9
DRUGS AND THE EYE

OBJECTIVES

As a primary care physician, you should be able to use pharmacologic agents to facilitate an eye examination, including staining the corneal surface with fluorescein, anesthetizing the cornea with a topical anesthetic, and dilating the pupil with one or more mydriatic drugs. You should be aware of the potential ocular complications of the eyedrops and systemic drugs that you prescribe and be able to recognize these ocular complications when they occur. In addition, you should be cognizant of the systemic effects of the topical ophthalmic drugs that an ophthalmologist might prescribe for your patients.

To achieve these objectives, you should learn

- The technique of applying drugs to the conjunctival sac
- The ocular effects and complications of common topical ocular drugs used for diagnosis and therapy, such as anesthetics, mydriatics, decongestants, antibiotics, and anti-inflammatory agents
- The systemic side effects of glaucoma medications: beta-adrenergic blockers, cholinergic stimulators, alpha-2 adrenoreceptor agonists, adrenergic-stimulators, prostaglandin analogs, and carbonic anhydrase inhibitors
- The ocular side effects of systemically administered amiodarone, biphosphanates, chloroquines, chlorpromazine, corticosteroids, digitalis, diphenylhydantoin, ethambutol, HMG-CoA reductase inhibitors (statins), rifabutin, sildenafil and tadalifil, thioridazine, and topiramate

RELEVANCE

You will need to use diagnostic drugs to perform a complete ocular examination, which entails skills that every primary care physician should possess. You must be familiar with the side effects and complications of diagnostic and

therapeutic drugs to minimize the potential for problems and to recognize them when they do occur. See Table 9.1 for a summary of common topical ocular drugs for diagnosis and treatment.

TABLE 9.1 Summary of Selected Topical Ocular Drugs*

Class	Compound (Brand Name)	Comment
Diagnostic		
Fluorescein dye	Sodium fluorescein	Helpful in detecting abrasions of the corneal surface. Contact lenses should be removed before instillation.
Anesthetics	Proparacaine hydrochloride 0.5% Tetracaine 0.5%	Surface-active compounds. Patients should not rub their eyes for at least 10 minutes after receiving to avoid inadvertent abrasions. Never prescribed for repeated use.
Mydriatics (dilators)	*Cholinergic-blocking drugs:* Tropicamide 0.5% or 1% Cyclopentolate hydrochloride 0.5%, 1%, or 2% Homatropine hydrobromide 2% or 5%	Dilation by paralyzing the iris sphincter.
	Adrenergic-stimulating drugs: Phenylephrine hydrochloride 2.5 or 10%	Dilation by stimulating the pupillary dilator muscle.
Therapeutic		
Decongestants	Naphazoline hydrochloride 0.012% Phenylephrine hydrochloride 0.12% Tetrahydrozaline hydrochloride 0.05%	Available over the counter. Designed to temporarily whiten the conjunctiva through their vasoconstrictor effect. Chronic use can result in rebound hyperemia.
Relief of allergic conjunctivitis	Naphazoline/antazoline drops (Vasocon-A)	Available over the counter. Provide decongestant action, antihistamine effects.
	Naphazoline/pheniramine drops (Naphcon- A, Opcon-A)	Available over the counter. Antihistamine.
	Cromolyn (Crolom) Pemirolast (Alamast)	Prevent the release of inflammatory mediators. Mast-cell stabilizer.
	Nedocromil (Alocril)	Antihistamine/mast-cell stabilizer.
	Lodoxamide (Alomide)	Mast-cell stabilizer.
	Ketotifen (Zaditor)	Acts as a mast-cell stabilizer and decreases eosinophil chemotaxis.
	Levocabastine (Livostin)	Antihistamine.
	Olopatadine (Patanol)	Antihistamine/mast-cell stabilizer.

