to build confidence in using an auto-injector and reduces their dread of using one.

The method of treating anaphylaxis in the intensive care unit

High-level care (on an intensive care unit) with continuous monitoring has the advantage of detecting and treating shock states sooner. The main approach does not alter from other settings if intensive care professionals become aware of anaphylaxis, whether due to hypotension, tachycardia, a warning signal from the monitor, or low oxygen saturation. On an intensive care unit, common elicitors of anaphylaxis include pharmaceuticals and blood products; consequently, the first step is to stop administering the probable allergen or elicitor. Following that, the priority-oriented ABCDE (airway, breathing, circulation, disability, and exposure) strategy [84] is used. Syringe pumps may need to be adjusted depending on the current manner of intravenous catecholamine administration. Because of its unique mast-cell stabilizing function among catecholamines, adrenaline should be given. It's important to remember that, in the presence of a continuous vasopressor, the standard intramuscular delivery of 0.3–0.5 mg adrenaline may be ineffective due to peripheral hypoperfusion. In intensive care, intravenous administration is given in 50 g bolus doses in adults and 1 g/kg bolus doses in children [58] until the patient is

stabilized, preferably via a central venous catheter; however, peripheral delivery is also possible.

Therapy control management

It is critical to monitor the anaphylactic patient until he or she is in definite long-term remission (Fig.3) It's important to consider the likelihood of a biphasic course of anaphylaxis. As a result, in-patient hospital observation is recommended for all severe anaphylactic responses (grade II and higher). Anaphylaxis with life-threatening systemic reactions should be monitored in a hospital's intensive care unit. On discharge, the need for a self-treatment emergency kit (adrenaline auto-injector, antihistamines, glucocorticosteroids, and maybe a topical bronchodilatory aerosol spray) should be evaluated. Educational programs should be used to teach the practical use of emergency self-treatment equipment, particularly the use of the epinephrine autoinjector (Tab. 7; see below). It is required to see an allergist for a more thorough diagnosis and perhaps long-term treatment.[89]

Table-7

Substance	Dosage and delivery method
Adrenaline	Body-weight-adjusted autoinjector for intramuscular use: 150 g adrenaline > 30 kg 300 g adrenaline
Antihistamine H1	Depending on the age of the patient and if they prefer a liquid or a fast-melting pill. A single dose of the each antihistamine's permitted daily dose is recommended. Dimetindene drops can be administered orally at a bodyweight-adjusted dose that is equivalent to the intravenous dose.
Glucocorticosteroid	Oral or rectal (tablets or liquid) with 50–100 mg Prednisolone equivalent, depending on the patient's age and choice.
Optional	agonists of 2 adrenoceptors in individuals with bronchial asthma An adrenaline preparation for inhalation with a spray head is recommended when airway blockage is likely (to be ordered especially from the pharmacist)

After an anaphylactic reaction, discharge management is something to think about

Following successful anaphylactic therapy, patients and/or their relatives should be informed about the condition and undergo proper allergy testing (Table 6). If anaphylaxis occurs during surgery, an anesthetic certificate must be produced, and the patients must be notified of the reaction. It's critical to keep track of reactions, as well as symptoms, co-factors, and potential elicitors. A first-aid kit for emergencies is required (see below).

Under the supervision of a nutritionist with allergy competence and the working group on dietetics in allergology, patients with food allergies should follow an individually customized therapeutic elimination diet. The idea of allergen-specific immunotherapy should be considered following reactions to insect stings.

If the elicitor of anaphylaxis with extracutaneous symptoms cannot be reliably avoided (e.g., insect stings, foods), patients should be recommended to carry an emergency first-aid kit with them at all times, as well as a written document, such as an anaphylactic passport (see section below on patient management and self-medication). The patient should be given information on how to handle an emergency and how to take emergency medication. If the elicitor is a medicine commonly used in hospitals, an allergy passport with thorough documentation of the reaction should be provided to assist allergy diagnoses. In the case of recurring reactions, long-term pharmacological treatment, such as antihistamines or an anti-IgE antibody like omalizumab, may be considered [90,91].

Management of anaphylaxis during surgery

Because the patient is unable to convey early complaints such as itch or nausea when under analgosedation or general anesthesia, it is critical to maintain constant supervision and monitoring of respiratory and cardiovascular function. Other suspected anaphylactic symptoms should be sought right once if unexpected hypotension or tachycardia occur during the perioperative period:

- Erythema, edema, or urticaria forming on the arm receiving the infusion, perhaps starting on the arm receiving the infusion
- There was a decrease in pulse oximetry oxygen saturation or a prolonged expiration with lower expiratory flow.
- Lung compliance was reduced.

In the context of viscerosurgical procedures, the differential diagnosis must distinguish eventeration syndrome, which might appear clinically as prostacyclin-mediated flushing, tachycardia, and hypotension.

When the working diagnosis of severe anaphylaxis or anaphylactic shock is confirmed, adrenaline treatment is started right away. Titrated adrenaline in 0.1- to 0.3-mg bolus doses is given to people with severe shock but normal circulation until their systolic blood pressure rises to 100 mm Hg . At the same time, volume treatment with 1–3 liters of balanced electrolyte solution is started. The histamine H1-receptor antagonists, as well as H2-antagonists and glucocorticoids, are subsequently given intravenously, as stated previously. It's a good idea to think about keeping an eye on your hemodynamics for a while. If these procedures are successful in stabilizing the patient, the next step is to determine whether or not the surgical procedure can be conducted and to what extent. Depending on the severity, more thorough monitoring is necessary.

Features of care in a medical clinic that are unique

In the medical office, common causes of anaphylaxis

Allergen solutions used in allergen-specific immunotherapy (hyposensitization), as well as natural rubber latex, local anesthetics, and medications utilized in the medical office, are all potential elicitors in the medical office (e.g., antibiotics, cyclooxygenase inhibitors, radiographic contrast media, vaccines, and intravenous iron). Patients who have had severe allergic reactions to hymenoptera venoms or foods should seek medical attention as soon as possible.

Process of preparing for an emergency treatment in a medical office

For the treatment of anaphylaxis, all medical offices should have emergency equipment on hand. Because anaphylactic episodes are uncommon in most medical offices, ongoing training in anaphylaxis recognition and treatment, both pharmacological and non-pharmacological, is

required (especially with regard to distribution of tasks, positioning, calling for help, oxygen, recording respiratory and cardiovascular function). Medical care in an emergency situation is improved by regular training of team protocols during anaphylaxis. It is highly advised that you create a documented, easily available emergency plan that includes a list of the necessary drugs and dosages. Patients should be treated in a separate room from other patients but within easy reach of many caregivers. Weight-adjusted dosages for emergency therapy in children receiving allergen-specific immunotherapy can already be recorded on the documentation sheet in the pediatric context.

In order to prepare for an emergency, it is beneficial to define the following specifications:

- Recognize the location where emergency equipment is kept.
- In the event of an emergency, you should be aware of the particular method.
- Find out who is in charge of that (inform the physician, take care of the patient, call for help, etc.)
- learn about the patient's treat

Equipment that allows a medical office to remain open in an emergency

In a medical office, the elements listed in Table 3 are recommended as emergency equipment. ECG and blood pressure monitors are not standard equipment in many medical offices, but a pulse oximeter should be provided.

