

OCULAR & VISUAL SIDE EFFECTS of SYSTEMIC DRUGS

Clinically Relevant Toxicology and Patient Management

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Abstract

Many systemic drugs have reported ocular and visual side effects that impact patient management. It is important to be familiar with the associated side effects which can be mild and transient or may seriously threaten vision. This article deals briefly with the mechanisms and reasons that account for the effects that systemic drugs can exert on the visual system. The remainder of the paper will cover major drug classes and serve as a guide to familiarize clinicians with important ocular and visual implications.

Key Words

Melanin binding, photosensitizer, systemic drugs, ocular toxicity, ocular and visual side effects

Many common systemic medications can affect ocular tissues and visual function. Adverse effects can have mild to more serious implications. The optometrist is in the ideal position to identify and manage such occurrences. In order to appropriately educate patients, prevent and minimize serious consequences, clinicians should keep in mind the potential effects from systemic drugs. While this is true for all optometrists, it is particularly important for those with special interest and expertise in the diagnosis and treatment of functional and behavioral visual problems. These practitioners are most apt to treat patients with special visual needs, such as those with learning disabilities and acquired brain injuries. These patients are quite frequently taking some type of medication(s).

Every year there are many new drugs approved by the FDA (Food and Drug Administration). It can be a formidable task to keep track of newly released drugs as well as those already on the market. There are some drugs that are well documented in terms of their ability to affect the eye. For example, it is well known that chloroquine and hydroxychloroquine can cause permanent, sight-threatening retinopathy.¹ However, side effects from newer drugs and commonly used drugs may not be universally known.

One of the most important aspects of the patient intake is obtaining a thorough medical history which includes specific medications, dosage, and duration of treatment. Some drugs have a greater propensity to cause toxicity the longer the drug is used. Others tend to affect the eyes more if used in higher dosages. In general, it is a good idea to identify the condition being treated since many drugs have multiple approved and off-label uses. For instance, beta-blockers are used to treat hypertension, arrhythmia, angina, and migraines.

The eye care practitioner can be instrumental in detecting and reporting ocular side effects, advising patients, plus collaborating with other members of the patient's healthcare team. One of the difficulties includes becoming familiar with the countless systemic medications prescribed for patients. Another is being able to correlate a particular side effect with a suspected drug. It is the vision care practitioner's responsibility for eye care practitioners to maintain current pharmacologic knowledge. This article will deal briefly with how and why systemic drugs can affect the eyes. The remainder of the paper will cover major drug classes and serve as a guide to familiarize clinicians with important ocular implications. Appendix A further delineates the commonly prescribed drugs in each class, while Ap-

pendix B can serve as a clinically relevant summary of the ocular and visual side effects of each class of drugs.

ANATOMY

The total area of the globe is relatively small compared to the rest of the body. When a systemic medication is taken to treat another part of the body, the eyes frequently are affected. After a drug molecule enters the systemic circulation, it can reach ocular tissues through uveal or retinal circulations.² The choroid, sclera and ciliary body have thin, fenestrated walls for drug molecules to pass. Small, lipid soluble molecules pass freely into the aqueous humor, and can further diffuse into avascular structures such as the lens, cornea, and trabecular meshwork.

At the ocular level, the ability of a drug to penetrate the major barriers determines its likelihood to affect ocular tissues and visual function. The first barricade is the blood-brain barrier where tight junctions called zonular occludens of endothelial cells in the retinal blood vessels prevent passage of drug molecules. Another blockade is the blood-aqueous barrier whose fenestrations sort by molecular size and lipid solubility. The blood-retinal barrier restricts entry of larger molecular weight drugs via Bruch's membrane and the zonular occludens of the retinal pigment epithelium (RPE).

Drug molecules that enter by means of the uveal circulation exit the eye from the Canal of Schlemm, ciliary body or may diffuse into adjacent anatomical structures. Drugs from the retinal circulation can reenter the systemic circulation, diffuse into the vitreous and anatomical structures, or get actively transported out.

In summary, drug molecules can enter the eye, contact various ocular tissues, and eventually accumulate in ocular tissues or exit the eye. There are three major accumulation sites including the cornea, lens and vitreous. The duration of drug in the eye is prolonged if deposited, increasing chances for toxicity.² The cornea has a permeable endothelium, and the stromal glycosaminoglycans (GAGs) can bind drug molecules, leading to edema and decreased transparency. Drug molecules can also bind to lens protein, and photosensitize the lens to ultraviolet (UV) radiation. Lastly, drug molecules tend to accumulate in the vitreous due to the slow rate of fluid exchange.

