

EYE DISEASES IN HOT CLIMATES

FIFTH EDITION



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Contents

Preface	v
Dedications	viii
Acknowledgements	ix
Chapter 1 Introduction	1
Chapter 2 Basic anatomy and physiology of the eye	29
Chapter 3 Clinical methods: history taking and eye examination	41
Chapter 4 Principles of treatment	81
Chapter 5 Ophthalmic optics and the correction of refractive errors	101
Chapter 6 The eyelids and the lacrimal apparatus	115
Chapter 7 Diseases of the conjunctiva, episclera and sclera	137
Chapter 8 Trachoma	165
Chapter 9 The cornea	187
Chapter 10 Xerophthalmia and nutritional corneal ulceration	227
Chapter 11 Diseases of the uvea	253
Chapter 12 Diseases of the lens	277
Chapter 13 Diseases of the retina	313
Chapter 14 Diseases of the optic nerve and visual pathways	355

Chapter 15	Glaucoma	369
Chapter 16	Onchocerciasis and other parasitic diseases	397
Chapter 17	Leprosy and the eye	419
Chapter 18	Squint and other disorders of eye movement	435
Chapter 19	Orbital diseases	453
Chapter 20	Human immunodeficiency virus and the eye	467
Chapter 21	Eye injuries	483
Chapter 22	Eye disease and visual impairment in children	501
Chapter 23	Diagnosis of common eye conditions	515
Appendix		525
Index		527



Often the simplest treatments are the best and most effective. This young boy is receiving an azithromycin tablet to treat and to prevent trachoma.

There are various ways of treating patients with disorders of the eye:

- Medical and surgical treatment: these are the two 'conventional' ways of treating illness. Anyone seeing eye patients must have a basic understanding of the medical and surgical treatment of eye disease.
- Correction of refractive error (see Chapter 5): this is mainly done with spectacles and is very important in poor countries, where there are few opticians and many people with untreated refractive error. Sometimes refractive error is also treated with contact lenses or surgery.
- Community health and preventive treatment: this is a crucial part of the management of some diseases, such as trachoma, onchocerciasis and vitamin A deficiency. These diseases are discussed in the relevant chapters.
- Traditional medicines: these are widely used in many countries with variable safety and success (see Chapter 1).

Medical treatment and ocular pharmacology

Medication can be applied to the eyes in several ways:

1. Topically: the drug is applied directly on the eye.

2. Systemically: the drug is given by mouth or injection and reaches the eye through the bloodstream.
3. Injections in or around the eye: medication can be given under the conjunctiva (sub-conjunctival), into the Tenon's space (sub-Tenon's), beneath the eyeball (orbital floor), around or behind the eye (peri- or retrobulbar) or even into the eye (intravitreal).

Topical treatment

Topical treatment can be given as drops or ointment. This form of treatment is more effective for treating the front of the eye, i.e. disease of the conjunctiva, cornea, anterior chamber and iris. Drops and ointments have different advantages and disadvantages:

Drops

Drops are the most convenient and common way of giving topical treatment to the eye. However, the active drug is only in contact with the conjunctiva and cornea for a short time. If it is necessary to maintain high levels of the drug, the drops must be applied frequently, e.g. every hour or half hour. Some drops also contain substances such as methylcellulose to make them more viscous, so that they stay in contact with the eye for longer.

Ointments

Ointments stay in contact with the eye for longer and are often used at night just before sleep. Some patients also find ointments easier to apply than drops. However, ointments blur the vision temporarily and are messier than drops. Another disadvantage is that the active drug is usually dissolved in the oily part of the ointment. It is not always predictable how quickly the active drug will pass out of the ointment into the tears, and then into the tissues.

Many patients need simple instructions on how to apply drops or ointment. **Figures 4.1 and 4.2** are examples of leaflets given out to patients with their eye medicines. You might like to photocopy these and give them to the patient. However, it is always better to explain and demonstrate how to use the treatment to the patient and their accompanying person. Most patients can apply their own drops or ointment with a little practice, but it is easier if someone else does this for them. Also, remember to tell patients, that if they are not sure if the drop went into the eye, they can try again, as a second drop is very unlikely to be harmful, whereas not getting the drop in at all may be unsafe.

