

## **Antiallergics and drugs used in anaphylaxis**

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The H<sub>1</sub>-receptor antagonists are generally referred to as antihistamines. They inhibit the wheal, pruritus, sneezing and nasal secretion responses that characterize allergy. Antihistamines thus relieve the symptoms of allergic reactions, such as urticaria, allergic rhinitis, and allergic conjunctivitis; they also control pruritus in skin disorders, such as eczema. Antihistamines are used to treat drug allergies, food allergies, insect stings and some of the symptoms of anaphylaxis and angioedema. Drug treatment and other supportive care should not be delayed in critically ill patients (see Allergic Emergencies below). Specific precipitants should be sought and if identified, further exposure avoided and desensitization considered.

Drowsiness and sedation are particular disadvantages of the older antihistamines and the patient should be warned against driving or operating machinery. Other central nervous depressants, including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytics and neuroleptics, may enhance the sedative effects of antihistamines. Since antihistamines interfere with skin tests for allergy, they should be stopped at least one week before conducting a skin test.

**Chlorphenamine** is a typical, older sedative antihistamine. Newer antihistamines do not cause significant sedation. In practice, all antihistamines are equally effective in relieving the symptoms of allergic reactions and differ mainly in the intensity of sedative and anticholinergic (more correctly antimuscarinic) effects. Selection of an antihistamine should thus be based on the intended therapeutic use, the adverse reaction profile, and the cost.

Corticosteroids, such as **dexamethasone**, **hydrocortisone**, or **prednisolone**, suppress or prevent almost all symptoms of inflammation associated with allergy. The route of administration depends on the particular type of allergic condition. For example, for a mild allergic skin reaction, the best therapy may be the use of a corticosteroid ointment or cream. If the skin reaction does not respond to topical corticosteroid therapy, it may be necessary to give a corticosteroid orally.

Allergic reactions of limited duration and with mild symptoms, such as urticaria or allergic rhinitis, usually require no treatment. If on the other hand, symptoms become persistent, antihistamines constitute the mainstay of treatment. However, oral corticosteroids may be required for a few days in an acute attack of urticaria or for severe skin reactions. Oral corticosteroids are also used to relieve severe exacerbations in chronic urticaria, but long-term use should be avoided.

Corticosteroids may be used topically to reduce inflammation in allergic rhinitis but should only be used systemically for this condition when symptoms are disabling.

Adverse effects associated with long-term use of corticosteroids include inhibition of growth in children, disturbances of electrolyte balance leading to oedema, hypertension and hypokalaemia, with osteoporosis, spontaneous fractures, skin thinning, increased susceptibility to infection, mental disturbances and diabetes mellitus. For further information on the disadvantages of corticosteroids, see section 18.1.

## Allergic emergencies

Anaphylactic shock and conditions such as angioedema are medical emergencies that can result in cardiovascular collapse and/or death. They require prompt treatment of possible laryngeal oedema, bronchospasm or hypotension. Atopic individuals are particularly susceptible. Insect stings and certain foods including eggs, fish, cow's milk protein, peanuts and nuts are a risk for sensitized persons. Therapeutic substances particularly associated with anaphylaxis include blood products, vaccines, hyposensitizing (allergen) preparations, antibiotics (especially penicillins), iron injections, heparin, and neuromuscular blocking drugs. Acetylsalicylic acid and other nonsteroidal anti-inflammatory drugs (NSAIDs) may cause bronchoconstriction in leukotriene-sensitive patients. In the case of drug allergy, anaphylaxis is more likely to occur after parenteral administration. Resuscitation facilities should always be available when injecting a drug associated with a risk of anaphylactic reactions.

First-line treatment of a severe allergic reaction includes administering epinephrine (adrenaline), keeping the airway open (with assisted respiration if necessary), and restoring blood pressure (laying the patient flat, raising the feet). Epinephrine (adrenaline) should immediately be given by intramuscular injection to produce vasoconstriction and bronchodilation and injection should be repeated if necessary at 5-minute intervals until blood pressure, pulse and respiratory function have stabilized. If there is cardiovascular shock with inadequate circulation, epinephrine (adrenaline) must be given cautiously by slow intravenous injection of a *dilute solution*. Oxygen administration is also of primary importance.

An antihistamine such as chlorphenamine is a useful adjunctive treatment given after epinephrine (adrenaline) injection and continued for 24 to 48 hours to reduce the severity and duration of symptoms and to prevent relapse. An intravenous corticosteroid such as hydrocortisone has an onset of action that is delayed by several hours but should be given to help prevent later deterioration in severely affected patients.

