Essential Drugs

WHO Model Formulary

As described in previous issues of this journal, work is now under way on the WHO Model Formulary and draft texts will be published regularly to obtain comments on the material proposed for publication. Observations concerning the following sections should be addressed to: Department of Essential Drugs and Other Medicines (EDM), World Health Organization, 1211 Geneva 27, Switzerland.

Anti-allergics and drugs used in anaphylaxis

Although there are three types of histamine receptors H_1, H_2 and H_3, it is the H_1 receptor antagonists which are generally referred to as antihistamines. They are responsible for inhibiting the wheal, pruritus, sneezing and mucous secretion responses that are characteristic of allergy. H_1 receptor antagonists thus relieve the symptoms of allergic reactions, such as urticaria, angioedema, allergic rhinitis, and allergic conjunctivitis. They are also used to treat drug allergies, food allergies and insect stings and some of the symptoms of anaphylaxis. Antihistamines also control the pruritus in skin disorders, such as eczema. However, they are ineffective in the treatment of acute asthmatic attacks.

Drowsiness and sedation are particular disadvantages of the early antihistamines and the patient should be warned against driving or operating any type of machinery. Other central nervous depressants, including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives and neuroleptics may enhance the sedative effects of antihistamines. Since they interfere with skin tests for allergy, therapy should be stopped at least one week before conducting a skin test. Rashes and photosensitivity reactions, palpitations and arrhythmias have also been reported.

Chlorphenamine is considered the prototype for antihistamine H_1 antagonists. This class includes drugs with less sedative action than the traditional antihistamines or with different therapeutic potencies. In practice, all antihistamines are equally effective in relieving the symptoms of allergic reactions and differ mainly in the intensity of sedative and anticholinergic effects. Selection of drugs in this class should thus be based on the intended therapeutic uses, 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 should depend on the particular type of allergic condition. For example, in the case of a mild allergic skin reaction, the best therapy may be to apply a glucocorticoid ointment or cream. If the skin reaction does not respond to topical corticosteroid therapy, it may be necessary to give corticosteroids orally. Allergic diseases of limited duration and with mild reactions, such as urticaria or allergic rhinitis, usually require no treatment. If, on the other hand, symptoms become persistent, antihistamines constitute the mainstay of treatment.

Corticosteroids should be considered as supplements to primary therapy and used to reduce inflammation. Oral corticosteroids may be required for a few days in an acute attack of urticaria. Oral corticosteroids are also used to relieve severe exacerbations in chronic urticaria, but long-term use of oral corticosteroids should be avoided. Corticosteroids may be used topically to reduce inflammation in allergic rhinitis but should not be used orally or parenterally for this condition.

The adverse effects of corticosteroids include inhibition of growth in children, disturbances of the electrolyte balance leading to oedema and hypertension and to potassium loss, production of osteoporosis and spontaneous fractures, skin thinning, increased susceptibility to infection, mental disturbances and diabetes.

Allergic emergencies

Anaphylactic shock is a medical emergency that can result in cardiovascular collapse and death. It requires prompt treatment of possible laryngeal oedema, bronchospasm or hypotension. Atopic individuals are particularly susceptible. Insect bites and certain foods including eggs, fish, peanuts and nuts are also a risk for sensitized persons. Drugs particularly associated with anaphylaxis include blood products, vaccines, antibiotics (especially penicillins), iron injections, heparin and neuromuscular blocking agents. Acetylsalicylic acid and other nonsteroidal anti-inflammatory drugs (NSAIDs) may cause bronchoconstriction in leukotreine-sensitive patients. In the case of drug allergy, anaphylaxis is more likely to occur after parenteral administration. Resuscitation facilities should always be available if injection of a drug is associated with a certain risk.

First-line treatment includes administering epinephrine, keeping the airway open (assisted respiration may be necessary) and restoring blood pressure. Epinephrine should immediately be given by deep intramuscular or subcutaneous injection to produce vasoconstriction and bronchodilatation and injections should be repeated every ten minutes until blood pressure and pulse have stabilized. If there is complete cardiovascular shock, epinephrine must be given by slow intravenous injection.

Further treatment of anaphylaxis often includes intravenous corticosteroids such as hydrocortisone, intravenous antihistamines, such as chlorphenamine, and may include intravenous fluids, oxygen, an intravenous vasopressor agent, such as dopamine, intravenous aminophylline, and an injected or nebulized bronchodilator, such as salbutamol. Chlorphenamine is a useful adjunctive treatment given after epinephrine 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 several hours, but should be given to help prevent later deterioration in severely affected patients.

Steps in anaphylactic shock management

1. Epinephrine:

- 0.1 ml/10 kg (strength 1:1000, 1 mg/ml) by deep intramuscular injection; the dose can be repeated 10–30 minutes later.
- If the patient is in shock:
  Adults: 1–3 ml (strength 1:10 000, 0.1 mg/ml) by slow intravenous infusion.

  Children: 0.1–0.5 ml (strength 1:10 000, 0.1 mg/ml) by slow intravenous infusion.

2. Vital functions: maintain an open airway; give oxygen by mask.

3. Corticosteroids–hydrocortisone

   Adult: 250–500 mg intravenously

   Child: 10 mg/kg intravenously.