(continued)

TABLE 9.1 Summary of Selected Topical Ocular Drugs* (continued)

Class	Compound (Brand Name)	Comment
Anti-inflammatory agents, nonsteroidal**	Diclofenac (Voltaren) Ketorolac (Acular) Flurbiprofen (Ocufen)	These used alone may not be potent enough to control significant ocular inflammation.
Relief of dry-eye symptoms	Over-the-counter lubricant eye drops	Preservative-free formulations should be used when drops are required more than 6 times a day.
	Cyclosporine A (Restasis)	May provide relief for chronic moderate-to-severe disease. Relatively expensive.
Antibiotics	Erythromycin Sulfacetamide Aminoglycosides Fluoroquinolones	Often used to treat common bacterial conjunctivitis.
Antiviral agents	Trifluridine (Viroptic)	Topical antiviral agents should be used only under the direction of an ophthalmologist; long-term use may be toxic to the cornea.

*See text for additional information. Before administering any medication, always ask patient about possible allergies.

**Although corticosteroids are used in treating various ocular conditions, they should never be prescribed by a primary care physician; see Chapter 4 for information about the possible complications.

BASIC INFORMATION

Using the proper technique to instill eyedrops ensures maximum patient cooperation and adequate delivery of medication to the eye. To instill topical ocular medications, follow these steps:

1. Wash your hands; wear disposable gloves if desired.
2. Instruct the seated patient to tilt the head back and to look up.
3. Expose the palpebral conjunctiva by gently pulling downward on the skin over the cheekbone (Figure 9.1). Avoid direct pressure on the eyeball.
4. Instill the correct amount of medication into the lower conjunctival fornix. Avoid applying drops directly to the cornea, which is the most sensitive part of the eye, and avoid touching the tip of the applicator to the patient's lids or eye.
5. Instruct the patient to close both eyes gently for a few seconds. Wipe any excess medication from the patient's skin with a tissue.

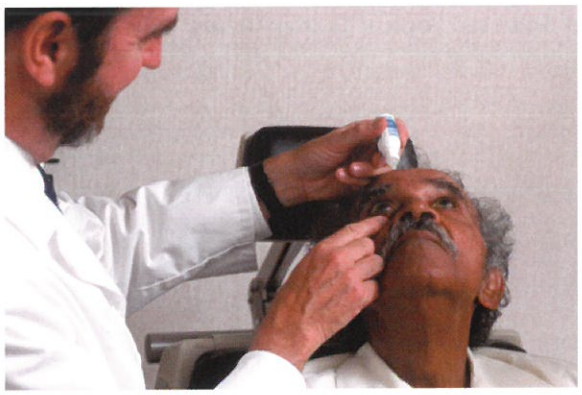

FIGURE 9.1 Instillation of topical drops.

TOPICAL OCULAR DIAGNOSTIC DRUGS

The drugs discussed in this section are used in executing a basic eye examination and assessing certain ocular complaints commonly encountered by the primary care physician. Before administering any medication, always ask patients if they may be allergic to the agent.

FLUORESCEIN DYE

Sodium fluorescein is a water-soluble, orange-yellow dye that becomes a brilliant green when viewed under cobalt-blue or fluorescent light. The dye, which does not irritate the eye, is extremely helpful in detecting abrasions of the corneal surface because fluorescein stains damaged epithelium (see Figures 1.12 and 1.13). To instill the dye, a sterile, individually packaged dry fluorescein strip is moistened with a drop of sterile water or saline and then applied to the inferior bulbar conjunctiva. A few blinks spread the now-visible tear film across the cornea. Although no systemic complications accompany the use of topical fluorescein, a local complication is the staining of a soft contact lens because of its porous structure. To avoid discoloration, contact lenses should be removed before the fluorescein is instilled.

ANESTHETICS

Among the topical anesthetics, the most widely used agents are proparacaine hydrochloride 0.5% and tetracaine 0.5%. The instillation of one drop of these surface-active compounds renders the corneal epithelium insensate within 15 seconds. Such anesthesia is useful to make surface manipulations painless; for example, to remove a superficial corneal foreign body or perform tonometry. Use of an anesthetic also facilitates the examination of a damaged cornea or saline irrigation for a chemical injury, which otherwise might be difficult because of the pain. Patients should be instructed not to rub their eyes for at least 10 minutes after receiving topical ocular anesthetics to avoid inadvertent corneal abrasions.