In case of an emergency, follow these steps

Acute treatment is carried out in the same way as stated above (in the hospital), with no significant variations.

Adrenaline is also given intramuscularly in the medical office by doctors who aren't trained in emergency medicine. If circulation does not improve, the procedure might be repeated. If a monitor is not available, heart rate and blood pressure can be recorded, and cardiovascular function can be determined by measuring capillary refill time on the sternum or fingertip.

Intravenous adrenaline delivery should be done with caution and under the supervision of a physician with experience. It also necessitates continuous blood pressure and pulse monitoring (exception: resuscitation situation with an i.v. catheter already in place).

Following the cessation of allergen exposure, emergency medical and rescue services should be notified as soon as possible if anaphylaxis with moderate to severe involvement of the respiratory or cardiovascular systems occurs .

In the medical office, the discharge management procedure is followed

Because patient monitoring options in the physician office are limited, it is suggested that severe or unclassifiable anaphylactic patients be transferred to a hospital for monitoring. Otherwise, discharge care is the same as it was when you were admitted to the hospital, as detailed above (Table 8).

Table-8

Aspects of anaphylaxis patients' discharge management

The elicitor's identity is determined.	Histories of allergies Referral to allergy testing (specific IgE and/or skin test) if necessary.
Recommendations for avoiding recurrences	Individually customized therapeutic elimination diet for food allergies Consider the indication for allergen-specific immunotherapy in the case of insect venom allergy. In the case of a medication allergy, avoidance and the use of an allergy passport are recommended.
Suggestions for pharmaceutical self-care	Pharmacological self-management plan in writing (anaphylaxis passport) Prescriptions for emergency medications in weight-adjusted doses Administration training
Recommendations for day-to-day administration	Information about patient organizations' support for issues with childcare, school, shopping, and travel. Food allergies that aren't listed on the label Information on allergy-trained dietitians, as well as referrals to them.

Childhood has unique characteristics

The particular dosages for children must be considered when administering various medications used in the treatment of anaphylaxis.

Chapter -7

Self-medication and patient care

Group of people to target

Every patient who has had anaphylaxis should be educated on the most essential behavioral steps that can help avoid and treat anaphylaxis. This is especially critical for individuals who are at a higher risk of anaphylaxis, such as people with mastocytosis or those who have a prognostically significant symptom constellation. When a patient successfully undergoes allergen-specific immunotherapy (ASIT), such as against insect venoms, this is also critical.

Self-help (“emergency set for self-help”) is a type of self-medication

Basically, all anaphylaxis survivors who cannot reliably avoid the elicitor, as well as all adult mastocytosis patients, should be given a "emergency kit for self-help" [91, 92]. An adrenaline autoinjector, H1 antihistamine, glucocorticosteroid, and, for asthma patients, an inhaled bronchodilator (Tab.7) are typically included in the emergency kit in Germany, Austria, and Switzerland. Patients who have a "emergency set for self-help" should be reminded to have it with them at all times. He or she must be advised about proper chemical storage and shelf life, as well as the potential for sedative side effects from older antihistamines (influence on driving performance). Patients, as well as others of their social circle – in the case of children, their parents and caregivers — must be taught how to utilize the drug. Anaphylaxis emergency plans that are standardized are available for this purpose.

Several adrenaline autoinjector formulations are available for intramuscular injection, with varying single doses (150 g for patients 15–30 kg bw, 300 g for patients over 30 kg bw). There is evidence that a dose of 150 g is safe in otherwise healthy children weighing between 10 and 15 kg. Off-label usage in this indication should be disclosed to parents. Patients receiving a second or subsequent adrenaline autoinjector should be prescribed a formulation that requires the same delivery strategy. It is beneficial to give patients and their social surroundings a dummy (without needle) and encourage them to practice frequently in order to train them in the use of the autoinjector.

The ease with which an H1 antihistamine can be ingested, as well as individual preferences, should be addressed when choosing an application form (drops for small children, tablets or fast-melt tablets for older children or adults). Liquid applications are suggested if swallowing difficulties (laryngeal angioedema) are present. The same parameters apply to glucocorticosteroids, with rectal administration being taken into account . Additional inhaled receptor agonists should be administered for asthma patients, as well as adrenaline for inhalation if there is a history of laryngeal edema.

Patients who are given an emergency set for self-help must be shown how to use it and have written instructions on how to do so. An emergency set or autoinjector is not required for all patients who have had an immediate-type allergic response. When the elicitor is known and easily avoided, as in drug-induced anaphylaxis, there is no need. Patients without extra risk factors had no higher risk of anaphylaxis after allergen-specific immunotherapy with insect venom, compared to the general population. As a result, these patients are not required to carry self-medication with them at all times. Tab.9 lists the indications for the prescription of an adrenaline autoinjector. A second autoinjector may be prescribed in some cases (e.g., very severe anaphylaxis, high body weight, mastocytosis, or a considerable distance to medical care).(Tab-10)

Table-9

Causes for prescribing an adrenaline auto-injector

Patients with bronchial asthma and systemic allergic responses (even with no history of anaphylaxis)
Symptoms of a systemic allergic reaction get more severe over time.
Anaphylactic reactions to elicitors in the past that couldn't be consistently avoided
Extracutaneous symptoms of systemic allergy to allergens such as peanuts, tree nuts, milk, and sesame.
Prior to allergy provocation testing, strong sensitization with an elevated risk of anaphylaxis was seen.
Patients who are allergic to trace quantities of an allergy
Mastocytosis affects adults (also without known anaphylaxis)

Table-10

Reasons for prescribing an additional (second) adrenaline auto-injector

Anaphylaxis with life-threatening consequences in the past
Obesity is defined as a body mass index (BW) of more than 100 kg.
Bronchial asthma that is uncontrolled
The nearest emergency medical care is inconveniently located.
Severe anaphylaxis is a distinct possibility (e.g., adults with mastocytosis after anaphylaxis)
Organizational: a second auto-injector for a childcare center, school, or, depending on the family situation, a second auto-injector

Patients with a high-grade suspicion of anaphylaxis are supplied an emergency first-aid kit before allergy testing

Children with atopic eczema (atopic dermatitis, eczema) are frequently susceptible to common food allergens, particularly following severe eczema at an early age [94, 95]. After the first oral exposure, patients with clinically meaningful sensitizations frequently have an anaphylactic reaction. An oral meal challenge is commonly undertaken in the inpatient environment to determine the therapeutic implications of this [96]. Patients can be administered an adrenaline auto-injector in the meantime because there is commonly a delay of many weeks or months between the time of indication and the conduct of oral challenge tests. It's crucial to get training on how to utilize an auto-injector with the help of a dummy. When considering the rationale for this approach, one must consider the time interval between oral challenge testing and the likelihood of a clinically relevant food allergy, as well as the likely severity of a reaction based on concomitant diseases such as asthma and the likelihood of accidental exposure.

The concentration of allergen-specific IgE antibodies against storage proteins enhances the probability of a systemic reaction in peanut or tree nut allergy [95, 97]. Specific IgE against 2S albumins is the strongest predictor of clinical significance . Even though these patients have never consumed this food allergen before, 2S albumin-specific IgE levels in some patients are so high that an anaphylactic reaction can be predicted with 90–95 percent certainty [95, 97]. Oral feeding challenges are frequently avoided or undertaken only later in these patients (e.g., at the time of school entrance). Without ever having had a clinical reaction, these patients can be diagnosed with "high-grade suspicion" of, for example, peanut or tree nut allergy. These patients should also be given an adrenaline auto-injector and therapeutic nutrition counseling in order to avoid the most questionable meals regularly and, if necessary, restore nutrients that are missing from their avoidance diet.