Side effects of topical treatment

Topical treatment is generally very safe. Side effects are not common or severe but they can occur.

- *Stinging or burning sensation on application*: this usually occurs because the pH (acid/base level) of the drop is different from that of tears. The pH level may be necessary to keep the active ingredient stable and dissolved.
- *Allergic reactions* (Figure 7.22): This will cause redness and irritation of the conjunctiva and surrounding skin. Allergic reactions are most

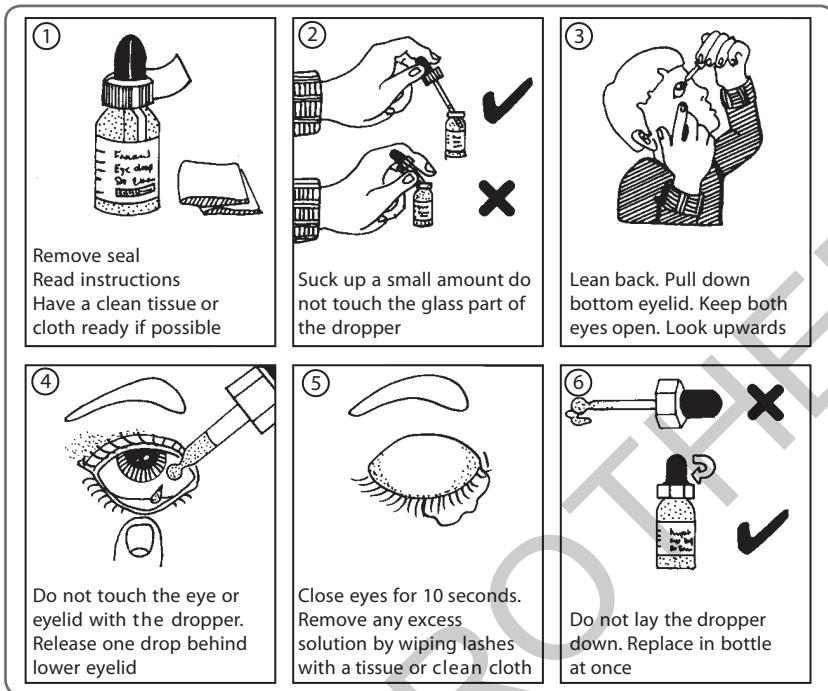


Figure 4.1 A leaflet explaining how to use eye drops.

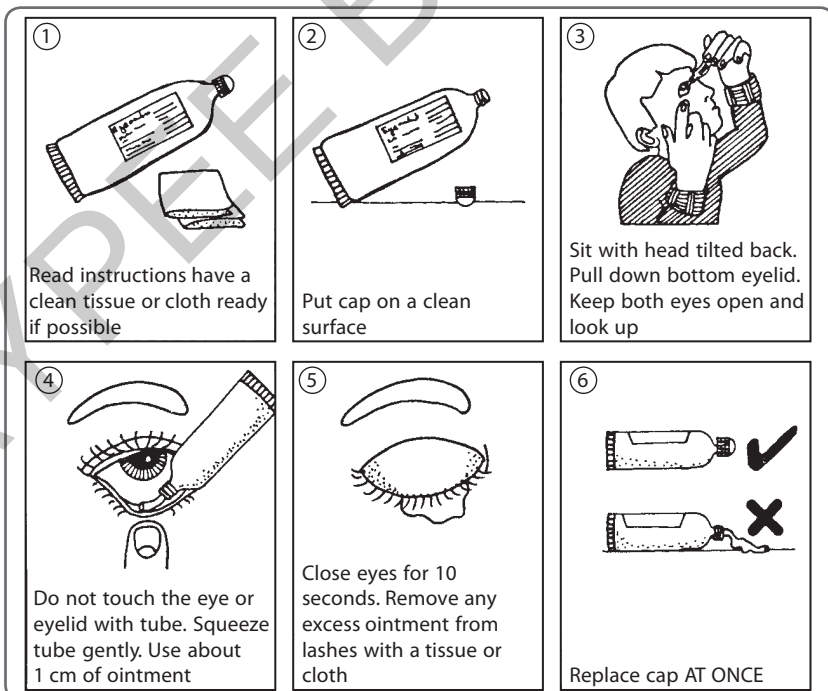


Figure 4.2 A leaflet explaining how to use eye ointment.

common with antibiotics, but may occur with almost any drug. Patients are sometimes allergic or intolerant to the preservative in the drops rather than the active ingredient. Preservative free drops can be used to avoid this, but they are much less widely available, more expensive and often need to be kept in the fridge.