Topical anesthetics may produce local or systemic allergy, but this is rare. They should never be prescribed for repeated use by patients because they are toxic to the corneal epithelium; they inhibit mitosis and cellular migration and can lead to corneal ulceration and permanent corneal scarring. (See Chapter 4 for a discussion of therapeutic warnings.)

MYDRIATICS

Mydriatics are drugs that dilate the pupil; dilation may be necessary for ophthalmoscopy. The two classes of mydriatics are cholinergic-blocking (or parasympatholytic) drugs and adrenergic-stimulating (or sympathomimetic) drugs.

Cholinergic-Blocking Drugs

Drugs in this category dilate the pupil by paralyzing the iris sphincter. Several such drugs are in regular use: tropicamide 0.5% or 1%; cyclopentolate hydrochloride 0.5%, 1%, or 2%; and homatropine hydrobromide 2% or 5%. Atropine sulfate 0.5% or 1% and scopolamine hydrobromide 0.25% are also available for topical ocular use, but they should never be used to dilate the pupil for diagnostic purposes because their effects may last 1 to 2 weeks.

Cholinergic-blocking drugs produce not only mydriasis but also cycloplegia, or paralysis of the muscles of the ciliary body. For this reason, these drugs are often referred to as *cycloplegics*. Cycloplegia produces paralysis of accommodation (focusing), so that patients find their near vision may be blurred until the effects of the cycloplegic wear off. Nevertheless, these drugs are widely employed by physicians because they produce excellent mydriasis and the cycloplegic effect facilitates refraction.

Tropicamide is a popular mydriatic with primary care physicians and ophthalmologists alike because of its rapid onset and short duration. Maximum pupillary dilation is attained about 30 minutes after instillation, and the effect diminishes within 4 to 5 hours. Cautions regarding pupillary dilation are discussed in Chapter 1. Systemic side effects of tropicamide are decidedly rare because of its brief duration of action, but they may be serious; they include nausea, vomiting, pallor, and vasomotor collapse. Cyclopentolate produces more complete cycloplegia and is used by ophthalmologists to perform refractions in children.

Adrenergic-Stimulating Drugs

These drugs dilate the pupil by stimulating the pupillary dilator muscle. Only one such drug is in regular use: phenylephrine hydrochloride 2.5%. One drop applied to the eye dilates the pupil in 30 to 40 minutes, but has no effect on accommodation; thus, phenylephrine is a mydriatic but not a cycloplegic. Because accommodation is not affected, the patient can use near vision after

instillation. However, the mydriasis produced is not as great as with tropicamide, and the pupil remains reactive to light. For these reasons, phenylephrine is seldom used alone as a mydriatic.

When maximum mydriasis is required—for example, when the far periphery of the retina must be examined—phenylephrine in combination with tropicamide is ideal because the effects are additive. This combination is often used to dilate the pupil of a brown iris as well, because mydriatics are less effective in dark-eyed individuals than in blue-eyed ones. The 2.5% solution of phenylephrine is much preferred to the 10% solution because the stronger preparation has been associated with acute hypertension and even with myocardial infarction in some patients.

In infants, the combination of cyclopentolate hydrochloride 0.2% and phenylephrine hydrochloride 1.0% (Cyclomydril) is the safest and most effective agent. Hypertension and reduced gastric emptying may occur if stronger agents are used.

TOPICAL OCULAR THERAPEUTIC DRUGS

The topically applied ocular drugs reviewed in this section are of clinical importance.

DECONGESTANTS

This group of drugs is important if only because more than a million bottles of over-the-counter (OTC) ocular decongestant are purchased each month in the United States. These weak adrenergic-stimulating drugs temporarily whiten the conjunctiva through vasoconstriction. They are advertised as effective in relieving eye redness due to minor eye irritations caused by smoke, dust, smog, wind, glare, swimming, contact lenses, or fatigue.