The first-aid kit includes the following items

Physicians recommend a combination of medications for patients to keep in an emergency first-aid kit, which should be carried with the anaphylaxis passport at all times. An adrenaline auto-injector, a histamine H1-receptor antagonist, a glucocorticoid, and, in patients with bronchial asthma or a history of bronchospasm, an inhaled bronchodilator (beta2-adrenoceptor agonist) are all recommended by the authors (Table 11).

Table-11

An anaphylactic patient's emergency first-aid kit

Adrenaline	>7.5–25 kg BW or >15–30 kg BW: 150 ga >25–50 kg BW or >30–50 kg BW: 300 ga Auto-injector for intramuscular, body weight-adjusted administration 300–500–600 g (BW >50 kg)
Antagonist of the histamine H1 receptor	Orally as fluid or (lozenge) tablet, depending on patient age and preference. The non-sedating antihistamine's dose can be adjusted up to four times. As with the intravenous formulation, a weight-adjusted dose can be advised as an oral dose for dimetindene drops (see Table 8)
Glucocorticoid	Oral (liquid or pill) or rectal (50–100 mg prednisolone equivalent) depending on the patient's age and preferences.

Swallowing ability and individual choice in terms of administration form should be taken into account when choosing a histamine H1-receptor antagonist (drops for small children, tablets or lozenges for older children and adults). If patient have a history of trouble swallowing (e.g., laryngeal edema), patient should take your medication in liquid form. The same parameters apply to glucocorticoids (1–2 mg/kg BW), which can also be administered recally. Antihistamines in higher doses should be used to treat anaphylaxis, according to the experts (up to four times the approved single dose). The new second-generation selective histamine H1-receptor antagonists are not approved for the treatment of anaphylaxis; however, because they have shown a rapid onset of action in placebo-controlled skin test studies and fewer side effects, such as sedation, they can be recommended alongside sedating antihistamines for oral emergency treatment. Inhaled beta2-adrenoceptor agonists are also prescribed for asthma sufferers. In the case of a previous history of laryngeal edema, an adrenaline inhalation preparation may be administered instead.

There are several types of adrenaline auto-injectors on the market, each with its own dose, handling, injection mechanism, and needle length. Special instructions are required, the preparations are difficult to substitute, and repeat prescriptions must be organized [98]. The “aut idem” box on the prescription must be checked.

Two adrenaline auto-injectors will be prescribed over a period of time.

Table 11 lists the indications for the use of two adrenaline auto-injectors.

Dosing adrenaline for anaphylaxis self-management is a less controlled first step that does not need to be the same as adrenaline administration under medical supervision and appropriate monitoring. Due to a lack of data, dose recommendations for self-management are based on body weight for children but not for adults [99]. The best adrenaline dose and number of adrenaline auto-injectors for self-management are unknown. In some cases, doctors or patients may decide that a second adrenaline auto-injector is necessary. The use of a second adrenaline injector is associated with the presence of co-existing bronchial asthma. For the indications listed in Table 9, the authors suggest prescribing a second adrenaline auto-injector[Tab10]

It's critical that patients receive a second auto-injector, also known as a replacement auto-injector, that uses the same technique as their previous device. Patients should keep their emergency first aid kit with them at all times in case of an emergency. It makes logical from an organizational standpoint to prescribe two adrenaline auto-injectors for various places in individual circumstances (e.g., school, childcare facility, workplace, and in the case of separated parents). When compared to patients who carry their auto-injector with them at all times, this can cause confusion and a lack of protection. As a result, the group suggests that a single auto-injector be prescribed and kept on hand at all times.

The time on the adrenaline auto-injector was no longer indicated

The European Academy of Allergy and Clinical Immunology (EAACI) has conducted extensive research on the need for patients with insect venom allergies to carry emergency self-medication at all times [100] and has developed recommendations for the prescription of adrenaline auto-injectors, which have been incorporated into current guidelines for the treatment of insect venom allergies. According to these guidelines, an adrenaline auto-injector prescription is no longer essential when the risk of a new systemic reaction is comparable to that of the general population. After successful immunotherapy and a well-tolerated sting reaction—either after a field sting or after a sting challenge—this can be expected.

In patients with only cutaneous/mucosal symptoms (grade I) or patients who have reacted with more than cutaneous symptoms (grade II), but no additional risk factors for non-response to venom immunotherapy, an adrenaline auto-injector prescription is no longer necessary after completion of allergen-specific immunotherapy [100]. Severe insect sting reactions (grade III or IV), bee venom allergy, high risk of exposure (e.g., beekeeper), a systemic response while on immunotherapy, mast cell disease, elevated basal serum tryptase, and ACE inhibitor therapy are all risk factors. It is debatable whether the auto-injector can be removed once the maintenance dose of venom immunotherapy has been reached. Patients with solely cutaneous/mucosal symptoms (grade I) would not need an auto-injector once the maintenance dose was attained, according to 70 to 80 percent of specialists. The indications for prescribing adrenaline auto-injectors are listed in Table 9.

Training for emergency first-aid kits includes:

The majority of anaphylactic reactions happen in the course of daily life, generally at home. As a result, emergency self-management training should encompass all steps that patients should consider or take on their own in the event of a (renewed) emergency. Instructions should be given to the patient on how to:

