Steroids and the eye

Corticosteroids are extremely valuable medications because of their potent ability to treat inflammatory, immune-mediated or allergic conditions. However, their therapeutic potential in ophthalmology is often limited by their numerous side effects. Also, the rapid symptom relief they produce can mask their adverse effects.

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Corticosteroid use in ophthalmology

Corticosteroids, if used correctly, can save sight; however, their inappropriate use is potentially blinding. There are many indications for corticosteroids in ophthalmology, and both systemic and topical therapies have been in use for more than 50 years. To prevent their indiscriminate use, corticosteroids should not be used without a definitive diagnosis.

Topical corticosteroid therapy

Indications for use

Indications for topical ophthalmic corticosteroids include:

- inflammatory and immune-mediated eye disease (such as uveitis, blepharitis, and noninfectious keratitis and conjunctivitis) as well as inflamed pterygia
- allergic eye disease – for example, simple allergic conjunctivitis or potentially blinding atopic keratoconjunctivitis in adults and vernal conjunctivitis in children (Figure 1)
- the prevention of inflammation after eye surgery and rejection after corneal grafting
- the control of inflammation after ocular trauma and chemical burns.

For many conditions, there are simple alternatives that should be trialled before corticosteroids are prescribed (Table 1).

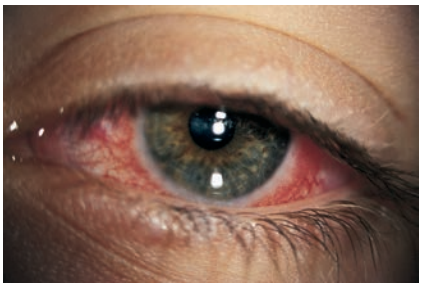
Effectiveness

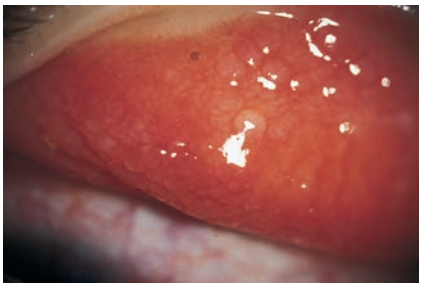
Many different corticosteroids are available for topical ophthalmic use (Table 2). Topical corticosteroids are formulated as solutions, suspensions or ointments. Suspensions must be shaken to avoid incorrect dosage, and compliance with shaking is reportedly poor.

The relative potencies (Table 3) and corneal penetrations of ophthalmic preparations vary. Fluorometholone, for instance, has high potency but poor corneal penetration and therefore is effective for superficial, but not for intraocular, inflammation. Prednisolone is less potent than fluorometholone; however, because of its high

IN SUMMARY

- **The correct use of corticosteroids for ophthalmic conditions can be sight saving; their incorrect use is potentially blinding.**
- **Corticosteroids should never be given for an undiagnosed red eye, when visual acuity is impaired or if there is a history of ocular herpes infection.**
- **Corticosteroids should be prescribed only when indicated, not casually for the relief of ocular discomfort.**
- **Topical corticosteroid treatment should not be repeated or renewed without regular review by an ophthalmologist.**
- **Patients on prolonged systemic corticosteroids should have six-monthly eye examinations by an ophthalmologist.**
- **Paediatric patients on corticosteroids require careful ophthalmological monitoring.**





Figures 1 a and b. a (left). Vernal conjunctivitis in an 8-year-old boy. b (right). Note the giant papillae on the everted upper eyelid.

corneal penetration it is more effective for intraocular inflammation.

Systemic corticosteroid therapy

The sight-threatening manifestations of conditions such as giant cell arteritis, rheumatoid arthritis and sarcoidosis require systemic corticosteroid therapy. In giant cell arteritis with visual symptoms, parenteral corticosteroids reduce the rate of permanent blindness by more than half. Systemic corticosteroids are also used when topical treatment fails and for severe potentially blinding ocular disease, such as scleritis.