Naphazoline hydrochloride 0.012%, phenylephrine hydrochloride 0.12%, and tetrahydrozaline hydrochloride 0.05% are the three major drugs in this category. The widespread belief that the use of these compounds is part of good ocular hygiene is a misconception. Red, burning eyes may benefit as much from a cold, wet compress to the closed eyelids as they would from these compounds. Nevertheless, these agents are purchased in high volume.

The most frequent complication of ocular decongestants arises from overuse, with rebound vasodilation of conjunctival vessels. In other words, when used in excess, these preparations can increase rather than decrease redness of the eyes. In rare instances, acute angle-closure glaucoma may be precipitated in susceptible eyes by the use of sympathomimetic drugs because they can dilate the pupil. However, these drugs may be used without harm by patients with chronic open-angle glaucoma because they do not produce a rise in pressure if the filtration angle is open.

AGENTS FOR RELIEF OF ALLERGIC CONJUNCTIVITIS

Combinations of naphazoline and antazoline or pheniramine drops are available as OTC remedies for redness and itching associated with seasonal allergic conjunctivitis. These provide decongestant action (see above) as well as antihistamine effects. Prescription medications are also available for management of these symptoms. The mast-cell stabilizers cromolyn, pemirolast (Alamast), nedocromil (Alocril), lodoxamide (Alomide), and olopatadine (Patanol) prevent the release of inflammatory mediators and are administered chronically for prevention of allergic symptoms. Ketotifen (Zaditor) acts as a mast cell stabilizer and an antihistamine, as well as decreasing eosinophil chemotaxis. Levocabastine (Livostin), an antihistamine, and nonsteroidal anti-inflammatory agents such as ketorolac (Acular), are helpful as needed for symptomatic relief.

ANTI-INFLAMMATORY AGENTS

Both corticosteroids and nonsteroidal topical preparations are useful in the management of various ocular situations. Topical ocular corticosteroids should never be prescribed by a primary care physician. The serious complications of this class of drugs are discussed in Chapter 4 and include promotion of viral, bacterial, and fungal infections as well as possible development of glaucoma and cataract. Nonsteroidal anti-inflammatory agents do not potentiate these complications. Topical ocular preparations include diclofenac, ketorolac, and flurbiprofen. These alone are generally not potent enough to control significant intraocular inflammation, however. They are also used by ophthalmologists for other specific indications, such as ocular itching, macular edema, or prevention of miosis during cataract surgery.

AGENTS FOR THE RELIEF OF DRY EYE SYMPTOMS

Millions of individuals have some level of dry eye symptoms. Palliative treatments with lubricating eyedrops or ointments are available over the counter. Some patients may develop allergies to common preservatives and require preservative-free formulations. The immunomodulatory agent cyclosporine A (Restasis) is now available as a topical medication and may affect the underlying inflammatory pathology of dry eye syndrome and provide relief to patients with chronic moderate to severe disease. Cyclosporine A is relatively expensive, and an ophthalmologist should be involved in the decision to use the medication.

ANTIBIOTICS

Topical antibiotics may be used for bacterial infections of the eyelids, conjunctiva, and cornea. The choice of agent is based on the suspected infecting

organism. Many commercial agents are available in ophthalmic preparations of drops or ointment.

Topical antibiotics are often used to treat common bacterial conjunctivitis. Useful antibiotics include erythromycin, sulfacetamide, aminoglycosides, and fluoroquinolones. Neomycin-containing agents, although effective as antibacterials, often cause increased redness and tearing because of topical allergic sensitivity. Antibiotics combined with corticosteroids should be used only under the direction of an ophthalmologist, because the combination may accelerate the progression of a herpes simplex or fungal infection and cause permanent damage.

ANTIVIRAL AGENTS

Topical antiviral agents such as trifluridine (Viroptic) are very effective in treating ophthalmic herpes simplex viral infections. These drugs should be used only under the direction of an ophthalmologist, as only short-term use is appropriate to avoid toxicity to the cornea.