- *Toxic reactions.* If a drug is being applied very frequently it may be toxic to the cornea and conjunctiva. For example, a patient may have an infected corneal ulcer and be treated with hourly antibiotic drops. These will kill the bacteria and sterilise the eye, but may affect the corneal epithelium, which might not heal until the drug is stopped or given less frequently.
- *Systemic reactions.* These are rare and one of the great advantages of topical treatment is that systemic reactions in the rest of the body are rare. Atropine (for dilatation of the pupil) and the beta-blockers (for glaucoma) are the main exception to this. Both of these can very occasionally cause serious and even life-threatening side-effects (see below).

Systemic treatment

Systemic treatment means that the drug is given by mouth or injection, and reaches the eye through the bloodstream. Systemic treatment is more effective for the back of the eye – the choroid, sclera, retina and optic nerve – as well as for the lacrimal passages and the orbit. It may be used in very severe cases of conjunctivitis.

Injections in and around the eye

Subconjunctival injections

Subconjunctival injection is a good way of quickly giving a high concentration to the front of the eye. The medication will be very active for about a day and may continue to have some effect for a few days. Subconjunctival injections may be helpful in the following situations:

- more serious or severe disease where a higher concentration of the drug is required
- to give a more continuous effect than intermittent drops
- if there is doubt that the patient will be able to administer drops frequently
- a subconjunctival injection of steroid (to suppress inflammation) and a mydriatic (to dilate the pupil) can be effective for treating acute anterior uveitis.

The technique for giving subconjunctival injections is given in **Box 4.1**. Not all antibiotics are suitable for subconjunctival injection. However, **Table 4.1** has a list of some antibiotics and other medications that can be used. The usual dose for a subconjunctival injection of antibiotic is 100 mg except for gentamicin for which the dose is 20 mg.

Intravitreal injections

Intravitreal injections are increasingly frequently used (**Figure 4.3**). They are used in two main situations:

Box 4.1 Subconjunctival injection technique (Figure 4.3)

Subconjunctival injections do not need to be painful if they are given with care. The technique for a subconjunctival injection is as follows:

1. Anaesthetise the conjunctiva with local anaesthetic drops. It is best to soak a tiny swab in local anaesthetic and leave it in the lower fornix for 1 minute, rather than just giving drops. This gives much better anaesthesia. A small injection of local anaesthetic first will lessen the pain of a subconjunctival injection, but if a local anaesthetic swab has been left in the conjunctiva for a minute this should not be necessary.
2. Ask the patient to look up and then insert a small hypodermic needle through the conjunctiva in the lower fornix.
3. Advance the needle a few millimetres just under the conjunctiva, and inject about 0.5 mL of the appropriate drug.

Table 4.1 Medicines that can be used for subconjunctival injection

Antibiotics (all 100 mg, except gentamicin)	Steroids
Gentamicin (20 mg)	Cortisone or hydrocortisone 20 mg
Penicillins: <i>Methicillin, Carbenicillin, Cloxacillin, Ampicillin, Crystalline penicillin</i>	Betamethasone 2–4 mg
Cephalosporins: <i>Cefuroxime, Cephazolin</i>	Depomedrone 20–40 mg (depomedrone is a prednisolon preparation which dissolves very slowly over a few weeks and gives long lasting treatment)
Chloramphenicol	

1. Antibiotics for endophthalmitis: this usually occurs post-operatively (mainly cataract surgery) and after a penetrating injury. Intravitreal treatment reduces the risk of blindness from endophthalmitis.
 2. Anti-VEGF drugs for wet macular degeneration: these are used to suppress macular degeneration (see Chapter 13).
- Intravitreal injections must be given in exactly the right amount and in the right way. Otherwise, they can cause great damage and even sight loss.