MELANIN BINDING

Melanin binding and storage of drug molecules has been postulated as a precursor to ocular toxicity.² It is possible that melanin absorbs light and damage results from the free-radical nature of melanin in structures such as the uveal tract and the RPE. Toxicity seems to occur in both albino and non-albino eyes. Certain drugs like chloroquine and chlorpromazine have a high affinity to melanin and tend to affect ocular tissues. Drugs binding to melanin may only be part of the problem, because prolonged exposure may affect adjacent, non-pigmented ocular tissues by slow release of drug from pigmented tissues. The melanin theory is still being debated, and is not completely explained.

DRUG METABOLISM

The body's ability to metabolize a drug directly correlates with toxicity. In patients with liver and kidney disease, there is a decreased rate of excretion, which allows drug molecules to accumulate to toxic levels.³ Also, toxic metabolites formed elsewhere like the liver, can reach the eye through systemic circulation or can be produced locally in ocular tissues.

PHOTOSENSITIZERS

The adult crystalline lens normally filters most ultra-violet (UV) radiation, so there is minimal risk of UV affecting the retina, where drug molecules can potentially bind.¹ UV radiation does affect anterior tissues like the cornea and lens when photosensitized by bound drug molecules. Exposed lens proteins, UV photosensitized by bound drug molecules, may denature, opacify and accumulate leading to cataract formation. UV radiation can potentially affect the retina in aphakic and pseudophakic patients, because UV can penetrate without the normal absorptive lens barrier. Well-known photosensitizers that cause anterior subcapsular lens changes include allopurinol, phenothiazine, amiodarone, and chloroquine.

CARDIOVASCULAR AGENTS

Beta-blockers

When patients report they have a "heart problem," it is important to determine the particular condition(s) for which they are being treated, e.g, hypertension, congestive heart failure, angina, arrhyth-

mia, or hyperlipidemia.⁴ Beta-blockers, used to treat hypertension, reduce tear lysozyme levels and immunoglobulin A (IgA).⁵ This causes a reduction in tear secretion, and patients complain of ocular irritation, dry eye symptoms, and contact lens intolerance. Management should include artificial tear supplementation and refitting the patient with lower water content soft lenses. More importantly, nonselective beta-blockers decrease intraocular pressure (IOP) by blocking the Beta-2 (B2) receptors on the nonpigmented ciliary epithelium.⁵ This results in reduced aqueous formation by the ciliary body. Topical B2 blockers produce little additional IOP reduction with concomitant administration of a nonselective (B1 and B2) systemic beta-blocker. Some patients may be misdiagnosed as normal tension glaucoma because the IOP is artificially reduced, appearing within normal limits. Patients should continue taking their medication, and the clinician should contact the prescribing physician. Management includes changing the dosage or the medication. Other antihypertensive drugs include angiotensin converting enzyme (ACE) inhibitors and alpha adrenergic antagonists. These rarely cause ocular side effects.

Diuretics

Thiazides or diuretics are often used to treat congestive heart failure. Hydrochlorothiazide (HCTZ) is a commonly used diuretic and sometimes causes dry eye by changing the tear film. Myopic shift and band keratopathy have been reported but rarely occur.⁴

Antiarrhythmics

There are many drugs used to treat angina including antiarrhythmics, calcium (Ca++) channel blockers, vasodilators, and nitroglycerine. A well known anti-arrhythmic drug causing significant ocular side effects is amiodarone.⁶ Amiodarone is a photosensitizer, with a tendency towards lipid storage in the cornea and lens. Studies found the presence of amiodarone in all ocular tissues when systemically administered.⁵ This medication is used when standard digitalis therapy fails, and tends to cause whorl-like corneal deposits in as early as six days of treatment, but more commonly in one to three months of treatment. The deposits appear whorl-like because epithelial cells

migrate centripetally from the limbus. This keratopathy occurs in the middle to lower third of the cornea, and Hudson-Stahle lines should be ruled out. Amiodarone can also cause anterior and posterior subcapsular lens changes since it is a photosensitizing agent. As a preventive measure, a UV blocker (400nm) should be prescribed. Visual acuity (VA) is not usually affected, but can be mildly reduced (20/25-20/30). Patient symptoms include glare, halos, and foggy vision. This is a dose and duration dependent drug, where toxicity increases with higher doses and longer therapy. Fortunately, the side effects usually regress as amiodarone is discontinued. There have been recent cases of optic neuropathy with vision loss as well as reports of pseudotumor cerebri, however these were also reversible with the discontinuation of amiodarone therapy.^{6,7} A dilated fundus exam, Amsler grid, and central visual-field screening test should be performed, and consultation is recommended with the patient's internist or cardiologist to consider alternative therapy.⁶