4. Intravenous fluids: start infusion with sodium chloride (500–1000 ml during the first hour).

5. If the patient has asthma-like symptoms, give aminophylline: 5 mg/kg by slow intravenous injection.

6. Antihistamine orally.

CHLORPHENAMINE

Tablet: 4 mg (hydrogen maleate)
Injection: 10 mg (hydrogen maleate) in 1-ml ampoule

Uses: Symptomatic relief of allergy, hay fever, allergic rhinitis and conjunctivitis, urticaria, insect stings, pruritus of allergic origin and angioedema. Adjunct in the emergency treatment of anaphylactic shock or in the emergency treatment of severe angioedema.

Dosage:
Adults: 4 mg every 4–6 hours, maximum 24 mg daily.

Children: 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).

Emergencies: by subcutaneous or intramuscular injection or slow intravenous injection

Contraindications: Patients with prostate enlargement since chlorphenamine may cause urinary retention. Patients with ileus or pyloric stenosis. Glaucoma. Children under one year.

Precautions: Use with caution in patients with epilepsy, hepatic disease and severe cardiovascular disorders. Ability to drive or operate machinery may be impaired.

Adverse effects: Drowsiness, hypotension, headache, palpitations, psychomotor impairment, urinary retention, dry mouth, blurred vision and gastrointestinal disturbances. Other adverse effects include rash and photosensitivity reactions, sweating and tremor. Injections may be irritant and may cause paradoxical central nervous system stimulation and hypotension.

Drug interactions: Effects of alcohol and other central nervous system (CNS) depressants may be additive. Other drug interactions will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.

DEXAMETHASONE

Tablet: 0.5 mg, 4 mg
Injection: 4 mg dexamethasone phosphate (as disodium) in 1-ml ampoule

Uses: Adjunct in the emergency treatment of anaphylaxis. Short-term suppression of inflammation in allergic disorders.

Dosage:
Orally: usual range 0.5–10 mg daily.

By intramuscular injection or slow intravenous injection or infusion:
Adults: 2–5 mg/kg daily.

Children: 200–500 µg/kg daily.

Contraindications, precautions and adverse effects: Because rare instances of anaphylactoid reactions such as bronchospasm have occurred in patients receiving parenteral corticosteroid treatment, appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to drugs.

EPINEPHRINE (ADRENALINE)

Injection: 1 mg (as hydrochloride or hydrogen tartrate) in 1-ml ampoule

Uses: Severe anaphylactic reaction or severe angioedema.

Dosage:
Caution: Different dilutions of epinephrine solution are used for different routes of administration. Use 1:1000 epinephrine solution for intramuscular or subcutaneous injection.

Anaphylaxis

Age	volume of epinephrine 1: 1 000 (1 mg/ml solution)
under 1 year	0.05 ml
1 year	0.1 ml
2 years	0.2 ml
3–4 years	0.3 ml
5 years	0.4 ml
6–12 years	0.5 ml
Adult	0.5–1.0 ml

Repeat the dose every 10 minutes as necessary, according to blood pressure and pulse, until improvement occurs.

Use 1:10 000 epinephrine solution for slow intravenous 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.

Adults: 500 µg (0.5 mg), i.e., 5 ml of a dilute 1: 10 000 epinephrine injection solution, given at an injection rate of 100 µg (1 ml)/minute stopping once a response is obtained.

Children: 10 µg/kg (0.1 ml/kg of a dilute 1:10 000 epinephrine injection solution) given over several minutes.

Contraindications: Hyperthyroidism, hypertension, diabetes mellitus, ischaemic heart disease, hypertension and closed angle glaucoma. Chronic bronchial asthma and substantial emphysema. Elderly patients.

Adverse effects: Tachycardia and arrhythmias, hypertension, tremor, anxiety, sweating, nausea, vomiting, weakness, dizziness and pulmonary oedema have all been reported. Headache is common.

Drug interactions: These will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.

HYDROCORTISONE

Powder for injection: 100 mg (as sodium succinate) in vial

Uses: Adjunct in the emergency treatment of anaphylaxis.

Dosage:
Anaphylactic emergency/by slow intravenous injection:
Adult: 100–300 mg three to four times in 24 hours as required.

Children: < 1 year, 25 mg; 1–5 years, 50 mg; 6–12 years, 100 mg three to four times in 24 hours as required.

Contraindications, precautions and adverse effects: Because rare instances of anaphylactoid reactions such as bronchospasm have occurred in patients receiving parenteral corticosteroid therapy, appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to drugs.

Drug interactions: These will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.

PREDNISOLONE

Tablet: 5 mg

Uses: Short-term suppression of inflammation in allergic disorders.

Dosage: Initial dose up to 10–20 mg daily. Severe allergy may require up to 60 mg daily. The maintenance dose is 2.5–15 mg daily. Higher doses may be necessary.

Contraindications: Known hypersensitivity to any corticosteroid. Active bacterial, viral or fungal infection. Unless the benefits outweigh the risks, systemic administration of corticosteroids is contraindicated in patients with peptic ulcer, osteoporosis, psychoses or severe psychoneuroses, congestive heart failure, hypertension, diabetes mellitus, epilepsy, glaucoma, ocular herpes simplex, chronic renal failure or uraemia.

Precautions: Children on corticosteroid therapy should be treated with immunoglobulin if they are exposed to a childhood viral infection to which they have no acquired immunity. They should not receive live-virus vaccines.

Adverse effects: Infections contracted during therapy can be fatal in the absence of effective treatment.

Drug interactions: These will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.