SYSTEMIC SIDE EFFECTS OF GLAUCOMA MEDICATIONS

The topically administered glaucoma drugs discussed in this section (Table 9.2) may have potent systemic side effects. Any drug instilled in the conjunctival cul-de-sac may be absorbed systemically by the conjunctiva, nasopharyngeal mucosa, or gastrointestinal tract (after saliva is swallowed in the nasopharynx). One class of agents, the carbonic anhydrase inhibitors, may also be given orally and may cause side effects as well. The systemic side effects of ocular glaucoma medication may be more prominent in the elderly, many of whom have multiple systemic conditions and are taking multiple other medications. The systemic side effects of glaucoma medications should be reviewed in particular with the elderly patient.

BETA-ADRENERGIC BLOCKERS

Topical Timolol, Levobunolol, Metapranolol, Carteolol

Nonselective beta-adrenergic antagonists reduce the formation of aqueous humor by the ciliary body and thereby reduce intraocular pressure. Timolol and its analogs levobunolol, metapranolol, and carteolol are highly effective and widely used. Because the systemic beta-adrenergic effects include bronchospasm, these drugs are contraindicated in patients with asthma or chronic obstructive pulmonary disease. Several deaths have been reported secondary to the pulmonary complications of topically administered timolol. Because of their cardiac effects, topical beta-adrenergic antagonists may precipitate or

TABLE 9.2 Selected Types of Glaucoma Medications*

Class	Agent
Beta-adrenergic blockers	Timolol (Timoptic, Timoptic-XE, Betimol)
	Levobunolol (Betagan)
	Metipranolol (Optipranolol)
	Carteolol (Ocupress)
	Betaxolol (Betoptic-S)
Cholinergic-stimulating drugs	Pilocarpine
	Pilocarpine gel
Alpha-2 adrenoreceptor agonists	Brimonidine tartrate (Alphagan-P)
	Apraclonidine (Iopidine)
Adrenergic-stimulating drugs	Epinephrine hydrochloride
	Dipivefrin (Propine)
Prostaglandin analogs	Latanoprost (Xalatan)
	Bimatoprost (Lumigan)
	Travoprost (Travatan)
	Unoprostone (Rescula)
Carbonic anhydrase inhibitors	Oral acetazolamide (Diamox)
	Oral methazolamide (Neptazane)
	Oral dichlorphenamide (Daranide)
	Dorzolamide (Trusopt)
	Brinzolamide (Azopt)
Combination	Timolol + dorzolamide (Cosopt)

*Topically applied unless noted. See "Systemic Side Effects of Glaucoma Medications" in this chapter for additional information.

worsen cardiac failure and must be used with caution if bradycardia or systemic hypotension would adversely affect the patient.

Topical Betaxolol

A cardioselective beta-1-adrenergic antagonist, betaxolol hydrochloride was developed to avoid the pulmonary complications of timolol. Betaxolol may be as effective as nonselective beta-adrenergic antagonists in lowering intraocular pressure. However, pulmonary effects have occasionally been noted, and caution should be used when this drug is employed in patients with excessive impairment of pulmonary function.

CHOLINERGIC-STIMULATING DRUGS

Topical Pilocarpine

Pilocarpine, available in drop and ointment forms, lowers intraocular pressure by increasing aqueous outflow through the trabecular meshwork. Because of

frequent local side effects, including diminished vision due to pupillary constriction and headaches from ciliary muscle spasm, this drop is a less popular glaucoma agent. Systemic side effects are rare, however, as systemic toxicity occurs only at 5 to 10 times the usual ocular dosage. Nevertheless, lacrimation, salivation, perspiration, nausea, vomiting, and diarrhea may occasionally occur, especially with overdosage.

ALPHA-2 ADRENORECEPTOR AGONISTS

Topical Brimonidine (Alphagan-P)

Brimonidine tartrate is a relatively selective alpha-2 agonist that lowers intraocular pressure by a presumed dual mechanism of decreased aqueous production and increased uveoscleral (nontrabecular meshwork) aqueous outflow. To date, systemic side effects of this new glaucoma medication have been few but may include oral dryness, headache, and fatigue and drowsiness, as it is lipid-soluble and crosses the blood–brain barrier. Brimonidine should not be given to infants because of the risk of severe hypotension and apnea. In adults it may cause a local allergic reaction.