Another drug commonly used for cardiac arrhythmia is digitalis (Digoxin). 11-25% of patients using this drug experience some ocular symptoms like change in color vision, visual sensation, or flickering vision.⁴ Early reports suggested retrobulbar optic neuritis toxicity.⁵ Later, high concentrations of the drug were found in the retina and choroid. Thus, the retina instead of the optic nerve is thought to be the site of digitalis toxicity. In particular, cone dysfunction is caused by inhibition of the enzyme, Na⁺-K⁺-activated ATPase, which plays a vital role in maintaining normal cone receptor function.⁵ Color vision can be monitored with the Farnsworth 100-hue test.⁴ Another side effect is reduction of IOP in glaucomatous and nonglaucomatous eyes.¹ Cardiac glycosides like Digoxin inhibit ouabain-sensitive Na⁺-K⁺-ATPase in the ciliary epithelium.¹ This enzyme is responsible for the active transport of sodium, necessary for aqueous secretion. Thus, its inhibition leads to reduced aqueous secretion and IOP. Along with the ocular side effects, there are numerous systemic side effects associated with this drug precluding its use in glaucoma treatment.

Antihyperlipidemics

Patients with high cholesterol are often treated with antihyperlipidemic drugs. One of the earlier investigations of lovastatin (Mevacor), showed a high rate of lens opacities.⁷ However, subsequent studies exonerated this drug showing no difference between the treated and placebo groups.⁸ Niacin (B3) is another drug that lowers triglycerides and low-density lipoproteins (LDLs). However 20% experience dry eye and several cases of cystoid macular edema have been reported. In addition, symptoms of lid edema and blurred vision may occur.

HYPERGLYCEMICS

Sulfonylureas, such as glipizide and glyburides are used to treat diabetes.³ For some patients, subcutaneous insulin treatment is necessary. Side effects from these drugs are rare and it may be difficult to differentiate them from secondary signs of diabetic state or from drug related hypoglycemia.⁹ These signs and symptoms include extraocular muscle paresis, diplopia, and optic neuritis.⁴

HORMONES

Synthetic hormones are commonly prescribed for replacement therapy. In patients with reduced thyroid function, levothyroxine (Synthroid) is given for management of thyroxine levels.³ Some patients have noticed visual hallucinations with the use of this drug.¹⁰ Other side effects are eyelid hyperemia and pseudotumor cerebri (PTC), which disappear with discontinuation of the drug.⁷ The patient's internist or endocrinologist should be notified to adjust the dosage, balancing adequate T-level control and reducing side effects.⁴

The use of oral contraceptives is commonly known to cause dry eye and contact lens intolerance from reduced tear secretion. The exact cause has not been proven, but may be associated with steepening of the corneal curvature, corneal edema from hypoxia, and decreased aqueous component of the precorneal tear film.¹ Also, there have been microvascular complications like artery and venous occlusions reported in the past. These may be related to changes in retinal vasculature, enhanced platelet adhesiveness, or increase in fibrinogen and clotting factors.¹ Other side effects include migraines, pseudotumor cerebri, macular edema, and

transischemic attacks (TIAs). Patients must discontinue oral contraception if they experience TIAs due to the increased risk of stroke.⁴

Lastly, women entering menopause frequently start estrogen replacement. Similar to oral contraception, steepening of corneal curvature and contact lens intolerance have been noted.¹ There can be increased risk of retinal thrombosis and optic neuritis in large doses.¹⁰

CENTRAL NERVOUS SYSTEM AGENTS

Central nervous system (CNS) agents are becoming the most commonly prescribed class of medication in the world. In general, visual acuity may be inexplicably reduced, color vision altered, pigmented deposits may be found on the endothelium or lens capsule, and optic neuritis may occur.

Antipsychotic

Phenothiazines are prescribed to manage schizophrenia. Thioridazine (Mellaril) has almost completely replaced previous chlorpromazine (Thorazine) use. These drugs have anticholinergic properties causing blurred vision, decreased accommodation and mydriasis. These symptoms are transient and dose-dependent. Reduced tearing and dry eye may also result from the anticholinergic effects. These drugs are photosensitizers and cause endothelial and lenticular pigment deposits. Doses greater than 500 mg/day given for prolonged periods have a higher incidence of irreversible corneal and lenticular deposits.⁸ Pigment deposits can occur on areas of the bulbar conjunctiva that are exposed to UV radiation. UV protection was found unsuccessful to reduce the prevalence, and these patients should simply be monitored on a yearly basis. More importantly, retinal and macular damage have been reported in higher doses.⁶ This can lead to permanent visual acuity and visual field loss if not closely monitored. However, some of these changes may be reversible if detected early.