Endophthalmitis: choice of medication

Ideally, two antibiotics should be used, one for gram-negative bacteria, and one for gram-positive bacteria. The recommended antibiotics for gram-negative bacteria are either ceftazidime 2.0 mg or amikacin 0.4 mg. As both of these may be difficult to obtain gentamicin 0.1 mg can also be used. The recommended antibiotics for gram-positive bacteria are either vancomycin or cephazolin 2 mg. The exact choice of antibiotics depends on what is available and what is recommended locally, however some possibilities are:

- Amikacin and vancomycin.
- Gentamycin and vancomycin.
- Ceftazidime and vancomycin.

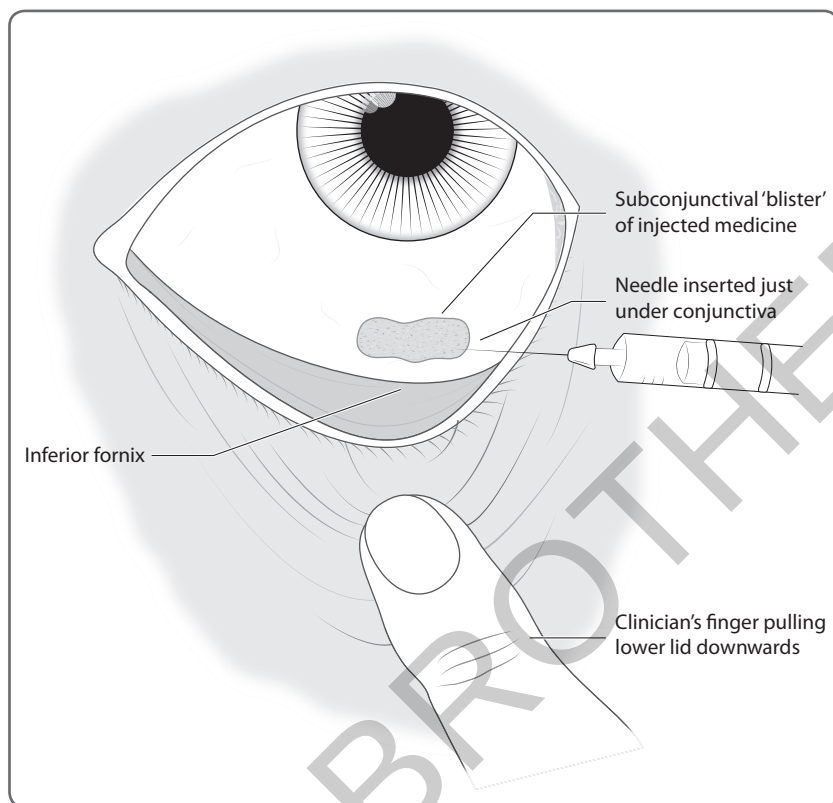


Figure 4.3 Subconjunctival injection technique.

Endophthalmitis: method of injection

The injections are made up in a 1.0 mL syringe; 0.9 mL is discarded leaving the last 0.1 mL to be injected. Therefore, the way to calculate how to make the injection is to put ten times the dose to be given in a 1.0 mL syringe and discard 9/10 of it. Make sure there is no 'dead space' in the needle when using such tiny amounts. Sterile preservative-free saline for injections must be used to dilute the active antibiotic. A 10 mL syringe is also needed to help dilute the antibiotic. **Table 4.2** explains how to make up the above medications. **Box 4.2** and **Figure 4.4** shows the technique of injection.

Endophthalmitis: vitreous samples

If good laboratory services are available then it is very important to aspirate a tiny amount of the vitreous for bacteriological examination and culture in an empty 1.0 mL syringe before making the injection.

Injections into the eye are upsetting both for the patient and the doctor and risk damaging the eye. If they are given carefully they should not cause too much pain and they are the best hope (almost the only hope) of saving the eye if there is established endophthalmitis.