1. Anaphylactic responses should be recognized.

2. Administer self-medication for symptom relief.

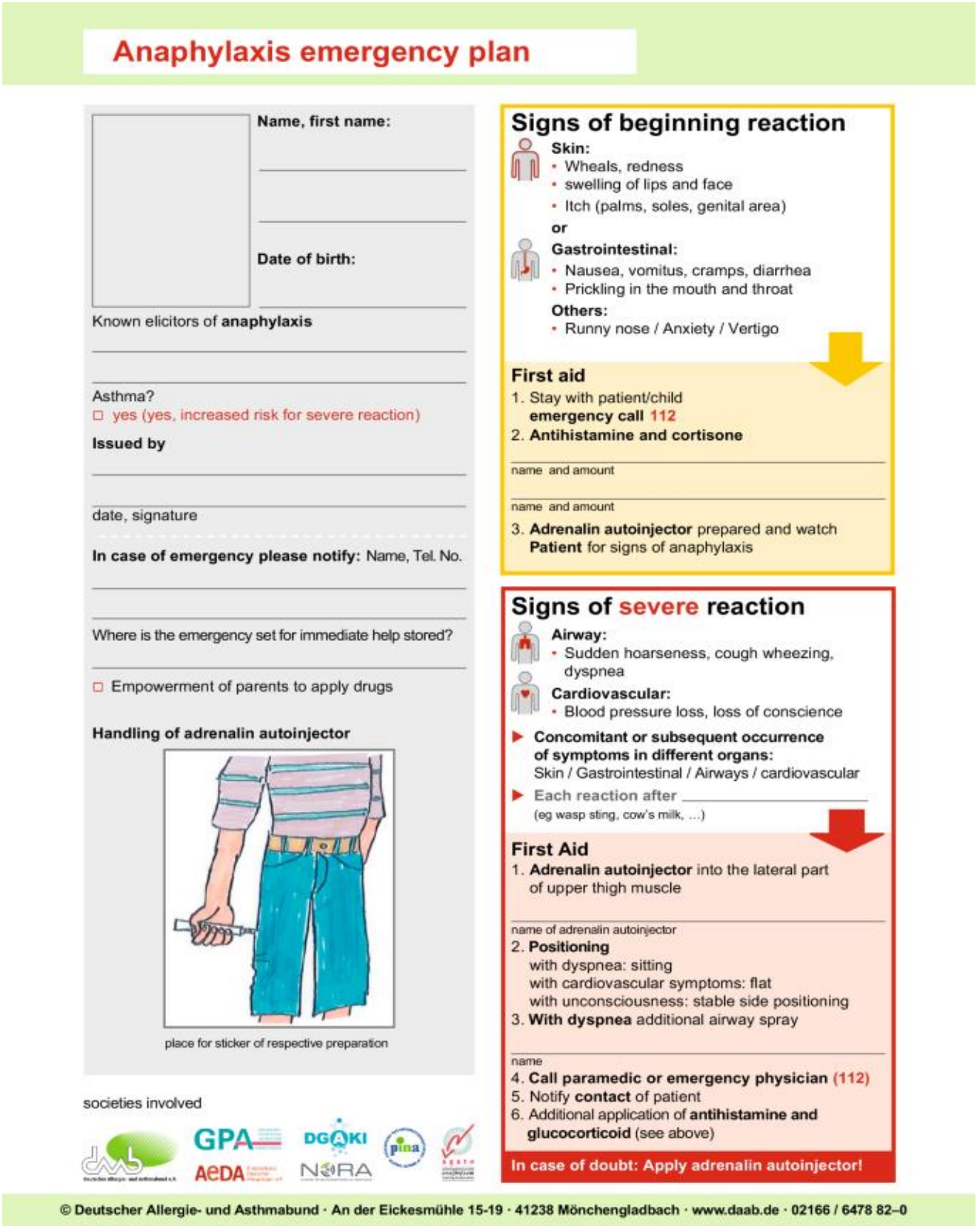
3. Drugs should be stored correctly.

4. Call for help in an emergency

If at all possible, potential elicitors (foods, insects, and medications) should be kept.

Self-medication is based on symptoms and the degree of certainty that allergen contact has occurred: the correct stage-appropriate administration of a number of drugs for acute medication is an essential part of patient information, as patients and their families have the most uncertainty in this regard. If an anaphylactic elicitor has been identified (insect sting without successful allergen-specific immunotherapy, eating allergy-eliciting food, or taking an allergy-eliciting medicine), the anaphylaxis emergency plan must be implemented (Fig. 4). An allergy sufferer should always have an emergency plan and an anaphylaxis passport with them.

Figure-4


Anaphylaxis emergency plan
Name, first name:
Date of birth:
Known elicitors of anaphylaxis
Asthma?
□ yes (yes, increased risk for severe reaction)
Issued by
date, signature
In case of emergency please notify: Name, Tel. No.
Where is the emergency set for immediate help stored?
□ Empowerment of parents to apply drugs
Handling of adrenalin autoinjector
place for sticker of respective preparation
societies involved
Signs of beginning reaction
Skin:
• Wheals, redness
• swelling of lips and face
• Itch (palms, soles, genital area)
or
Gastrointestinal:
• Nausea, vomitus, cramps, diarrhea
• Prickling in the mouth and throat
Others:
• Runny nose / Anxiety / Vertigo
First aid
1. Stay with patient/child
emergency call 112
2. Antihistamine and cortisone
name and amount
name and amount
3. Adrenalin autoinjector prepared and watch Patient for signs of anaphylaxis
Signs of severe reaction
Airway:
• Sudden hoarseness, cough wheezing, dyspnea
Cardiovascular:
• Blood pressure loss, loss of conscience
Concomitant or subsequent occurrence of symptoms in different organs:
Skin / Gastrointestinal / Airways / cardiovascular
Each reaction after
(eg wasp sting, cow's milk, ...)
First Aid
1. Adrenalin autoinjector into the lateral part of upper thigh muscle
name of adrenalin autoinjector
2. Positioning
with dyspnea: sitting
with cardiovascular symptoms: flat
with unconsciousness: stable side positioning
3. With dyspnea additional airway spray
name
4. Call paramedic or emergency physician (112)
5. Notify contact of patient
6. Additional application of antihistamine and glucocorticoid (see above)
In case of doubt: Apply adrenalin autoinjector!
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At the time of prescription, all patients with a history of anaphylaxis, as well as their families and guardians, should get specific instruction, including a practical demonstration of how to use the emergency kit.

This training covers the following topics: anaphylaxis elicitors, how to avoid them, how to refer to a nutritionist with allergy experience for advice on a therapeutic elimination diet in the case of food-induced anaphylaxis, anaphylaxis symptoms, and theoretical and practical knowledge (including a demonstration) on how to administer emergency drugs in the event of a renewed anaphylaxis .Each new prescription for an adrenaline auto-injector should include these instructions. The patient, as well as individuals in their social milieu, particularly child caretakers, must be taught how to use self-medication. Standardized anaphylactic emergency plans, as well as anaphylaxis documentation and recommendations for emergency management in childcare facilities and schools, are available to this end (Fig. 4). The anaphylactic passport also includes a summary of self-management guidelines, which include, in addition to triggers, medicine dosage and route of administration based on clinical symptoms.

Locate further resources for managing anaphylaxis on a daily basis

Other information materials (such as brochures, shopping guides, restaurant maps with information on specific food allergies for the kitchen, documents for air travel, and so on) can be made available by patient organizations in addition to standardized written anaphylaxis emergency plans and the anaphylaxis passport.

It appears to be critical to include not only affected patients and their social environments (e.g., parents), but also allergy and anaphylaxis specialists, as well as other occupational groups such as paramedics, emergency services, hospital emergency departments, first-aid course organizers, and patient organizations [101].

Overall, the acute management of anaphylaxis patients in Germany can be rated positively; however, there are still significant issues with long-term management, particularly in children in daycare centers and schools, as well as deficiencies in the prompt administration of adrenaline, further diagnostics, training, and education [40, 101].

It is critical to raise awareness of this potentially life-threatening condition among medical professionals and to familiarize them with intramuscular adrenaline delivery, including the use of adrenaline auto-injectors for self-medication.

COVID-19 vaccination-induced anaphylaxis

Vaccination initiatives against COVID-19 have recently begening in a number of nations. Rare occurrences of severe allergic reactions have been reported in the United Kingdom and the United States, causing concern and worry among patients and clinicians who administer vaccines. As a result, the guideline group and allergological societies developed position statements [102,103] emphasizing that some patients with defined allergic conditions, particularly those with severe allergic reactions to drugs or vaccines and known hypersensitivities to vaccine ingredients, may be at increased risk for anaphylaxis after COVID-19 vaccination. In cases where allergies are unknown, allergy testing should be done prior to COVID-19 vaccination, and patients should be monitored for at least 30 minutes after receiving the vaccine. Physicians and other health professionals working in vaccination clinics should be informed of the risks of anaphylaxis and the emergency treatment options available [102,103].