Lithium is a medication used to treat bipolar affective disorders, e.g., manic depression. Drugs in this class (manic depressives) can cause downbeat jerk nystagmus which may not reverse when the drug is stopped.² Blurred vision sometimes occurs due to cortical involvement.

Other ocular complications include diplopia, keratitis sicca and contact lens intolerance.

Antianxiety

There are numerous drugs used to treat extreme tension. Ocular side effects like blurred vision and diplopia are usually rare and reversible.¹⁰ Mydriasis can result with diazepam (Valium) use. Allergic conjunctivitis may onset after 30 minutes due to antigenic factors in this drug class.

Antidepressant

The tricyclic antidepressants are "dirty" drugs in that they produce many anticholinergic side effects. Symptoms of blurred vision, cycloplegia and dry eye are transient and reversible.¹¹ Clinicians should use caution with sympathomimetics along with tricyclics and also with monoamine oxidase (MAO) inhibitors. It is important to correlate the patient's medication with the time frame of symptoms when possible. Reducing or changing the medication may improve the symptoms. In some cases, near vision lenses may be helpful.

The newer antidepressants, with fewer systemic side effects are the selective serotonin re-uptake inhibitors like fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil) and citalopram (Celexa).¹¹ These do not have any significant ocular effects.⁹

Barbiturate

Barbiturates are used to sedate or induce sleep. Many OTC drugs are marketed heavily and can be easily purchased. Ptosis is common in habitual users.⁸ Extraocular muscle problems and nystagmus can also occur.

Anticonvulsant

These drugs are prescribed not only for chronic epilepsy but for pain as well. Phenytoin (Dilantin) and carbamazepine (Tegretol) are very commonly prescribed. These drugs can cause nystagmus, glare and conjunctivitis.¹²

CNS Stimulant

Methylphenidate (Ritalin) is a mild cortical stimulant with CNS actions similar to amphetamines or adrenergic agonists. In adults, this drug stimulates the sympathetic system and is helpful in cases of narcolepsy. However, this drug has a paradoxical effect on children, and is frequently used to calm children with At-

tention Deficit Hyperactivity Disorder (ADHD). The visual side effects include accommodative dysfunctions and blurred vision.¹³

ANTIMIGRAINE AGENTS

Beta-blockers, discussed previously, are sometimes used to treat migraines. The recently popular sumatriptan (Imitrex) is a serotonin receptor antagonist. Not many side effects have been reported, however corneal opacities were found in dogs. As with newer drugs, reporting of side effects may not be current or accessible. Thus, it is best to take a careful history and monitor any changes.

ANTIULCER AGENTS

Blocking histamine-2 (H₂) receptors in the stomach reduces acid production, helpful for thousands of patients with gastroesophageal reflux disease (GERD), peptic ulcer and gastritis.^{3,10} Cimetidine and ranitidine, better known as Tagamet and Zantac, are common over-the-counter (OTC) H₂ blockers. Some patients have complained of visual hallucinations, blurred vision, photophobia, conjunctivitis and color change.⁴ However, these side effects are usually rare and reversible.

ANTICOAGULANTS

Blood thinners are used to treat venous thrombosis and to prevent embolic induced stroke.⁵ The coumadin-derived medications, like warfarin and heparin, potentiate retinal hemorrhaging due to their blood thinning effect.⁴ This is a particular concern in patients with diabetic retinopathy or age-related macular degeneration. It is important to closely follow diabetic patients for proliferative retinal changes. The managing physician should be advised on the potential for retinal hemorrhages. Also, spontaneous anterior chamber hyphema can occur in any patient on anticoagulant treatment. Routinely, blood thinners are discontinued before ocular surgery in diabetic and hypertensive patients. This may not be necessary in a healthy patient.