In optic neuritis, intravenous corticosteroids reduce the risk of recurrence. In contrast, recurrence of optic neuritis is more common in patients with multiple sclerosis or those who have been treated with oral corticosteriods.

Corticosteroids are also used for Graves' ophthalmopathy, alone or with immunosuppressives, radiation or surgery.

Side effects of corticosteroid therapy

The side effects of corticosteroids are dependent on the route of administration, dosing schedule and total cumulative dose. The numerous side effects may affect any organ system including the visual system.

Systemic side effects usually occur from oral or parenteral administration but can occur with topical or even inhaled corticosteroids. The rapid withdrawal of corticosteroids may also lead to side effects – after prolonged therapy the dose should be reduced by no more than half the current dose at a time.

Ocular side effects typically arise from the prolonged use of topical, inhaled or systemic corticosteroids (Table 4). Prolonged topical therapy for the skin in the periorbital region, such as for atopic dermatitis, can have ocular side effects.

Cataracts

Topical, systemic and even inhaled corticosteroids can induce posterior subcapsular cataract (Figure 2). This is one of the most visually disabling types of cataract

Table 1. Alternatives to corticosteroids for ocular disorders

Allergic conjunctivitis
- Tear substitutes to dilute and wash away allergens
- Cold packs applied to the eyelids
- Topical H_1 antihistamine and vasoconstrictor combinations as needed during the allergy season
- Topical mast cell stabilisers to prevent attacks

Blepharitis
- Lid scrubs with sodium bicarbonate solutions (1 teaspoon of sodium bicarbonate in 600 mL of water – boiled then allowed to cool)
- Heat and massage of the eyelids
- Complete removal of make-up each day
- Low dose systemic tetracyclines, especially if rosacea is present

Pterygia
- Wide-brimmed hat
- Sunglasses with UV filters and side protection
- Ocular lubricants
- Topical nonsteroidal anti-inflammatory agents

Table 2. Common topical ophthalmic corticosteroids

Prednisolone
- Prednisolone acetate 1% (Prednefrin Forte)
- Prednisolone sodium phosphate 0.5% (Minims Prednisolone, Predsol Eye Drops)

Dexamethasone
- Dexamethasone 0.1% (Maxidex)

Progesterone-like agents
- Medrysone 1% (HMS Liquifilm)
- Fluorometholone 0.1% (Flucon, FML)
- Fluorometholone acetate 0.1% (Flarex)

Hydrocortisone
- Hydrocortisone acetate 0.5% and 1.0% (Hycor Eye Ointment)
- Hydrocortisone suspension 0.5% and 1.0% (Hycor Eye Drops)

Table 3. Anti-inflammatory and IOP-elevating properties of topical and local corticosteroids

Corticosteroid	Relative potency	Rise in IOP (mmHg)
Dexamethasone 0.1%	24	22
Fluorometholone 0.1%	21	6
Prednisolone 1%	2.3	10
Medrysone 1%	1.7	1
Triamcinolone* 0.25%	1.4	2
Hydrocortisone 0.5%	1.0	3

*Triamcinolone is used by ophthalmologists for local steroid injections (e.g. subconjunctival).
IOP=intraocular pressure.

and accounts for a significant proportion of cataract extractions.

Cataracts occur when the daily systemic dosage of corticosteroid exceeds 15 mg over one year, such as in the treatment of chronic arthritis, asthma and eczema, and after renal transplantation. Prolonged topical therapy is used for vernal or atopic conjunctivitis, or after corneal grafting. However, cataracts may follow even short term therapy. Children and people with diabetes are more susceptible.

Limited evidence suggests that cataract regression may occur if therapy is stopped or the dose reduced. However, the indication for treatment must be considered. In renal transplant patients, if the maintenance corticosteroid dose is kept as low as possible to suppress rejection, it should not necessarily be reduced further, for fear of rejection.