Management of long-term therapy and prevention

Allergy diagnostics should be performed after an anaphylactic reaction. All preventive strategies include the identification of the elicitor, the targeted issuance of an anaphylaxis passport, and specific counseling regarding risks and dangers (bellow). Diagnostics refers to any approach that can be used to identify an elicitor with certainty. Relevant anaphylactic risk factors (such as asthma, mastocytosis, or drug interactions) should be identified and their significance conveyed to the patient. Allergen-specific immunotherapy should be initiated as soon as possible [104]. Regular monitoring and long-term medication (e.g. anti-IgE, omalizumab) should be considered in the case of recurring anaphylactic reactions [90].

A) Avoidance

1. An anaphylaxis passport and an anaphylaxis emergency plan are issued.

2. Always have an emergency kit, anaphylaxis-passport, and a cell phone on hand.
3. Understanding anaphylactic symptoms and being able to identify them from other symptoms (e.g. fear)

4. Autonomous training with the adrenalin-autoinjector (dummy without needle and drug) should be repeated every 3–6 months if possible (caveat: do not confuse with the “real” autoinjector!)

5. Substances' shelf lives must be examined on a regular basis. The manufacturer's reminder service can be used with the Adre nalin-autoinjector.

6. Inform the social network: plan assistance and allocate jobs in the event of an emergency (emergency call, application of drugs, receiving the emergency physician etc.)

7. Potentially more counseling, information materials, and patient interchange through patient organizations .

B) Self-treatment in an emergency

1. Use of the emergency kit (see Anaphylaxis emergency plan / Anaphylaxis passport)

2. Positioning is number nine.

    a) with predominant heart and circulatory symptoms: lie down with legs up (shock positioning);

    b) with predominant respiratory symptoms: sit (“coachman position”).

    c) In the event of insanity: recovery posture

3. The word "anaphylaxis/anaphylactic shock" should be mentioned first, and the conversation should be guided by the rescue central office.

4. Seek assistance and support from your social circle.

Chapter -8

The importance of Anaphylaxis in future recommendations and research

The therapy of anaphylaxis and molecular allergy diagnostics, in particular, are on track to improve the management of patients with severe allergic reactions. National and international norms, as well as the establishment of training programs, are essential components for their implementation.

The data and collaboration of the anaphylaxis registry's participating centers contribute significantly to this. The development of a severity-measurement tool in the future should allow for a better differentiation of affected patients.

The IgE epitopes of the 56-kDa protein are determined by both the heat stable CCD and the protein structure, according to the research. Sadly, the structure of these glycosylated 56-kDa allergens has yet to be determined.

As a result, this is something that researchers should think about for future studies and validation.

Also included is a proposal for the design of future anaphylaxis epidemiology studies —

Table -12

Risk Assessment	Factors that are at risk Comorbidties Medications Taken at the Same Time Cofactors Disorders of the mast cell
Classification	Definition, diagnosis, and severity grading are all based on the same criteria.
Intensive Care	The use of biomarkers in diagnosis and treatment Prescription for an adrenaline auto injector
Pathogenesis	Mechanisms for Triggers and Reactions (Immunologic pathways ,effector cells , mediators)

Conclusion

Anaphylaxis is a life-threatening allergic reaction. Bee stings, medicines, meals, and exercise are all potential causes. The onset is usually abrupt, and a delayed reaction can occur many hours later. Fluid expanders, epinephrine, and oxygen are used to keep the airway open and boost blood pressure. Additional medications such corticosteroids, antihistamines, vasopressors, glucagon, atropine sulfate, and isoproterenol hydrochloride may help. The most crucial aspect of anaphylactic care is prevention.

Reference

1. Okubo, Y., Nochioka, K., & Testa, M. A. (2019). Nationwide survey of hospitalization due to pediatric food-induced anaphylaxis in the United States. *Pediatric emergency care*, *35*(11), 769-773.

2. Castilano, A., Sternard, B., Cummings, E. D., Shi, R., Arnold, T., & Bahna, S. L. (2018, July). Pitfalls in anaphylaxis diagnosis and management at a university emergency department. In *Allergy & Asthma Proceedings* (Vol. 39, No. 4).

3. Akenroye, A. T., Ajala, A., Azimi-Nekoo, E., & de Vos, G. S. (2018). Prevalence of anaphylaxis among adults admitted to critical care for severe asthma exacerbation. *Emergency Medicine Journal*, *35*(10), 623-625.

4. Bresser, H., Sander, C. H., & Rakoski, J. (1995). Emergencies by insect stings in Munich in 1992. *Allergo J*, *4*, 373-6.

5. Mehl, A., Wahn, U., & Niggemann, B. (2005). Anaphylactic reactions in children–a questionnaire-based survey in Germany. *Allergy*, *60*(11), 1440-1445.

6. Sampson, H. A., Muñoz-Furlong, A., Campbell, R. L., Adkinson Jr, N. F., Bock, S. A., Branum, A., ... & Decker, W. W. (2006). Second symposium on the definition and management of anaphylaxis: summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *Journal of Allergy and Clinical Immunology*, *117*(2), 391-397.

7. Tejedor Alonso, M. A., Moro Moro, M. M. G. M., & Múgica García, M. V. (2015). Epidemiology of anaphylaxis. *Clinical & Experimental Allergy*, *45*(6), 1027-1039.

8. Yocum, M. W., Butterfield, J. H., Klein, J. S., Volcheck, G. W., Schroeder, D. R., & Silverstein, M. D. (1999). Epidemiology of anaphylaxis in Olmsted County: a population-based study. *Journal of Allergy and Clinical Immunology*, *104*(2), 452-456.

9. Moneret-Vautrin, D. A., Morisset, M., Flabbee, J., Beaudouin, E., & Kanny, G. (2005). Epidemiology of life-threatening and lethal anaphylaxis: a review. *Allergy*, *60*(4), 443-451.

10. Helbling, A., Hurni, T., Mueller, U. R., & Pichler, W. J. (2004). Incidence of anaphylaxis with circulatory symptoms: a study over a 3-year period comprising 940 000 inhabitants of the Swiss Canton Bern. *Clinical & Experimental Allergy*, *34*(2), 285-290.

11. Decker, W. W., Campbell, R. L., Manivannan, V., Luke, A., Sauver, J. L. S., Weaver, A., ... & Li, J. T. (2008). The etiology and incidence of anaphylaxis in Rochester, Minnesota: a report from the Rochester Epidemiology Project. *Journal of Allergy and Clinical Immunology*, *122*(6), 1161-1165.

12. Sheikh, A., Hippisley-Cox, J., Newton, J., & Fenty, J. (2008). Trends in national incidence, lifetime prevalence and adrenaline prescribing for anaphylaxis in England. *Journal of the Royal Society of Medicine*, *101*(3), 139-143.

13. Poulos, L. M., Waters, A. M., Correll, P. K., Loblay, R. H., & Marks, G. B. (2007). Trends in hospitalizations for anaphylaxis, angioedema, and urticaria in Australia, 1993-1994 to 2004-2005. *Journal of allergy and clinical immunology*, *120*(4), 878-884.

14. Zubeldia, J., & Baeza, M. (2015). Anaphylaxis in adolescent/adult patients treated in the emergency department: differences between initial impressions and the definitive diagnosis. *J Investig Allergol Clin Immunol*, *25*(4), 288-294.