ANALGESICS

Salicylate, or aspirin, has multiple therapeutic uses. Not only is it effective for pain and fever reduction, but aspirin also works well as a platelet inhibitor. This anticoagulant property is helpful in acute myocardial infarction and embolic

stroke patients. In addition, it is prescribed for gout and rheumatoid arthritis. Aside from irritation of the gastric lining, aspirin has few systemic and ocular side effects. In terms of management, aspirin should not be used in patients with traumatic hyphema due to the increased risk of rebleed. In contrast to blood thinners, it does not increase risk of vitreal or panretinal hemes in diabetics.⁴ It should be noted that chronic use may cause yellowing of vision.

ANTIINFLAMMATORIES

Corticosteroids

Corticosteroids are used to treat inflammatory and allergic conditions. They are very effective for acute disease states as well as chronic conditions such as asthma and chronic obstructive pulmonary disease (COPD). Cataracts resulting from steroid use are well known and occur with topical, systemic, and nasal administration.¹⁴ The etiology is unknown, but these drugs may react with amino groups of crystalline lens fibers causing protein complexes to aggregate.¹ Posterior subcapsular lens opacity is the most frequent and critical side effect, especially in children since it is irreversible and amblyopia may result. Careful evaluation of each patient, regardless of duration or dosage is important. If significant changes are noted, the prescribing physician should be informed to weigh the risk versus benefit of steroid treatment. Another significant side effect from steroid use is increased IOP. The incidence is greater with topical versus systemic administration.¹ There is increased aqueous humor formation and reduction in aqueous outflow. The latter occurs with long term treatment. Excessive amounts of mucopolysaccharides accumulate in the trabecular meshwork, obstructing aqueous outflow by hydrating the trabeculum. This results in resistance to aqueous outflow and should be managed with IOP lowering drugs, as well as changing or tapering the steroid medication. Other side effects include iris microcysts, exacerbation of herpetic keratitis, papilledema, and retinopathy.¹

NSAIDs

There are much fewer side effects associated with nonsteroidal anti-inflammatory drugs (NSAIDs) compared to corticosteroids. Ibuprofen, a common

OTC medication, can cause blurred vision, refractive changes, diplopia, color vision changes and dry eye. With chronic use, permanent vision and visual field loss have been reported.⁴ The patient's internist should be notified, and a neurological workup may be indicated if there are visual field changes. Indomethacin (Indocin) is a prescription medication that causes whorl-like stromal opacities in 11-16% of patients. Patients may complain of light sensitivity, and RPE or retinal changes can occur. These usually improve with discontinuation of the drug. In addition, pseudotumor cerebri can occur with any NSAID, and a dilated exam should be performed.

ANTIRHEUMATICS

One of the treatments for rheumatoid arthritis and lupus involves gold salts (Ridaura).¹⁵ Gold deposits can reach the cornea and lens by circulation through the aqueous in the anterior chamber. This can lead to numerous, minute colored deposits on the eyelids, conjunctiva and corneal stroma.¹ The color of these deposits can vary from yellow-brown to violet or red. These deposits are benign, so there is no need to discontinue or reduce the dosage. If the patient stops taking this medication, the deposits usually disappear in three to six months.

Recently, physicians have frequently been prescribing the new Cox-2 inhibitors, Celebrex and Vioxx, to treat rheumatoid arthritis and osteoarthritis. These drugs seem effective in reducing inflammation with less risk of peptic ulcer in chronic users as compared to NSAIDs. Ocular side effects are rare. Only blurred vision has been mentioned.

ANTIALLERGY AGENTS

Blocking histamine-1 (H1) receptors alleviates allergic conditions of rhinitis, dermatopathies, urticaria, and systemic allergies. Benadryl and Chlor-trimeton are common OTC medications, the latter causing less sedation. The drugs in this class reduce mucous and tear secretion which aggravates keratitis sicca and causes contact lens intolerance.¹¹ Antihistamines have weak atropine action, acting as cholinergic antagonists. This can cause mydriasis, anisocoria, decreased accommodation and blurred vision.

ANTICHOLINERGICS

Anticholinergics and antihistamines are present in many OTC medications such as sedatives, sleep aids, cold preparations, antiarrhythmals and nasal decongestants.¹⁶ They often inhibit glandular secretions in a dose-dependent manner. Ocular effects include dry eye, mydriasis and decreased pupil response to bright light.

Atropine and related drugs are included in this category. Scopolamine patches contain an antiemetic used to prevent motion sickness, and are frequently dispensed on cruise lines. Passengers may directly contaminate their eyes after applying the transdermal patch. This leads to anisocoria or mydriasis. Practitioners can easily rule out any neurological association like a third nerve palsy because there is no extraocular palsy and the dilated pupil will not constrict to 1% Pilocarpine.