Further treatment of anaphylaxis may include intravenous fluids, an intravenous vasopressor such as dopamine, intravenous aminophylline or injected or nebulized bronchodilator, such as salbutamol.

### Steps in the management of anaphylaxis:

#### 1. Sympathomimetic

Epinephrine (adrenaline) by *intramuscular injection* using epinephrine injection 1 in 1000, **ADULT** and **ADOLESCENT**, 500 micrograms (0.5 ml); **INFANT** under 6 months 50 micrograms (0.05 ml); **CHILD** 6 months–6 years 120 micrograms (0.12 ml), 6–12 years 250 micrograms (0.25 ml)

*Note.* The above doses may be repeated several times if necessary at 5-minute intervals, according to blood pressure, pulse, and respiratory function

If circulation inadequate, *by slow intravenous injection* using epinephrine injection 1 in 10 000 (given at a rate of 1 ml/minute), **ADULT** 500 micrograms (5 ml); **CHILD** 10 micrograms/kg (0.1 ml/kg), given over several minutes

## 2. Vital functions

Maintain an open airway; give oxygen *by mask*, restore blood pressure (lay patient flat, raise feet)

3. **Antihistamine** such as chlorphenamine *by intravenous injection* over 1 minute, **ADULT** 10–20 mg, repeated if required (maximum total dose 40 mg in 24 hours)
4. **Corticosteroids** such as hydrocortisone *by slow intravenous injection*, **ADULT** 100–300 mg; **CHILD** up to 1 year, 25 mg; 1–5 years, 50 mg; 6–12 years, 100 mg
5. **Intravenous fluids:** start infusion with sodium chloride (0.5–1 litre during the first hour)
6. If the patient has asthma-like symptoms, give salbutamol 2.5–5 mg by nebulization or aminophylline 5 mg/kg *by intravenous injection* over at least 20 minutes.

## Antihistamine

### Chlorphenamine maleate

Chlorphenamine is a representative sedative antihistamine. Various drugs can serve as alternatives

*Tablets*, chlorphenamine maleate 4 mg

*Elixir* (Oral solution), chlorphenamine maleate 2 mg/5 ml [not included on WHO Model List]

*Injection* (Solution for injection), chlorphenamine maleate 10 mg/ml, 1-ml ampoule

#### Uses:

symptomatic relief of allergy, allergic rhinitis (hay fever) and conjunctivitis, urticaria, insect stings and pruritus of allergic origin; adjunct in the emergency treatment of anaphylactic shock and severe angioedema

#### Contraindications:

prostatic enlargement, urinary retention; ileus or pyloroduodenal obstruction; glaucoma; child under 1 year

**Precautions:**

pregnancy and breastfeeding (Appendices 2 and 3); renal and hepatic impairment (Appendices 4 and 5); epilepsy; **interactions:** Appendix 1

*SKILLED TASKS.* May impair ability to perform skilled tasks, for example operating machinery, driving

**Dosage:**

Allergy, *by mouth*, **ADULT** 4 mg every 4–6 hours (maximum 24 mg daily); **CHILD** under 1 year not recommended, 1–2 years 1 mg twice daily, 2–5 years 1 mg every 4–6 hours (maximum 6 mg daily), 6–12 years 2 mg every 4–6 hours (maximum 12 mg daily)

Allergic reactions, *by subcutaneous or intramuscular injection*, **ADULT** 10–20 mg, repeated if required (maximum 40 mg in 24 hours); *by subcutaneous injection* **CHILD** 87.5 micrograms/kg, repeated if necessary up to 4 times daily

Anaphylaxis (adjunct), *by intravenous injection* over 1 minute, **ADULT** 10–20 mg; **child** under 1 year 250 micrograms/kg, 1–5 years 2.5–5 mg, 6–12 years 5–10mg

**Adverse effects:**

drowsiness (rarely paradoxical stimulation with high doses, or in children or elderly), hypotension, headache, palpitations, psychomotor impairment, urinary retention, dry mouth, blurred vision, gastrointestinal disturbances; liver dysfunction; blood disorders; also rash and photosensitivity reactions, sweating and tremor, hypersensitivity reactions (including bronchospasm, angioedema, anaphylaxis); injections may be irritant

**Sympathomimetic**

**Epinephrine (adrenaline)**

*Injection* (Solution for injection), epinephrine (as hydrochloride or hydrogen tartrate) 1 mg/1 ml, 1-ml ampoule