15. Worm, M., Edenharter, G., Rueff, F., Scherer, K., Pföhler, C., Mahler, V., ... & Hompes, S. (2012). Symptom profile and risk factors of anaphylaxis in Central Europe. *Allergy*, *67*(5), 691-698.

16. Smith, P. L., Kagey-Sobotka, A. N. N. E., Bleecker, E. R., Traystman, R. I. C. H. A. R. D., Kaplan, A. P., Gralnick, H. A. R. V. E. Y., ... & Lichtenstein, L. M. (1980). Physiologic manifestations of human anaphylaxis. *The Journal of clinical investigation*, *66*(5), 1072-1080.

17. Vadas, P., Perelman, B., & Liss, G. (2013). Platelet-activating factor, histamine, and tryptase levels in human anaphylaxis. *Journal of Allergy and Clinical Immunology*, *131*(1), 144-149.

18. Lee, J. K., & Vadas, P. (2011). Anaphylaxis: mechanisms and management. *Clinical & Experimental Allergy*, *41*(7), 923-938.

19. Korhonen, H., Fisslthaler, B., Moers, A., Wirth, A., Habermehl, D., Wieland, T., ... & Offermanns, S. (2009). Anaphylactic shock depends on endothelial Gq/G11. *Journal of Experimental Medicine*, *206*(2), 411-420.

20. Peavy, R. D., & Metcalfe, D. D. (2008). Understanding the mechanisms of anaphylaxis. *Current opinion in allergy and clinical immunology*, *8*(4), 310.

21. Griffin, T. (2014). Anaphylaxis in general dental practice. *Primary dental journal*, *3*(1), 36-40.

22. Muraro, A., Roberts, G., Clark, A., Eigenmann, P. A., Halken, S., Lack, G., ... & EAACI Task Force on Anaphylaxis in Children. (2007). The management of anaphylaxis in childhood: position paper of the European academy of allergology and clinical immunology. *Allergy*, *62*(8), 857-871.

23. Ring, J., & Messmer, K. (1977). Incidence and severity of anaphylactoid reactions to colloid volume substitutes. *The Lancet*, *309*(8009), 466-469.

24. Simons, F. E. R., Ardusso, L. R., Bilò, M. B., El-Gamal, Y. M., Ledford, D. K., Ring, J., ... & World Allergy Organization. (2011). World allergy organization guidelines for the assessment and management of anaphylaxis. *World Allergy Organization Journal*, *4*(2), 13-37.

25. Muraro, A., Roberts, G., Worm, M., Bilo, M. B., Brockow, K., Fernandez Rivas, M., ... & Sheikh, A. (2014). Food allergy and anaphylaxis guidelines. *Allergy*, *69*(8), 1026-1045.

26. Marx, J., Hockberger, R., & Walls, R. (2013). *Rosen's Emergency Medicine-Concepts and Clinical Practice E-Book: 2-Volume Set*. Elsevier Health Sciences.

27. Simons, F. E. R. (2009). Anaphylaxis: recent advances in assessment and treatment. *Journal of Allergy and Clinical Immunology*, *124*(4), 625-636.

28. Isbister, G. K., Brown, S. G., Page, C. B., McCoubrie, D. L., Greene, S. L., & Buckley, N. A. (2013). Snakebite in Australia: a practical approach to diagnosis and treatment. *Medical journal of Australia*, *199*(11), 763-768.

29. Boden, S. R., & Wesley Burks, A. (2011). Anaphylaxis: a history with emphasis on food allergy. *Immunological reviews*, *242*(1), 247-257.

30. Pravettoni, V., & Incorvaia, C. (2016). Diagnosis of exercise-induced anaphylaxis: current insights. *Journal of asthma and allergy*, *9*, 191.

31. Dewachter, P., Mouton-Faivre, C., Emala, C. W., & Riou, B. (2009). Anaphylaxis and anesthesia: controversies and new insights. *The Journal of the American Society of Anesthesiologists*, *111*(5), 1141-1150.

32. Castells, M. C. (Ed.). (2010). *Anaphylaxis and hypersensitivity reactions*. Springer Science & Business Media.

33. Stratton, K. R., Howe, C. J., & Johnston, R. B. (1994). Adverse events associated with childhood vaccines other than pertussis and rubella: summary of a report from the Institute of Medicine. *Jama*, *271*(20), 1602-1605.

34. Simons, F. E. R., Ebisawa, M., Sanchez-Borges, M., Thong, B. Y., Worm, M., Tanno, L. K., ... & Sheikh, A. (2015). 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. *World Allergy Organization Journal*, *8*, 32.

35. Modena, B., White, A. A., & Woessner, K. M. (2017). Aspirin and nonsteroidal antiinflammatory drugs hypersensitivity and management. *Immunology and Allergy Clinics*, *37*(4), 727-749.

36. Drain, K. L., & Volcheck, G. W. (2001). Preventing and managing drug-induced anaphylaxis. *Drug safety*, *24*(11), 843-853.

37. Klotz, J. H., Dorn, P. L., Logan, J. L., Stevens, L., Pinnas, J. L., Schmidt, J. O., & Klotz, S. A. (2010). "Kissing bugs": potential disease vectors and cause of anaphylaxis. *Clinical Infectious Diseases*, *50*(12), 1629-1634.

38. Brown, S. G., Wu, Q. X., Kelsall, G. R. H., Heddle, R. J., & Baldo, B. A. (2001). Fatal anaphylaxis following jack jumper ant sting in southern Tasmania. *Medical journal of Australia*, *175*(11-12), 644-647.

39. Bilò, B. M., & Bonifazi, F. (2008). Epidemiology of insect-venom anaphylaxis. *Current opinion in allergy and clinical immunology*, *8*(4), 330-337.

40. Worm, M., Francuzik, W., Renaudin, J. M., Bilo, M. B., Cardona, V., Scherer Hofmeier, K., ... & Dölle, S. (2018). Factors increasing the risk for a severe reaction in anaphylaxis: An analysis of data from The European Anaphylaxis Registry. *Allergy*, *73*(6), 1322-1330.

41. Schwartz, L. B. (2001). Clinical utility of tryptase levels in systemic mastocytosis and associated hematologic disorders. *Leukemia research*, *25*(7), 553-562.

42. Jacobs, R. L., Rake Jr, G. W., Fournier, D. C., Chilton, R. J., Culver, W. G., & Beckmann, C. H. (1981). Potentiated anaphylaxis in patients with drug-induced beta-adrenergic blockade. *Journal of Allergy and Clinical Immunology*, *68*(2), 125-127.

43. Newman, B. R., & Schultz, L. K. (1981). Epinephrine-resistant anaphylaxis in a patient taking propranolol hydrochloride. *Annals of allergy*, *47*(1), 35-37.

44. Hepner, M. J., Ownby, D. R., Anderson, J. A., Rowe, M. S., Sears-Ewald, D., & Brown, E. B. (1990). Risk of systemic reactions in patients taking beta-blocker drugs receiving allergen immunotherapy injections. *Journal of allergy and clinical immunology*, *86*(3), 407-411.

45. Lang, D. M., Alpern, M. B., Visintainer, P. F., & Smith, S. T. (1991). Increased risk for anaphylactoid reaction from contrast media in patients on β-adrenergic blockers or with asthma. *Annals of internal medicine*, *115*(4), 270-276.