DERMATOLOGIC AGENTS

Dermatologists prescribe isotretinoin (Accutane) to treat acne. This systemic medication is a Vitamin A analog and frequently causes blepharoconjunctivitis.⁹ Decreased meibomian gland function and contact lens intolerance result from its use. Since meibomian glands are modified sebaceous glands, suppression of these glands by Accutane causes deficiency of the normal lipid layer in the tear film. Along with artificial tears, treatment includes decreasing the dosage or discontinuing the medication. Other reversible side effects include keratitis, corneal neovascularization, pseudotumor cerebri, optic neuritis, night blindness and retinotoxicity.¹

ANTIINFECTIVES

Sulfonamides

Sulfacetamides are effective against gram-positive and gram-negative organisms. Conjunctivitis and optic neuritis are rare, but myopic shifts commonly occur. Symptoms resolve within days to weeks of dose reduction or cessation. The mechanism for myopic shifting is similar to anticholinergic effects where the ciliary body becomes edematous, resulting in thickening and anterior movement of the lens. A major hypersensitivity reaction to systemic and topically administered

sulfonamide drugs is Stevens-Johnson syndrome.⁸

Tetracyclines

Tetracycline is also an effective bacteriostatic drug against gram-positive and gram-negative organisms. Sometimes, the periorbital area becomes hyperpigmented and dark deposits may occur in the palpebral conjunctiva. Tetracycline and its derivative, minocycline, can also cause pseudotumor cerebri with extraocular muscle paresis especially in children.⁸ Symptoms usually develop between 12 hours and four days after beginning therapy. After discontinuing the drug, these symptoms regress. Other reported side effects include transient myopia, decreased vision, photophobia and diplopia.

Antimalarials

In addition to malaria, these drugs are used to treat rheumatoid arthritis and lupus. The optimal dosage is 3.5-4.0 mg/kg/day for chloroquine (Aralen) and 6.0-6.5 mg/kg/day for hydroxychloroquine (Plaquenil).⁷ Chloroquine tends to be more toxic than hydroxychloroquine. The risk of irreversible retinal damage is dose-dependent. The likelihood increases when the total cumulative dose exceeds 300g.⁸ Toxic macular changes have been well documented. This bull's-eye maculopathy starts as fine pigmentary mottling within the macular area, with or without the loss of the foveal reflex. The end result can range from reduced vision to possible blindness. Differentials include retinitis pigmentosa and age-related macular degeneration. The pigmented tissues of the eye continue to hold the drug for a prolonged period after the drug has been discontinued according to the melanin binding theory. This leads to degenerative changes in the RPE. Neurosensory retina has also been shown to bind the drug.

Transient and reversible corneal changes occur typically when the patient receives more than 250 mg daily.⁸ Whorl-like pigment deposits within the corneal epithelium can occur from reversible binding of the drug to intracellular nucleoproteins in the corneal epithelium.⁷

In addition to the macular changes, optic nerve pallor, cycloplegia and ptosis can occur. A baseline exam should be performed before the patient starts treatment. Amsler grid to detect paracentral

scotomas, color vision, contrast sensitivity and central red-white visual field can be used to follow the patient for changes.⁷ Fundus photos are excellent for documentation and useful for detecting subtle changes in pigmentation.

Antitubercular

Isoniazid (INH) is used to treat mycobacterial diseases like tuberculosis.⁶ It is less toxic than other drugs such as ethambutol, and INH is now considered the drug of choice. Patients with renal insufficiency, or impaired ability to excrete the drug, may be at greater risk for developing ocular toxicity. An uncommon but serious complication of antitubercular drug therapy is acquired optic neuropathy.⁶ Both INH and ethambutol can cause retrobulbar optic neuritis, but most cases were reversible with INH only.¹⁷

ERECTILE DYSFUNCTION

Sildenafil (Viagra) is a new oral medication to treat males with erectile dysfunction. It inhibits phosphodiesterase-5 (PDE-5) which results in vasodilation of smooth muscle.¹⁸ Visual disturbances are a common side effect of this medication. Viagra blocks hyperpolarization of photoreceptors.⁷ Eleven percent of patients on 100mg perceived a blue haze up to four hours after administration. This may cause difficulty in distinguishing between blue and green. Since pilots and aviators need to see blue runway lights, they should be cautioned for safety. The Federal Aviation Administration has recommended that pilots not fly within six hours of taking the drug.¹⁸ Caution should also be used in patients with retinitis pigmentosa due to the uncertainty about long-term retinal damage.