Topical Apraclonidine (Iopidine)

Apraclonidine, a derivative of clonidine, decreases aqueous formation and increases uveoscleral outflow. It is primarily utilized for temporary intraocular pressure control in critical situations or as prophylaxis against pressure spikes after glaucoma laser procedures, but it may also be used chronically to treat glaucoma. Its most concerning systemic side effects include promotion of orthostatic hypotension and vasovagal episodes. Locally it has a fairly high rate of sensitivity reaction and may cause an impressive contact dermatitis of the lids and conjunctiva. Use of topical apraclonidine is associated with mild pupillary dilation, whitening of the conjunctiva, and elevation of the upper eyelid.

ADRENERGIC-STIMULATING DRUGS

Topical Epinephrine, Dipivefrin

Epinephrine hydrochloride and dipivefrin (Propine), an epinephrine prodrug, are infrequently used in the treatment of glaucoma. Epinephrine in particular may cause cardiac arrhythmia or an increase in systemic blood pressure in some patients due to its adrenergic stimulation.

PROSTAGLANDIN ANALOGUES

Topical Latanoprost (Xalatan), Bimatoprost (Lumigan), Travoprost (Travatan), Unoprostone (Rescula)

This new class of glaucoma medications increases aqueous outflow through the uveoscleral pathway, a supplemental route through which a small portion of aqueous normally drains. No major systemic toxic effects of these drugs have been reported thus far, but there are unique ocular effects. Patients may acquire darkening of the iris that may be more noticeable in patients with light brown, green, or hazel irides. Lengthening and thickening of the eyelashes also may occur, usually after several months of therapy. In addition, inflammation in the eye and swelling of the macula causing decreased vision may occur, especially in those predisposed to this condition after cataract surgery or following vascular disease in the eye (eg, central retinal vein occlusion).

CARBONIC ANHYDRASE INHIBITORS

Oral Acetazolamide (Diamox), Methazolamide (Neptazane), Dichlorphenamide (Daranide)

These aqueous suppressants are the only oral drugs utilized for glaucoma management. Their use, particularly on a chronic basis, is limited by a number of side effects, which include paresthesias, anorexia, gastrointestinal disturbances, headaches, altered taste and smell, sodium and potassium depletion, and a predisposition to form renal calculi, and rarely, bone marrow suppression.

Topical Dorzolamide (Trusopt), Brinzolamide (Azopt)

Topical carbonic anhydrase inhibitors lower intraocular pressure by the same mechanism as oral carbonic anhydrase inhibitors but with a much lower (but still possible) incidence of systemic side effects. Altered taste sensation is the most common systemic effect. A fixed combination of timolol and dorzolamide (Cosopt) is commercially available.

OCULAR SIDE EFFECTS OF SYSTEMIC DRUGS

The drugs covered in this section are systemically administered medications that may have profound ocular or neuro-ocular effects.

AMIODARONE

Amiodarone is a cardiac arrhythmia drug that has recently been associated with optic neuropathy. Patients present with mildly decreased vision, visual field defects, and bilateral optic disc swelling. Discontinuation of the drug may allow resolution of the nerve changes in some patients. Amiodarone also produces

whorl-shaped, pigmented deposits in the corneal epithelium. These deposits are dosage-related and reversible if the dosage is decreased or the drug is discontinued entirely. Visual symptoms are rare from the epithelial deposits.

BIPHOSPHONATES

Biphosphonates are used to treat osteoporosis and other conditions associated with increased bone absorption. Conjunctivitis, scleritis, and uveitis have been associated with biphosphonate use. Symptoms include red eye, photophobia, decreased vision, and deep, "boring" eye pain. In decreasing order of side-effect frequency are pamidronate, alendronate, etidronate, risedronate, and clodronate.