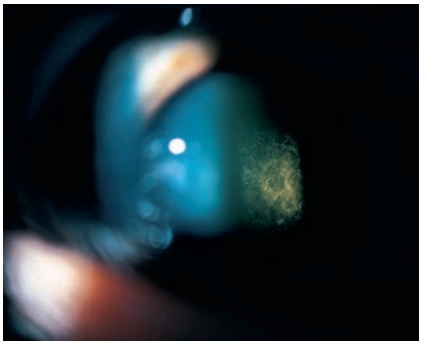


Figure 2. Posterior subcapsular cataract.

Glaucoma

Corticosteroids (again, systemic, topical and even inhaled) may raise intraocular pressure (IOP), resulting in secondary open-angle glaucoma. Raised intraocular pressure has been reported in up to a third of patients on topical ophthalmic corticosteroids – these patients are said to be corticosteroid 'responders'. The propensity of topical corticosteroids to raise intraocular pressure varies (Table 3).

Corticosteroid-induced glaucoma is similar to chronic open-angle glaucoma. There is a moderate rise in pressure that over the years damages the optic nerve head, leading to an insidious loss of visual field (Figure 3). Typically, there is no pain and the eye is not red. The damage can be so great that the eye may be left blind. A personal or family history of glaucoma and high myopia increases the risk of corticosteroid-induced glaucoma.

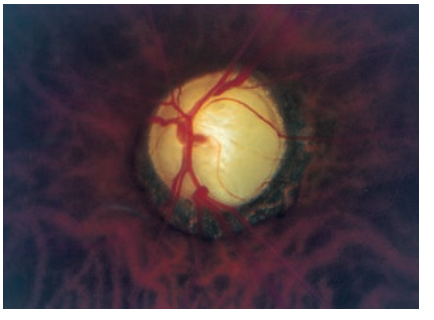


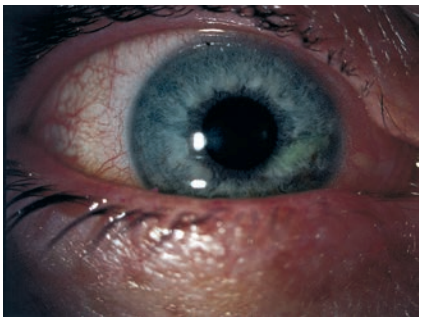
Figure 3. An optic nerve head damaged by glaucoma.

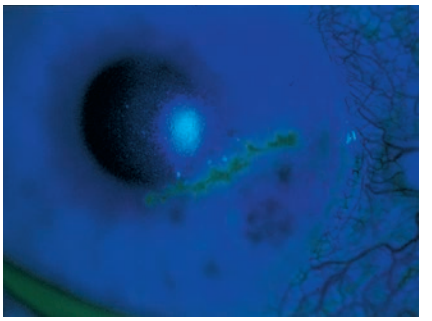
Table 4. Ocular complications of corticosteroids

- Cataract
- Glaucoma
- Opportunistic infection
- Corneal melt and perforation*
- Delayed corneal epithelialisation (e.g. after traumatic corneal abrasion)
- Delayed wound healing
- Ptosis with moon facies
- Exophthalmos
- Ocular muscle palsy
- Refractive changes, typically myopia
- Scleral therapy and thickening
- Papilloedema with pseudotumour cerebri
- Lid chemosis and swelling
- Slight mydriasis
- Exacerbation/recurrence of ocular toxoplasmosis
- Rebound inflammation†
- Corticosteroid-induced uveitis‡
- Hypertensive retinopathy
- Eyelid depigmentation§
- Eyelid necrosis§
- Central retinal artery occlusion§
- Subcutaneous fat atrophy§
- Intraocular injection§
- Retrobulbar haemorrhage§

*May occur when corticosteroids are used in conditions that cause corneal or scleral thinning.
†An acutely red eye after sudden corticosteroid withdrawal; it presents as conjunctivitis, which resolves after a few days without treatment.
‡Topical corticosteroids may rarely induce a nongranulomatous anterior uveitis.
§May occur with periocular corticosteroid injection.