46. Lang, D. M., Alpern, M. B., Visintainer, P. F., & Smith, S. T. (1993). Elevated risk of anaphylactoid reaction from radiographic contrast media is associated with both ß-blocker exposure and cardiovascular disorders. *Archives of internal medicine*, *153*(17), 2033-2040.

47. Mullins, R. J., Dear, K. B., & Tang, M. L. (2009). Characteristics of childhood peanut allergy in the Australian Capital Territory, 1995 to 2007. *Journal of Allergy and Clinical Immunology*, *123*(3), 689-693.

48. Pouessel, G., Dumond, P., Liabeuf, V., Tanno, L. K., Deschildre, A., Beaumont, P., ... & Network, A. V. (2019). Gaps in the management of food-induced anaphylaxis reactions at school. *Pediatric allergy and immunology: official publication of the European Society of Pediatric Allergy and Immunology*, *30*(7), 767-770.

49. De Schryver, S., Halbrich, M., Clarke, A., La Vieille, S., Eisman, H., Alizadehfar, R., ... & Ben-Shoshan, M. (2016). Tryptase levels in children presenting with anaphylaxis: temporal trends and associated factors. *Journal of Allergy and Clinical Immunology*, *137*(4), 1138-1142.

50. Brockow, K., Vieluf, D., Püschel, K., Grosch, J., & Ring, J. (1999). Increased postmortem serum mast cell tryptase in a fatal anaphylactoid reaction to nonionic radiocontrast medium. *The Journal of allergy and clinical immunology*, *104*(1), 237-238.

51. Ring, J., Klimek, L., & Worm, M. (2018). Adrenaline in the acute treatment of anaphylaxis. *Deutsches Ärzteblatt International*, *115*(31-32), 528.

52. Westfall, T. C. (2006). Adrenergic agonists and antagonists. *Goodman and Gilman's the pharmacological basis of therapeutics*.

53. Monsieurs, K. G., Nolan, J. P., Bossaert, L. L., Greif, R., Maconochie, I. K., Nikolaou, N. I., ... & Xanthos, T. T. (2015). European resuscitation council guidelines for resuscitation 2015: section 1. Executive summary. *Resuscitation*, *95*, 1-80.

54. Thomas, M., & Crawford, I. (2005). Glucagon infusion in refractory anaphylactic shock in patients on beta-blockers. *Emergency Medicine Journal*, *22*(4), 272-273.

55. Faisst, M., Stuhr, M., Savinsky, G., & Kerner, T. (2020). Notfallmedizinische Versorgung adipöser Menschen. *Der Notarzt*, *36*(06), 346-356.

56. Perkins, G. D., Olasveengen, T. M., Maconochie, I., Soar, J., Wyllie, J., Greif, R., ... & Nolan, J. P. (2018). European resuscitation council guidelines for resuscitation: 2017 update. *Resuscitation*, *123*, 43-50.

57. Simons, F. E. R., & Schatz, M. (2012). Anaphylaxis during pregnancy. *Journal of allergy and clinical immunology*, *130*(3), 597-606.

58. Perkins, G. D., Olasveengen, T. M., Maconochie, I., Soar, J., Wyllie, J., Greif, R., ... & Nolan, J. P. (2018). European resuscitation council guidelines for resuscitation: 2017 update. *Resuscitation*, *123*, 43-50.

59. Bellomo, R., Chapman, M., Finfer, S., Hickling, K., & Myburgh, J. (2000). Low-dose dopamine in patients with early renal dysfunction: a placebo-controlled randomised trial. Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group. *Lancet (London, England)*, *356*(9248), 2139-2143.

60. Adhikari, N. K., Burns, K. E., Friedrich, J. O., Granton, J. T., Cook, D. J., & Meade, M. O. (2007). Effect of nitric oxide on oxygenation and mortality in acute lung injury: systematic review and meta-analysis. *Bmj*, *334*(7597), 779.

61. Gronemeyer, W. (1980). Noradrenalin statt Adrenalin beim anaphylaktischen Schock. *Dtsch Med Wochenschr*, *102*, 101.

62. Schummer, C., Wirsing, M., & Schummer, W. (2008). The pivotal role of vasopressin in refractory anaphylactic shock. *Anesthesia & Analgesia*, *107*(2), 620-624.

63. Emran, M. A., Hossain, S. S., Salek, A. K. M., Khan, M. M., Ahmed, S. M., Khandaker, M. N., & Islam, M. T. (2014). Drug abuse in sports and doping. *Bangladesh Medical Journal*, *43*(1), 46-50.

64. Ring, J., Beyer, K., Biedermann, T., Bircher, A., Fischer, M., Fuchs, T., ... & Brockow, K. (2021). Guideline (S2k) on acute therapy and management of anaphylaxis: 2021 update. *Allergo journal international*, *30*(1), 1-25.

65. Channelopathies, I., Cardiomyopathies, R., Cardiomyopathies, S., Pulmonale, C., Pericarditis, E., & Pericarditis, T. C. (2012). Cardiac Diseases. *Anesthesia and Uncommon Diseases: Expert Consult-Online and Print*, 28.

66. Walther, A., & Böttiger, B. W. (2004). Anaphylaktoide Reaktionen in der Prähospitalphase. *Der Internist*, *45*(3), 296-304.

67. Vincent, J. L. (2013). De. Backer D. *Circulatory shock. N Engl J Med*, *369*, 1726-34.

68. Muraro, A., Roberts, G., Clark, A., Eigenmann, P. A., Halken, S., Lack, G., ... & EAACI Task Force on Anaphylaxis in Children. (2007). The management of anaphylaxis in childhood: position paper of the European academy of allergology and clinical immunology. *Allergy*, *62*(8), 857-871.

69. Martin, C., Jacob, M., Vicaut, E., Guidet, B., Van Aken, H., & Kurz, A. (2013). Effect of waxy maize-derived hydroxyethyl starch 130/0.4 on renal function in surgical patients. *Anesthesiology*, *118*(2), 387-394.

70. Myburgh, J. A., Finfer, S., Bellomo, R., Billot, L., Cass, A., Gattas, D., ... & Webb, S. A. (2012). Hydroxyethyl starch or saline for fluid resuscitation in intensive care. *New England Journal of Medicine*, *367*(20), 1901-1911.

71. Ring, J., Beyer, K., Biedermann, T., Bircher, A., Fischer, M., Fuchs, T., ... & Brockow, K. (2021). Guideline (S2k) on acute therapy and management of anaphylaxis: 2021 update. *Allergo journal international*, *30*(1), 1-25.

72. Sheikh, A., Ten Broek, V., Brown, S. G. A., & Simons, F. E. R. (2007). H1-antihistamines for the treatment of anaphylaxis: Cochrane systematic review. *Allergy*, *62*(8), 830-837.

73. Pragst, F., Herre, S., & Bakdash, A. (2006). Poisonings with diphenhydramine—a survey of 68 clinical and 55 death cases. *Forensic science international*, *161*(2-3), 189-197.

74. Zuberbier, T. (2009). Dermatology Section of the European Academy of Allergology and Clinical Immunology; Global Allergy and Asthma European Network; European Dermatology Forum; World Allergy Organization. EAACI/GA^ 2LEN/EDF/WAO guideline. management of urticaria. *Allergy*, *64*, 1427-1443.