CHLOROQUINES

Chloroquine phosphate and hydroxychloroquine sulfate, originally used to treat malaria, are now also used to treat rheumatoid arthritis, lupus erythematosus, and other autoimmune disorders. Chloroquines can produce corneal deposits and retinopathy. The corneal deposits are usually asymptomatic, but can produce glare and photophobia. The deposits regress when the drug is discontinued, but the retinopathy is much more serious. This drug-induced retinal damage is insidious, slowly progressive, and usually irreversible. The typical bull's-eye macular lesions do not become visible ophthalmoscopically until serious retinal damage has already occurred.

Chloroquines are rarely used for the treatment of autoimmune disease due to their greater toxicity and have been replaced by the safer drug hydroxychloroquine (Plaquenil). At the standard dosages used, 200 to 400 mg daily, Plaquenil maculopathy is uncommon. All patients beginning Plaquenil therapy should have a baseline dilated examination to document fundus appearance, visual field testing, and any other ocular conditions (eg, macular degeneration, retinal dystrophy). The exam should include counseling about the risk of retinal damage and the establishment of other risks based on the patient's age, physique, drug dosage and duration of use, and any presence of renal or liver disease. A complete dialated exam should be performed with baseline visual field testing and optional color vision, fundus photography, and other testing. Low-risk patients may be followed at a minimum 2 years from baseline. Patients at higher risk should be screened at intervals determined by their level of risk. Follow-up examinations include visual acuity, color vision, Amsler grid or formal visual field testing, ophthalmoscopic examination and other testing as indicated. Patients on Plaquenil with visual complaints should be referred for ocular examination.

CHLORPROMAZINE

This psychoactive drug produces punctate opacities in the corneal epithelium after long-term use. Occasionally, opacities develop on the lens surface as well. These opacities rarely cause symptoms and are reversible with discontinuation of the drug.

CORTICOSTEROIDS

Corticosteroids or, more properly, adrenocorticosteroids, when given long-term in moderate dosage produce posterior subcapsular cataracts. This phenomenon has been commonly observed in people with asthma, renal transplant, or rheumatoid arthritis. Patients with rheumatoid arthritis may develop posterior subcapsular cataracts in the absence of corticosteroid therapy, but the incidence increases with corticosteroid therapy. The use of systemic or inhaled corticosteroids is associated with elevated intraocular pressures (steroid-induced glaucoma) in susceptible individuals. Oral and inhaled steroids may also precipitate or aggravate acute or chronic central serous retinopathy, a condition resulting in pooling of fluid under the macula.

DIGITALIS

Intoxication with this widely used cardiovascular drug almost always produces blurred vision or abnormally colored vision (ie, chromatopsia). Classically, normal objects appear yellow with the overdosage of digitalis, but green, red, brown, or blue vision can also occur. White halos may be perceived on dark objects, or objects may seem frosted in appearance. Usually, fatigue and weakness develop concomitantly with digitalis intoxication, but the visual disturbances often dominate the patient's complaints.

DIPHENYLHYDANTOIN

Still widely used for the control of seizures, diphenylhydantoin sodium causes dosage-related cerebellar-vestibular effects. Horizontal nystagmus in lateral gaze, vertical nystagmus in upgaze, vertigo, ataxia, and even diplopia occur with mildly elevated blood levels of the drug. More complex forms of nystagmus and even ophthalmoplegia may accompany extremely high blood levels. These effects are reversible if the drug is discontinued.

ETHAMBUTOL

Ethambutol is useful in the chemotherapy of tuberculosis. As a side effect, ethambutol produces a dosage-related optic neuropathy. With dosages of 15 mg/kg/day, optic neuropathy occurs in less than 1% of patients, but increases to 5% of patients receiving 25 mg/kg/day and to 15% receiving 50 mg/kg/day. The onset of visual loss may be within 1 month of starting the drug.

Recovery usually occurs when the drug is stopped, but may take months; occasionally, visual loss is permanent.