Stopping the corticosteroid usually lowers the intraocular pressure; however, this may take weeks to months. In situations where corticosteroid therapy must be continued, drugs that lower intraocular pressure – such as betaxolol (Betoptic, Betoquin), brimonidine (Alphagan), latanoprost (Xalatan), timolol (Optimol, Tenopt, Timoptol) – are used in combination.





Figures 4 a and b. a (left). An acute red eye. b (right). Fluorescein staining shows a dendritic ulcer due to herpes simplex infection.

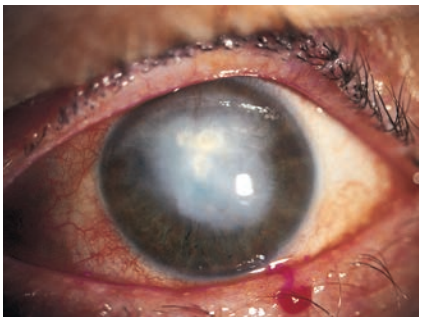


Figure 5. Permanent corneal scarring from herpes simplex keratitis.

Ocular herpes simplex

Superficial ocular infections presenting as a red eye may actually be herpes infection (Figure 4). Topical corticosteroids, if used incorrectly, can transform a simple herpetic dendritic lesion into an extensive amoeboid ulcer involving all layers of the cornea. This requires prolonged, complicated management, with a possibility of permanent corneal scarring and visual loss (Figure 5).

Herpes simplex involving the corneal stroma may be treated, by an ophthalmologist, with topical corticosteroids, as it is usually immune mediated. Stromal disease is diagnosed by slit lamp examination because the typical finding of a dendritic lesion is usually absent.

Viral conjunctivitis

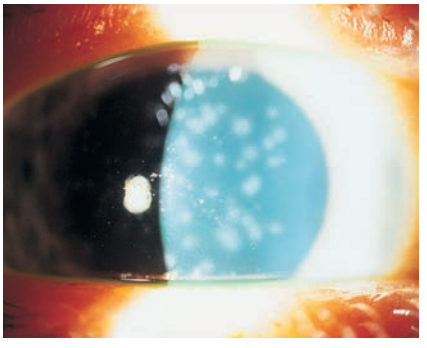
Debate surrounds topical corticosteroid use for adenoviral conjunctivitis. Topical corticosteroids can improve comfort and reduce erythema; however, they prolong viral shedding and clinical infection.

An immune-mediated keratitis may follow epidemic adenoviral conjunctivitis (Figure 6). This can be treated with topical corticosteroids.

Bacterial, fungal and protozoal eye infections

For ocular infections, corticosteroid use must be given careful consideration because it can potentiate infection. Misdiagnosis, delays in diagnosis, uncontrolled infection or superinfection can then occur, with disastrous results.

A painful red eye after trauma is commonly due to a corneal abrasion. If corticosteroids are given, fungal infection may supervene (Figure 7). Less commonly, if bacterial infection occurs after an abrasion and corticosteroids are applied, panophthalmitis can follow within hours.



COURTESY OF DR PATRICK VERSACE, SYDNEY

Figure 6. Adenoviral keratitis. Note the superficial corneal opacities.

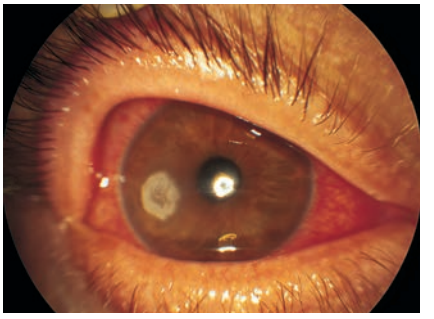


Figure 7. Corneal ulcer due to *Aspergillus*; the result of a traumatic corneal abrasion treated with corticosteroids.