Table 4.2 How to prepare intravitreal injections for endophthalmitis treatment

BACTERIAL INFECTIONS	
Gentamicin. Dose 0.1 mg in 0.1 mL (prepare 1.0 mg in 1.0 mL)	Vancomycin. Dose 2 mg in 0.1 mL (prepare 20 mg in 1.0 mL)
1. An ampoule of gentamicin contains 40 mg/mL. Take 0.25 mL (i.e. 10 mg of gentamicin) from this and make up to 10 mL with normal saline in the 10.0 mL syringe (i.e. 10 mg in 10 mL = 1.0 mg/mL) 2. Draw up 1.0 mL of this in a 10 mL syringe (i.e. 1 mg in 1.0 mL). 3. Discard 0.9 mL (i.e. 0.1 mg in 0.1 mL remains)	1. Dissolve 500 mg of powder in 10 mL of normal saline (concentration = 50 mg/mL) 2. Discard 8 mL, leaving 2 mL (i.e. 100 mg in 2 mL remains). 3. Add 3 mL of normal saline (i.e. 100 mg in 5 mL, concentration = 20 mg/mL) 4. Draw up 1.0 mL of this in a 1.0 mL syringe (i.e. 20 mg in 1 mL) 5. Discard 0.9 mL leaving 0.1 mL (i.e. 2 mg in 0.1 mL remains)
Amikacin. Dose 0.4 mg in 0.1 mL (prepare 4 mg in 1 mL)	Cephazolin and ceftazidime. Dose for both: 2 mg in 0.1 mL (prepare 20 mg in 1.0 mL)
1. A vial of amikacin contains 500 mg in 2 mL (250 mg/mL). Take 1.6 mL (i.e. 400 mg in 1.6 mL) 2. Make up to 10 mL with normal saline (i.e. 400 mg in 10 mL = 40 mg/mL) 3. Discard 9 mL leaving 1 mL (i.e. 40 mg in 1 mL) 4. Make up to 10 mL with normal saline (i.e. 40 mg in 10 mL = 4 mg/mL). 5. Draw up 1.0 mL of this in a 1.0 mL syringe (i.e. 4 mg in 1 mL) 6. Discard 0.9 mL. The remaining 0.1 mL = 0.4 mg.	1. Dissolve 500 mg of powder in 10 mL of normal saline (concentration = 50 mg/mL). 2. Discard 8 mL, leaving 2 mL (i.e. 100 mg in 2 mL remains). 3. Add 3 mL of normal saline (i.e. 100 mg in 5 mL, concentration = 20 mg/mL) 4. Draw up 1.0 mL of this in a 1.0 mL syringe (i.e. 20 mg in 1 mL) - Discard 0.9 mL leaving 0.1 mL (i.e. 2 mg in 0.1 mL remains)
FUNGAL INFECTIONS	
Amphotericin (prepare 5 µg in 0.1 mL)	
1. Dissolve 50 mg of powder in 10 mL of normal saline (concentration = 5 mg/mL) 2. Withdraw 0.1 mL and discard the rest (i.e. 0.5 mg in 0.1 mL). 3. Make up to 10 mL with normal saline (i.e. 0.5 mg in 10 mL) Discard 9.9 mL. The remaining 0.1 mL = 5 microgram.	

Box 4.2 Technique for giving intravitreal injections in endophthalmitis treatment

1. Insert a sterile speculum to hold open the eyelids. Apply local anaesthetic drops to the conjunctiva, and then leave a small sponge swab soaked in local anaesthetic on the surface of the conjunctiva for at least a minute. This greatly increases the anaesthesia. A small amount of local anaesthetic can be injected under the conjunctiva but this should not be necessary. If the topical anaesthetic is given time to work intravitreal injections should not normally be painful.
2. Put a few drops of iodine or betadine 5% in the eye
3. Use a fine (e.g. 25 gauge orange needle), short hypodermic needle on the 1.0 mL syringe containing the antibiotic. Make sure there is no dead space containing air in the needle. Insert the needle 4 mm

Box 4.2 Continued

back from the limbus in the outer and upper quadrant of the eye, aim the point of the needle towards the centre of the eye and do not insert it more than 1 cm into the eye. (Most needles with 1.0 mL syringes are only 1 cm long). You can ask the patient to look towards their nose to help expose an optimal area to insert the needle.