75. Lin, R. Y., Curry, A., Pesola, G. R., Knight, R. J., Lee, H. S., Bakalchuk, L., ... & Westfal, R. E. (2000). Improved outcomes in patients with acute allergic syndromes who are treated with combined H1 and H2 antagonists. *Annals of emergency medicine*, *36*(5), 462-468.

76. Ring, J., Rothenberger, K. H., & Clauss, W. (1985). Prevention of anaphylactoid reactions after radiographic contrast media infusion by combined histamine H1-and H2-receptor antagonists: results of a prospective controlled trial. *International Archives of Allergy and Immunology*, *78*(1), 9-14.

77. Brockow, K., Kiehn, M., Riethmüllerb, C., Vieluf, D., Berger, J., & Ring, J. (1997). Efficacy of antihistamine pretreatment in the prevention of adverse reactions to Hymenoptera immunotherapy: a prospective, randomized, placebo-controlled trial. *Journal of allergy and clinical immunology*, *100*(4), 458-463.

78. Aouam, K., Bouida, W., Ben Fredj, N., Chaabane, A., Boubaker, H., Boukef, R., ... & Nouira, S. (2012). Severe ranitidine-induced anaphylaxis: a case report and literature review. *Journal of clinical pharmacy and therapeutics*, *37*(4), 494-496.

79. Winbery, S. L., & Lieberman, P. L. (2002). Histamine and antihistamines in anaphylaxis. *Histamine and H1-antihistamines in allergic disease*, 303-334.

80. Ahnefeld, F. W., Bartholeyns, J., Dick, W., Doenicke, A., Fuchs, T., Gervais, H., ... & Mehrkens, H. H. (1994). Akuttherapie anaphylaktoider Reaktionen. Ergebnisse einer interdisziplinären Consensuskonferenz [Acute therapy of anaphylactoid reactions. Results of an intradisciplinary consensus conference]. *Der Anaesthesist*, *43*(4), 211-222.

81. Choo, K. J. L., Simons, E., & Sheikh, A. (2010). Glucocorticoids for the treatment of anaphylaxis: Cochrane systematic review. *Allergy*, *65*(10), 1205-1211.

82. Alqurashi, W., & Ellis, A. K. (2017). Do corticosteroids prevent biphasic anaphylaxis?. *The Journal of Allergy and Clinical Immunology: In Practice*, *5*(5), 1194-1205.

83. VARGA19, M. W., & BROCKOW, K. Guideline for acute therapy and management of anaphylaxis.

84. Ring, J., Beyer, K., Biedermann, T., Bircher, A., Fischer, M., Fuchs, T., ... & Brockow, K. (2021). Guideline (S2k) on acute therapy and management of anaphylaxis: 2021 update. *Allergo journal international*, *30*(1), 1-25.

85. Cheng, A., Canadian Paediatric Society, & Acute Care Committee. (2011). Emergency treatment of anaphylaxis in infants and children. *Paediatrics & child health*, *16*(1), 35-40.

86. Przybilla, B., Rueff, F., Walker, A., Rawer, H. C., Aberer, W., Bauer, C. P., ... & Wedi, B. (2012). Diagnosis and therapy of bee and wasp venom allergy.

87. Lommatzsch, M., Buhl, R., & Korn, S. (2020). The treatment of mild and moderate asthma in adults. *Deutsches Ärzteblatt International*, *117*(25), 434.

88. Morita, E., Kunie, K., & Matsuo, H. (2007). Food-dependent exercise-induced anaphylaxis. *Journal of dermatological science*, *47*(2), 109-117.

89. Klimek, L., Goebel, U., & Glowania, A. (2012). Management der Anaphylaxie. *HNO*, *60*(12), 1103-1113.

90. Lieberman, J. A., & Chehade, M. (2013). Use of omalizumab in the treatment of food allergy and anaphylaxis. *Current allergy and asthma reports*, *13*(1), 78-84.

91. El-Gamal, Y. Patient Risk Factors: Vulnerable Groups.

92. Hartmann, K., Biedermann, T., Brockow, K., Grabbe, J., Horny, H. P., & Lippert, U. (2009). Mastocytosis. Guideline of the German Society for Allergology an Clinical Immunology (DGAKI) and the German Society for Dermatology (DDG). *Allergo J*, *18*, 196-207.

93. Simons, F. E. R., Ardusso, L. R., Dimov, V., Ebisawa, M., El-Gamal, Y. M., Lockey, R. F., ... & World Allergy Organization. (2013). World Allergy Organization Anaphylaxis Guidelines: 2013 update of the evidence base. *International archives of allergy and immunology*, *162*(3), 193-204.

94. Roesler, V. H. (2019). *Bedeutung diagnostischer Parameter in der Diagnostik funktioneller Bauchschmerzen im Kindesalter* (Doctoral dissertation, Universität Ulm).

95. Sood, P., & Wood, R. A. (2015). Predictive Values of Component-Specific IgE for the Outcome of Peanut and Hazelnut Food Challenges in Children. *Pediatrics*, *136*(Supplement 3), S242-S242.

96. Worm, M., Reese, I., Ballmer-Weber, B., Beyer, K., Bischoff, S. C., Classen, M., ... & Kleine-Tebbe, J. (2015). Guidelines on the management of IgE-mediated food allergies. *Allergo journal international*, *24*(7), 256-293.

97. Lange, L., Lasota, L., Finger, A., Vlajnic, D., Büsing, S., Meister, J., ... & Beyer, K. (2017). Ana o 3-specific IgE is a good predictor for clinically relevant cashew allergy in children. *Allergy*, *72*(4), 598-603.

98. Guerlain, S., Hugine, A., & Wang, L. (2010). A comparison of 4 epinephrine autoinjector delivery systems: usability and patient preference. *Annals of Allergy, Asthma & Immunology*, *104*(2), 172-177.

99. Ring, J., Beyer, K., Dorsch, A., Biedermann, T., Fischer, J., & Friedrichs, F. (2012). Anaphylaxis school–a new educational program for tertiary prevention in patients with anaphylaxis. *Allergo J*, *21*, 96-102.

100. Bilò, M. B., Cichocka-Jarosz, E., Pumphrey, R., Oude-Elberink, J. N., Lange, J., Jakob, T., ... & Rueff, F. (2016). Self-medication of anaphylactic reactions due to Hymenoptera stings—an EAACI Task Force Consensus Statement. *Allergy*, *71*(7), 931-943.

101. Ring, J., Brockow, K., Kugler, C., Gebert, N., Grando, K., Götz, D., ... & Gieler, U. (2017). New aspects in allergy education with special emphasis on anaphylaxis. *Allergo Journal International*, *26*(7), 267-272.

102. Worm, M., Ring, J., Klimek, L., Jakob, T., Lange, L., Treudler, R., ... & Brockow, K. (2021). Anaphylaxie-Risiko bei der COVID-19-Impfung: Empfehlungen für das praktische Management. *MMW-Fortschritte der Medizin*, *163*(1), 48-51.

103. Ring, J., Beyer, K., Biedermann, T., Bircher, A., Fischer, M., Heller, A., ... & Brockow, K. (2021). Leitlinie zu Akuttherapie und Management der Anaphylaxie-Update 2021. *Allergo Journal*, *30*(1), 20-49.

104. Przybilla, B., Rueff, F., Walker, A., Rawer, H. C., Aberer, W., Bauer, C. P., ... & Wedi, B. (2012). Diagnosis and therapy of bee and wasp venom allergy.