Contact lens wearers are susceptible to infection with, at times, devastating visual results. The red eye has many possible causes in the contact lens wearer, and prompt ophthalmological attention is needed because of both the complexity of diagnosis and the risk of vision-threatening infection. Corticosteroids can promote potentially serious infections – for example, with *Pseudomonas* and *Acanthamoeba* species, which are of particular concern because of their virulence and difficulty of eradication.

Side effects in children

Ocular side effects of corticosteroids should not be forgotten in children. About half of the children treated with prednisone for inflammatory bowel disease may develop either cataract or raised intraocular pressure, and children with cataract or raised intraocular pressure often do not complain of the symptoms. Development of the visual system continues during childhood, such that cataract may lead to amblyopia; this may be difficult to treat, resulting in irreversible poor vision.

Use in pregnancy

Systemic corticosteroid therapy late in pregnancy has been associated with intrauterine growth retardation and adrenal suppression in the baby. The safety of intense or prolonged use of topical ophthalmic corticosteroids in pregnancy has not been established. In animal studies,

Guidelines for corticosteroid use in general practice

- Never give corticosteroids for an undiagnosed red eye.
- Never give corticosteroids if visual acuity is impaired and there is no diagnosis.
- Review the patient the day after starting corticosteroids and refer him or her to an ophthalmologist if the condition is getting worse rather than better.
- Avoid issuing a repeat prescription for corticosteroids without ophthalmological review, because the patient may be a corticosteroid 'responder' (responding with a raised intraocular pressure).
- Avoid corticosteroids if there is a history of a herpetic dendritic ulcer.
- Be more wary if the ocular problem is unilateral, because herpes simplex or microbial keratitis are typically unilateral.
- Always check the cornea with fluorescein before prescribing any therapy.
- Arrange for review every six months by an ophthalmologist if a patient is on prolonged systemic, inhaled or topical corticosteroid therapy.
- Do not forget the ocular side effects of corticosteroids in children.

an increased incidence of cleft palate followed corticosteroid application to the mother's eye.

Corticosteroids, the GP and the eye

The general practitioner is involved in the treatment of less serious ocular conditions, patient education regarding the potential side effects of ocular medications, and reinforcement of the need for supervision by an ophthalmologist when corticosteroids are used.

General practitioners are frequently advised against starting corticosteroids for ophthalmic conditions because, without access to a slit lamp, it may be difficult to make the correct diagnosis and identify side effects. Similarly, treatment should not be repeated or renewed without slit lamp review and intraocular pressure measurement by an ophthalmologist.

Patient education regarding the risks of corticosteroids is imperative to ensure patients present early with complications and to deter long term unsupervised corticosteroid use. Patients may exert pressure for corticosteroids because the symptom relief is rapid, but they may misuse them. Prescribing topical corticosteroids is further complicated because the smallest volume produced by most pharmaceutical companies is 5 mL, which is enough for more than one month, even when used four times daily.

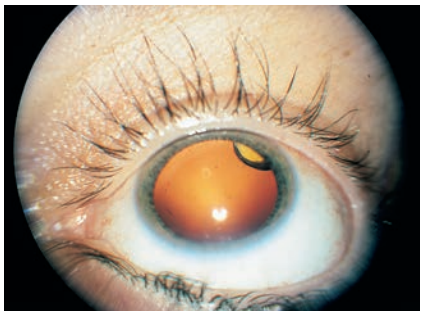


Figure 8. An intraocular ganciclovir implant used for cytomegalovirus retinitis. Similar implants are under investigation for corticosteroid delivery.

Some guidelines for ocular corticosteroid use in general practice are listed in the box on this page.

Reducing the risks of corticosteroid therapy

Use of corticosteroid-sparing agents, new corticosteroids or new modes of

administration can reduce the risk of complications.