4. Hold the needle steady with the same hand that you used to insert the needle into the eye and use the other hand to press the plunger of the syringe to inject the antibiotic. If as recommended, two different antibiotics are used, the needle can be left in place while the syringe is delicately removed and replaced with the syringe with the second antibiotic. However, you may find it easier to make two separate injections.

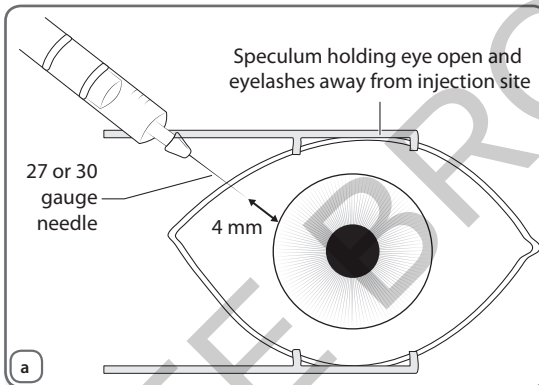
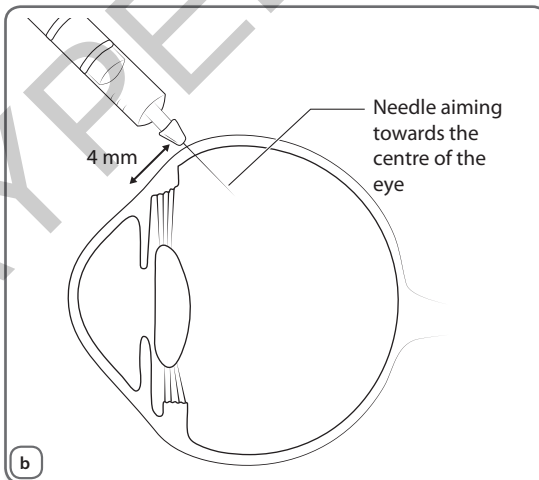


Figure 4.4 The location of an intravitreal injection.



Commonly used drugs in ophthalmology

Antibiotics

Antibiotics are used for treating bacteria. Most eye infections from bacteria occur in the conjunctiva or cornea. Therefore, antibiotics are usually applied topically to the eye. This avoids the possible side effects of giving them systemically and a very wide range of antibiotics to be used for eye treatment.

Chloramphenicol is the most popular antibiotic for topical use in the eye. It has a wide range of activity, good penetration, and it is cheap. Systemic chloramphenicol has a risk of causing aplastic anaemia, but this is not thought to occur following topical use. It is sometimes avoided in younger children because of this theoretical risk, and *fucithalmic* (fusidic acid) is often used instead. It is widely available as a drop and an ointment.

Tetracycline ointment is widely used in poor countries, because it is effective against *Chlamydia trachomatis*, which causes trachoma (see Chapter 8).

Other topical antibiotics that are particularly useful for treating corneal ulcers include penicillin, neomycin, gentamicin, polymyxin, framycetin, ciprofloxacin, ofloxacin, tobramycin, and sulphacetamide (or mixtures of these).

If the antibiotic is only available as powder for injection, it is possible in an emergency to dilute it to make a 1% solution in water. This can be used as eye drops (see also page 204).

Antiviral and antifungal drugs

Antiviral drops and ointments are available to treat viral infections of the cornea (see page 194), but they are quite expensive. Antifungal drops and ointment are needed to treat fungal infections of the cornea (see page 207). These are available in a few countries but may be very difficult to obtain. This is a pity because fungal corneal ulcers are common in tropical climates. Systemic antiviral and antifungal drugs are now available. They are used mostly in patients with AIDS and unfortunately are currently very expensive.

In patients with acute eye infections, topical treatment with antibiotics, antiviral or antifungal drugs should be given frequently, especially if the cornea is involved. This means that drops should be applied at least every hour and ointments every 2 hours. Antibiotic drops and ointments are also widely used to prevent conjunctival and corneal infections. These treatments are also used to prevent eye infections after minor eye injuries, corneal foreign bodies and eye surgery. When given to prevent infection rather than to treat it, the drops or ointment need only be applied three or four times a day.

Anti-inflammatory agents

Steroids

Corticosteroids are the most powerful anti-inflammatory drugs that are widely available. Hydrocortisone, prednisolone, betamethasone and

dexamethasone are all used extensively for both topical and systemic eye treatment.