SUMMARY

A careful and detailed case history is important to reveal a patient's medication history. The ocular and visual side effects from a patient's systemic medication can range from mild to severe. These side effects may or may not be serious enough to warrant discontinuing treatment. Recognition of ocular and visual side effects is important for prompt management to prevent and minimize serious complications. Familiarity with medications improves by routinely paying attention to concomitant medications. While these considerations should be in the minds of all optometrists,

they are particularly important for those who are increasingly called upon to diagnose and treat the functional visual problems of at risk populations.

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Appendix A. Common Systemic Medications and Uses

ANTI-HYPERTENSIVES

Ace inhibitor

CAPOTEN	captopril
VASOTEC	enalapril
ZESTRIL	lisinopril

Alpha agonist

ALDOMET	methyldopa
CATAPRES	clonidine
MINIPRESS	prazosin

Bblockers

COGARD	nadolol
INDERAL	propranolol
LOPRESSOR	metoprolol
TENORMIN	atenolol

CHF

Thiazides/Diuretics

HCTZ	hydrochlorothiazide
LASIX	furosemide

ANTI-ANGINAL

Antiarrhythmia

CORDARONE	amiodarone
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Ca++Channel Blocker

CALAN	verapamil
NORVASC	amlodipine
PROCARDIA	nifedipine

Vasodilators

ISOSORDIL	isosorbide
LONITEN	minoxidil

Nitroglycerin

NITROBID	nitroglycerin
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CHF / ARRHYTHMIA

Cardiac Glycosides

DIGOXIN	digitalis
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CHOLESTEROL

MEVACOR	lovastatin
ZOCOR	simvastatin
NIACOR	niacin (B3)

DIABETES

Sulfonylureas

DYMEJOR	acetohexamide
DIABINESE	chlorpropamide
GLUCOTROL	glipizide
MICRONASE	glyburide
GLUCOPHAGE	metformin
TOLINASE	tolazamide
ORINASE	tolbutamide

Insulin

HUMULIN
NOVOLIN

ORAL CONTRACEPTIVES

DEMULEN
LOESTRIN
LO-OVRAL
MODICON
NORDETTE
NORINYL
ORTHO-NOVUM
ORTHO-TRICYCLEN
OVCON
OVRAL

THYROID HORMONE

SYNTHROID	levothyroxine
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ESTROGEN HORMONE

ESTRADERM	estradiol
PREMARIN	estrogen

ANTI-PSYCHOTICS

Phenothiazines

MELLARIL	thioridazine
THORAZINE	chlorpromazine
STELLAZINE	trifluoperazine

Manic Depressives

HALDOL	haloperidol
CIBALITH-S	lithium
ESKALITH	
LITHIONATE	

ANTI-ANXIETY

ATIVAN	lorazepam
HALCION	triazolam
LIBRIUM	chlordiazepoxide
KLONOPIN	clonazepam
VALIUM	diazepam
VERSED	midazolam
XANAX	alprazolam

ANTI-DEPRESSANTS

Heterocyclics

EFFEXOR	venlafaxine
DESYREL	trazodone

Tricyclics

ELAVIL	amitriptyline
ADAPIN	doxepin
SINEQUAN	
PAMELOR	nortriptyline
AVENTYL	

Serotonin inhibitor

PROZAC	fluoxetine
ZOLOFT	sertraline

BARBITURATES

AMYTAL	amobarbital
BUTISOL	butabarbital
SECONAL	secobarbital

ANTI-CONVULSANTS

DILANTIN	phenytoin
TEGRETOL	carbamazepine

CNS STIMULANT

RITALIN
methylphenidate

ANTI-MIGRAINE

Serotonin agonist

IMITREX	sumatriptan
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ANTI-ULCER

PEPCID	famotidine
AXID	nizatidine
PRILOSEC	omeprazole
CARAFATE	sucralfate

ANTI-COAGULANTS

Coumadin derived

COUMADIN (po)
HEPARIN (iv)
PANWARFIN (po)

Platelet inhibitor

PLAVIX	clopidogrel
TICLID	ticlopidine

ANALGESICS

ASPIRIN	salicylate
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CORTICOSTEROIDS

Systemic

DECADRON	dexamethasone
DELTAONE	prednisone

Inhalers

NASALIDE	flunisolide
VANCENASE	beclomethasone

NSAIDS

ADVIL	ibuprofen
INDOCIN	indomethacin
ORUDIS	ketoprofen
ALEVE	naproxen

ARTHRITIS

RIDAURA	auranofin
CELEBREX	celecoxib
VIOXX	refecoxib

ALLERGY

BENADRYL	diphenhydramine
CHLORTRIMETON	chlorpheniramine

ANTI-CHOLINERGIC

TRANSDERM SCOP	scopolamine
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DERMATOLOGICS