- Topical nonsteroidal anti-inflammatory drugs (NSAIDs) are useful for allergic conjunctivitis and inflamed pterygia. They include flurbiprofen (Ocufen), ketorolac trometamol (Acular Eye Drops) and diclofenac (Voltaren Ophtha).
- Topical cyclosporin A and systemic immunosuppressives are corticosteroid sparers.
- Pulse corticosteroid therapy is particularly useful for scleritis.
- Loteprednol etabonate is a new corticosteroid with greater specificity for the ocular surface and lesser effect on intraocular pressure. It is not yet available for use in Australia.

New alternatives to corticosteroids

Immune modulators, tolerance inducers, anticytokines, antiadhesion molecules and antichemokines are currently under investigation as more specific immunosuppressives.

Implantable intraocular devices, for the slow release of corticosteroids or immunosuppressives, are under development. Ganciclovir implants are already in use for cytomegalovirus retinitis (Figure 8).

Conclusion

The proper use of corticosteroids can be sight saving; their inappropriate use is potentially blinding. They produce rapid symptom relief and this can mask their adverse effects. Cataract, glaucoma and the potentiation of infection are serious ocular side effects. Topical ophthalmic corticosteroids can have systemic side effects. Their prescription requires: slit-lamp examination with monitoring of intraocular pressure; assurance of appropriate follow up; patient education; and knowledge of the differential diagnosis, evaluation and treatment of ophthalmic conditions. All patients on systemic or topical corticosteroids require regular review by an ophthalmologist. MT

Further reading

1. Baratz KH, Hattenhauer MG. Indiscriminate use of corticosteroid-containing eyedrops. Mayo Clin Proc 1999; 74: 362-366.
2. Claoue CM, Stevenson KE. Incidence of inappropriate treatment of herpes simplex keratitis with topical steroids. BMJ 1986; 292: 1450-1451.
3. Cumming RG, Mitchell P, Leeder SR. Use of inhaled corticosteroids and the risk of cataracts. N Engl J Med 1997; 337: 8-14.
4. Evans TM. Ocular pharmacology and therapeutics. J Occup Med 1971; 13: 92-96.
5. Gilkes MJ. The GP and the specialist: ophthalmology. BMJ 1982; 285: 1247-1248.
6. Jones BR, Coster DJ, Falcon MG. Prospects of prevention of recurrent herpetic eye disease. Trans Ophthalmol Soc UK 1977; 97: 350-355.
7. Kersten RC. Ophthalmic drugs. Prim Care 1982; 9: 743-756.
8. Krupin T, Le Blanc RP, Becker B, Kolker AE, Podos SM. Uveitis in association with topically administered corticosteroid. Am J Ophthalmol 1970; 70: 883-885.
9. Loredo A, Rodriguez RS, Murillo L. Cataracts after short-term corticosteroid treatment. N Engl J Med 1972; 286: 160.
10. McCluske,y P, Wakefield D. Intravenous pulse methylprednisolone in scleritis. Arch Ophthalmol 1987; 105: 793-797.
11. O'Dowd TC, Beck L. Steroids, the eye, and general practitioners. BMJ 1986; 293: 265.
12. Chalam KV, ed. Ocular pharmacology. In: Tripathi RC, chief ed. Fundamentals and principles of ophthalmology. San Francisco: American Academy of Ophthalmology, 1997: 415-421.
13. Renfro L, Snow JS. Ocular effects of topical and systemic steroids. Dermatol Clin 1992; 10: 505-512.
14. St Clair Roberts D. Steroids, the eye, and general practitioners. BMJ 1986; 292: 1414-1415.
15. Tripathi RC, Kipp MA, Tripathi BJ, et al. Ocular toxicity of prednisone in paediatric patients with inflammatory bowel disease. Lens Toxic Res 1992; 9: 469-482.