Topical and subconjunctival steroids

Topical steroid treatment is used frequently for keratitis, anterior uveitis, allergic types of conjunctivitis and after surgery. There are no significant systemic side effects, but unfortunately topical steroids quite often cause serious side effects in the eye. Steroids can also be given by subconjunctival injection (see above).

The side effects of topical and subconjunctival steroids

1. *Infection risk:* steroids act by suppressing the inflammatory response in the tissues, but they also suppress the defences of the body to infection. Topical steroid treatment therefore encourages any micro-organisms in the conjunctiva and cornea to multiply. The infection may continue to spread, but because the inflammatory responses are suppressed the patient's symptoms improve. This complication is especially serious if there is a herpes simplex viral infection of the cornea (see page 192). The wrong treatment with topical steroids will make a herpes simplex corneal ulcer very severe and persistent.
2. *Cataracts and glaucoma:* patients who receive topical steroid treatment over a long period of time are at risk of cataract (particularly posterior subcapsular) and glaucoma (these patients are called 'steroid responders'). The stronger the steroids, the greater the risk of both cataracts and glaucoma. These side effects are most common with dexamethasone, and least common with hydrocortisone. Rimexolone, clobetasone and fluoromethalone are all topical steroid preparations that are thought to be less likely to raise the intraocular pressure. They may be useful for patients who need long-term topical steroid treatment but who tend to get raised intraocular pressure from the steroids.

Topical steroid preparations are more misused than any other eye treatment. Almost all patients with a red inflamed eye will get relief of symptoms by using topical steroids, as the inflammation will subside. Unfortunately, the result can be disastrous if the inflammation results from herpetic or bacterial corneal infections. Before giving topical steroid treatment every patient should have the cornea carefully inspected with fluorescein dye. In general, if a corneal ulcer is present topical steroid treatment should not be given, unless it is done very carefully and with regular review by someone with expertise in corneal ulcer management. If there is no corneal ulcer, it is usually safe to give a short course of topical steroids. It is both a common and a bad habit to treat an inflamed eye with a mixture of antibiotics and steroids, without trying to diagnose the cause. If the disease is caused by an infection, only antibiotics should be used; if it is caused by inflammation, without any infection, only steroids should be used.

Systemic steroids

Systemic steroids are used to treat inflammations of the choroid, and occasionally the optic nerve and orbit. Unfortunately, systemic steroid treatment,

especially when it is prolonged, may cause numerous side effects throughout the body (Table 4.3).

Topical non-steroidal anti-inflammatory drugs, mast cell stabilisers and anti-histamines

There are several other groups of drugs that can be used to suppress various inflammatory responses of the eye. They are all weaker than steroids but they do not have the same serious side effects especially from long-term usage. The different groups of drugs have different pharmacological actions and are therefore used for different eye conditions.

Antihistamines

Antazoline, azelastine, levocabastine and emedastine are all topical antihistamines. They are very useful for allergic conjunctivitis. Sometimes, they are combined with a vasoconstricting drug.

Mast cell stabilisers

Cromoglycate, nedocromil and olopatidine prevent histamine release and are also used in allergic conjunctivitis, especially vernal conjunctivitis.

Prostaglandin inhibitors (topical non-steroidal anti-inflammatory drugs)

Diclofenac, ketorolac and flurbiprofen have an anti-inflammatory action. They have a specific use in suppressing pain after injury or surgery, and they keep the pupil dilated during intraocular surgery. They are also used for treating cystoid macular oedema, which can occur after cataract surgery (see page 302).

Systemic 'steroid-sparing' immunosuppressive drugs

These drugs are sometimes used systemically to treat severe sight-threatening inflammatory disease in the eye, such as uveitis or choroiditis. Cyclophosphamide, cyclosporine, methotrexate and azathioprine are the most commonly used of these drugs. They must be given with very great care, monitored carefully with regular blood tests and preferably prescribed and monitored by an experienced clinician because they can have serious and even fatal side effects.