HMG-COA REDUCTASE INHIBITORS (STATINS)

Hydroxymethylglutaryl coenzyme reductase inhibitors (statins) include pravastatin, lovastatin, simvastatin, fluvastatin, atorvastatin, and rosuvastatin. Statins are cholesterol-lowering agents that have been shown to decrease myocardial infarction, stroke, and cardiovascular mortality in patients with coronary artery disease. Studies in dogs have shown that some statins are associated with cataract when given in excessive dosages. In humans, long-term use of these drugs has not been shown to increase the risk of cataract. However, concurrent use of erythromycin and simvastatin has been associated with increased risk of cataract. Other medications that affect statin metabolism in the liver should also be monitored.

RIFABUTIN (MYCOBUTIN)

Rifabutin is an antiviral agent used in the prophylactic therapy for disseminated *Mycobacterium avium* complex infection in patients with HIV infection and decreased CD4 lymphocyte counts. Severe uveitis has been associated with rifabutin treatment in these as well as immunocompetent patients.

SILDENAFIL (VIAGRA) AND TADALIFIL (CIALIS)

Sildenafil is a medication for the treatment of men with erectile dysfunction. At the time of peak plasma levels, patients may experience transient, mild impairment of color discrimination, often noted as blue color tinge of vision. The ocular effects of sildenafil have been carefully studied in healthy volunteers and patients with eye disease, and no long-term effects have been identified to date. Tadalafil is a long-acting drug and can have the same visual side effects as sildenafil.

THIORIDAZINE

Thioridazine, commonly used to treat patients with psychoses, produces a pigmentary retinopathy after high dosage, usually at least 1000 mg/day. The current recommendation is 800 mg/day as the maximum dose.

TOPIRAMATE (TOPIMAX)

Topiramate is used for the treatment of seizure disorder and has recently been shown to induce acute angle-closure glaucoma. Side effects include acute eye pain, redness, blurred vision, and halos around lights, usually within days of initiation of the medication. This association is important to recognize, as the

mechanism of glaucoma is not resolved by an iridectomy, but instead with cycloplegia and topical corticosteroids as well as discontinuing the medication. This type of angle-closure glaucoma associated with ciliary body swelling can also be seen in other sulfa-derived agents.

POINTS TO REMEMBER

- When applying eyedrops, avoid dropping them onto the sensitive central cornea. Instead, release the drops into the lower conjunctival fornix.
- Never give a patient a prescription or a sample of a topical anesthetic.
- Never use atropine or scopolamine to dilate the pupil for a fundus exam.
- Never use or prescribe a topical ocular corticosteroid unless you have a precise diagnosis for which the drug is specifically indicated. You must be prepared to monitor the patient for serious side effects, such as glaucoma or cataract.

SAMPLE PROBLEMS

1. A 52-year old attorney with a history of open-angle glaucoma treated by a local ophthalmologist calls your office because she purchased some over-the-counter medication for her allergic rhinitis that has a warning about glaucoma in the package insert. The pharmacist instructed her to contact you. What do you tell her?
   a. Never take any medication that has a warning about glaucoma.
   b. Reassure her that she has open-angle glaucoma and there is no contraindication to this medication.
   c. Take the medication with caution only if her allergy symptoms are severe. If she develops any eye pain or blurred vision, contact her ophthalmologist immediately as blindness could result in a short period of time.

   Answer: **b**. All systemic medications that have sympathomimetic effects can dilate the pupil. In patients with undiagnosed narrow-angle glaucoma (who have not had an iridotomy) this may precipitate an attack of acute angle-closure glaucoma. However, patients who are followed by an ophthalmologist for glaucoma would be treated prophylactically if the angles are narrow and occludable. Thus, patients who are followed by an ophthalmologist regularly with or without glaucoma are cleared to take such medications. In contrast, it is patients who are undiagnosed and unaware who may develop such complications!

2. A 65-year old woman seeking a second opinion reports noted fatigue and decreased exercise tolerance. Her physician informed her that her heart rate was "a little slow" and she may need a pacemaker someday. A med-