AC CUTANE	isoretinoin
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ANTI-TUBERCULAR

LANIAZID	isoniazid
MYAMBUTOL	ethambutol
RIFATER	rifampin

ERECTILE DYSFUNCTION

VIAGRA	sildenafil
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Appendix B. Summary of the Ocular

CARDIOVASCULAR	TEARS	LIDS/CONJ	EOMS	CORNEA	PUPIL	ACCOM
BBlockers	Dry Eye		Diplopia			
Diuretics	Dry Eye					Myopia
Amiodarone	Dry Eye		Nystagmus	Whorl-like deposits		
Nitroglycerin						
Digoxin			Diplopia	Edema	Mydriasis	
HYPERLIPIDEMICS						
Niacin	Dry Eye	Edema	Diplopia			
HYPERGLYCEMICS						
			Paresis,Diplopia			
HORMONES						
Thyroid replacement		Hyperemia				
Oral Contraceptives	Dry Eye		Diplopia		Mydriasis	
Estrogen replacement	CL intol					
CNS						
Phenothiazines (chlorpromazine)	Dry Eye	Blue conj	Diplopia	Endothelial pigment	Mydriasis	Cycloplegia
Manic-depressives (lithium)	CL intol		Jerk nystagmus Diplopia			Decr accom
Antianxiety	Dry Eye	Allergic CJ	Diplopia		Mydriasis	Decr accom
Antidepressants (TCAs)	Dry Eye		Diplopia			Cycloplegia
Barbiturates		Ptosis	Nystagmus		Mydriasis	
Anticonvulsants		Chronic CJ	Nystagmus		Mydriasis	
CNS stimulant (Ritalin)					Mydriasis	Decr accom
ANTIULCER		Hyperemia,CJ				Decr accom
ANTICOAGULANTS						
ANALGESICS		Allergic CJ	Nystagmus	Exacerbates HSK	Mydriasis	
CORTICOSTEROIDS		Blue conj	Diplopia	Stromal opacities	Mydriasis	
NSAIDS	Dry Eye		Diplopia			
ANTIRHEUMATIC						
Gold salts		Gold deposits	Nystagmus	Chrysiasis		
Cox 2 inhibitors						
ANTIHISTAMINES	Dry Eye		Nystagmus		Mydriasis	Decr accom
DERMATOLOGIC (isoretinoin)	Dry Eye	Blepharo CJ		Keratitis, Deposits, Neovascularization		Myopia
ANTI-INFECTIVES						
Sulfonamides		CJ, Edema				Myopia
Tetracyclines		Dark deposits	Paresis,Diplopia			
Antimalarials		Ptosis	Nystagmus	Whorl-like deposits		Cycloplegia
Antitubercular (ethambutol)			Diplopia		Mydriasis	
Antiviral (acyclovir)						
OTHER						
Viagra						

and Visual Side Effects of Drugs

LENS	IOP	RETINA	COLOR	ON	Other
	Decr IOP				Visual hallucinations
			Color change		
ASC			Color change	Optic neuropathy	Halos, Blurred vision, Photophobia
					Yellow/Blue halos
	Decr IOP		Yellowing		Flickering vision
		CME			Blurred vision
				Optic neuritis	
				PTC	Visual hallucinations
		Macular edema, Vascular occlusions		PTC	
ASC	Incr IOP	RPE changes			Blurred vision
					Blurred vision
		Retinal hemes			Blurred vision
	Incr IOP				
			Color change		Glare
Cat				Color change	Blurred vision
					Visual hallucinations, Blurred vision
			Color change		Spontaneous AC hyphema
		Retinal hemes			
		Retinal hemes		Yellowing	Iris microcysts
PSC	Incr IOP	Retinopathy	Color change	PTC	VAVF loss, Blurred vision
		RPE changes	Color change	Optic neuritis	
ASC		Ret hemes			Blurred vision
					Blurred vision
	Incr IOP	Ret hemes			
Cat		Night blindness / retinotoxicity		PTC / Optic neuritis	
		Ret hemes		Optic neuritis	
		Ret hemes		PTC	
		Toxic maculopathy	Color change	Optic atrophy	
			Color change	Retrobulbar Optic neuritis	
					Visual hallucinations
					Blue haze