Table 4.3 Possible complications from systemic steroid treatment

Fluid and electrolytes: sodium and water retention, therefore increased blood pressure
Endocrine and metabolic: weight gain and swollen (Cushingoid) appearance to face and abdomen
Growth suppression: children
Dermatological: thin skin bruising, acne, striae, mild hirsutism
Haematological: increased bleeding, increased white cell count
Musculoskeletal: bone thinning (osteoporosis), fractures, osteonecrosis (bone death, most commonly of the head of the femur)
Behavioural: agitation, mood swings, poor sleep
Increased infection risk, especially tuberculosis
Gastrointestinal: stomach ulcer, pancreatitis, Candidiasis
Drug interactions: many, but particularly important: HIV treatments, rifampicin (for TB), diabetic treatments, epilepsy treatments
Eye: cataract, glaucoma

Mydriatics

Mydriatics are substances that dilate the pupil. There are two ways in which they act:

1. *Blocking the parasympathetic nervous system:* this makes the pupil sphincter muscle relax and relaxes the ciliary muscle. This prevents the eye from accommodating causing blurring of near vision. This is called 'cycloplegia'. Therefore this group of mydriatics are called cycloplegics. There are cycloplegics that dilate the pupil for a short time (a few hours), e.g. homatropine, cyclopentolate and tropicamide. There are also 'long-acting' cycloplegics, such as atropine (normal dose one drop of a 1% solution once a day) which may dilate the pupil for up to 2 weeks. Excessive use of atropine can cause systemic side effects: drying of the mouth, loss of sweating and tachycardia. Old patients may become confused even with normal doses.
2. *Stimulation of the sympathetic nervous system:* this stimulates the pupil dilator muscle. Phenylephrine 2.5–10% is the most effective drop for this. This does not cause cycloplegia, but can cause a rise in blood pressure, particularly the 10% concentration and must be used very cautiously in people who are known to already have high blood pressure.

The uses of mydriatics

Mydriatics have several very important uses in ophthalmology:

- **Examination:** dilating the pupil allows examination of the fundus. It is possible to use any of the short-acting mydriatics, but the best dilatation is achieved by using both types of agent, e.g. cyclopentolate 1% and phenylephrine 2.5%.
- **Intraocular surgery:** the pupil is dilated for cataract surgery and intraocular retinal surgery (see Chapters 12 and 13).
- **Treatment:** cycloplegics relax the smooth muscle in the iris and ciliary body, and are therefore used in the treatment of inflammatory eye disease. This has two benefits. Firstly, it stops the iris sticking to the lens (synechiae) and secondly can reduce the pain slightly as some of the pain comes from spasm of the iris.

Drugs used in the treatment of glaucoma

Miotics

Substances that constrict the pupil are called 'miotics.' They act by stimulating the parasympathetic system, which makes the iris sphincter muscle constrict.

Miotics are mainly used to treat glaucoma. Constricting the pupil opens up the angle of the anterior chamber (see page 390), which helps to relieve angle closure glaucoma. Miotics also increase the flow of aqueous through the trabecular meshwork, which lowers the intraocular pressure in open angle glaucoma as well. The most commonly used miotic is pilocarpine (1–4% drops), and its effect lasts for about 8 hours. Eserine and carbachol have



EYE DISEASES IN HOT CLIMATES FIFTH EDITION

This well-established textbook focuses on the management of preventable and treatable causes of blindness in developing countries.

Written specifically to address the needs of doctors, nurses and medical assistants involved in managing eye patients in tropical and developing nations, *Eye Diseases in Hot Climates Fifth Edition* is designed to support those working with limited specialist supervision and equipment.

Introductory chapters on anatomy, physiology and clinical skills are followed by chapters devoted to specific conditions such as xerophthalmia, leprosy and HIV. Also included are chapters on paediatric eye disease and the diagnosis of common eye disorders.

Thoroughly revised and updated, *Eye Diseases in Hot Climates Fifth Edition* continues to provide practical advice for healthcare providers caring for eye patients in nations where blindness and visual impairment remain prevalent.

- Incorporates many new treatments that are increasingly accessible in poorer countries, particularly for retinal disease, trachoma and HIV
- Includes an updated review of the epidemiology of visual impairment and blindness worldwide
- Features new photographs and illustrations throughout



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