**Uses:**

severe anaphylactic reaction; severe angioedema; cardiac arrest (section 12.2)

**Precautions:**

hyperthyroidism, hypertension, diabetes mellitus, heart disease, arrhythmias, cerebrovascular disease; second stage of labour; elderly; **interactions:** Appendix 1

**Dosage:****Caution: Different dilutions of epinephrine injection are used for different routes of administration**

Anaphylaxis, *by intramuscular or subcutaneous injection* of 1:1000 epinephrine injection, see Steps in the Management of Anaphylaxis for doses

Anaphylaxis, *by slow intravenous injection* of 1:10 000 epinephrine injection. This route should be reserved for severely ill patients when there is doubt about the adequacy of circulation and absorption from the intramuscular site, see Steps in the Management of Anaphylaxis for doses

**Adverse effects:**

tachycardia and arrhythmias, hypertension, tremor, anxiety, sweating, nausea, vomiting, weakness, hyperglycaemia, dizziness, pulmonary oedema have all been reported; headache common

**Corticosteroids****Dexamethasone**

*Tablets* , dexamethasone 500 micrograms, 4 mg [not on WHO Model List]

*Injection* (Solution for injection), dexamethasone phosphate (as sodium salt), 4 mg/ml, 1-ml ampoule

**Uses:**

adjunct in the emergency treatment of anaphylaxis; short-term suppression of inflammation in allergic disorders; for other indications see section 18.1

**Contraindications:**

untreated systemic infection (unless condition life-threatening); administration of live virus vaccines

**Precautions:**

increased susceptibility to and severity of infection; activation or exacerbation of tuberculosis, amoebiasis, strongyloidiasis; risk of severe chickenpox in non-immune patient (varicella-zoster immunoglobulin required if exposed to chickenpox); avoid exposure to measles (normal immunoglobulin possibly required if exposed); diabetes mellitus; peptic ulcer; hypertension; for further precautions relating to long-term use of corticosteroids see section 18.1

**Dosage:**

Allergy (short-term use), *by mouth* , **ADULT** and **CHILD** , usual range 0.5–10 mg daily as a single dose in the morning

Anaphylaxis, *by slow intravenous injection or infusion* , **ADULT** 0.5–20 mg;  
**CHILD** 200–500 micrograms/kg

**Adverse effects:**

nausea, dyspepsia, malaise, hiccups; hypersensitivity reactions including anaphylaxis; perineal irritation after intravenous administration; for adverse effects associated with long-term corticosteroid treatment see section 18.1

**Hydrocortisone**

*Injection* (Powder for solution for injection), hydrocortisone (as sodium succinate), 100-mg vial

**Uses:**

adjunct in the emergency treatment of anaphylaxis; inflammatory skin conditions (section 13.3); inflammatory bowel disease (section 17.4); adrenocortical insufficiency (section 18.1)

**Contraindications:**

not relevant to emergency use but for contra-indications relating to long-term use see section 18.1

**Precautions:**

not relevant to emergency use but for precautions relating to long-term use see section 18.1

**Dosage:**

Anaphylaxis, *by slow intravenous injection* as a single dose, see Steps in the Management of Anaphylaxis (above)

**Adverse effects:**

for adverse effects associated with long-term corticosteroid treatment see section 18.1

**Prednisolone**

Prednisolone is representative corticosteroid. Various drugs can serve as alternatives

*Tablets* , prednisolone 5 mg, 25 mg

**Uses:**

short-term suppression of inflammation in allergic disorders; longer-term suppression (section 18.1); malignant disease (section 8.3); eye (section 21.2)

**Contraindications:**

untreated systemic infection; administration of live virus vaccines

**Precautions:**

increased susceptibility to and severity of infection; activation or exacerbation of tuberculosis, amoebiasis, strongyloidiasis; risk of severe chickenpox in non-immune patient (varicella–zoster immunoglobulin required if exposed to chickenpox); avoid exposure to measles (normal immunoglobulin possibly required if exposed); diabetes mellitus; peptic ulcer; hypertension; for further precautions relating to long-term use of corticosteroids see section 18.1

**Dosage:**

Allergy (short-term use), *by mouth* , **ADULT** and **CHILD** , initially up to 10–20 mg daily as a single dose in the morning (in severe allergy up to 60 mg daily as a short course of 5–10 days)

**Adverse effects:**

nausea, dyspepsia, malaise, hiccups; hypersensitivity reactions including anaphylaxis; for adverse effects associated with long-term corticosteroid treatment see section 18.1