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The Eyes Have It! Update on Common Conditions Affecting the Eye

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LEARNING OBJECTIVES

Upon completion of this module, the subscriber will be able to:

1. Identify the parts of the eye and the function of each part.
2. Summarize various eye disorders including ocular hypertension, glaucoma, infections, dry eyes, conjunctivitis, age-related macular degeneration, macular edema following retinal vein occlusion, and diabetic macular edema.
3. Discuss brand/generic substitutions, possible side effects, and proper administration of ophthalmic medications.
4. Describe the roles of various ophthalmic agents including those used to treat the following conditions: ocular hypertension, glaucoma, infections, dry eyes, conjunctivitis, age-related macular degeneration, macular edema following retinal vein occlusion, and diabetic macular edema.
5. Classify the available over-the-counter medications available to treat ocular disorders.

ACCREDITATION

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Dr. Evoy's clinical practice largely consists of diabetes management, smoking cessation, obesity, and metabolic syndrome. His research interests are diverse, but have focused on smoking cessation, prescription drug abuse and MRSA infections most recently.

The Eyes Have It! Update on Common Conditions Affecting the Eye

Introduction and Anatomy of the Eye

The eye is a small, yet complex organ.[1]

Approximately 1-inch wide, the eyeball is housed within a socket, a hollow area formed by two bones that are lined with fat.[1] This socket serves to protect the eyeball. Six muscles allow the eyeball to move.[1] The term ocular refers to something relating to the eyes, so these are known as ocular muscles. **Figure 1** provides a picture of the ocular muscles.

The outer coat of the eye is made up of the sclera, conjunctiva, and cornea (**Figure 2**). The sclera is the white of the eye.[1] The conjunctiva is a thin mucous membrane that covers the outside of the sclera and lines eyelids. Inflammation of blood vessels inside the conjunctiva is known as conjunctivitis (commonly called pinkeye). The cornea is a clear layer with no blood vessels that protects the front of the eye and focuses light rays on the retina.

Figure 1. Muscles of the Human Eye

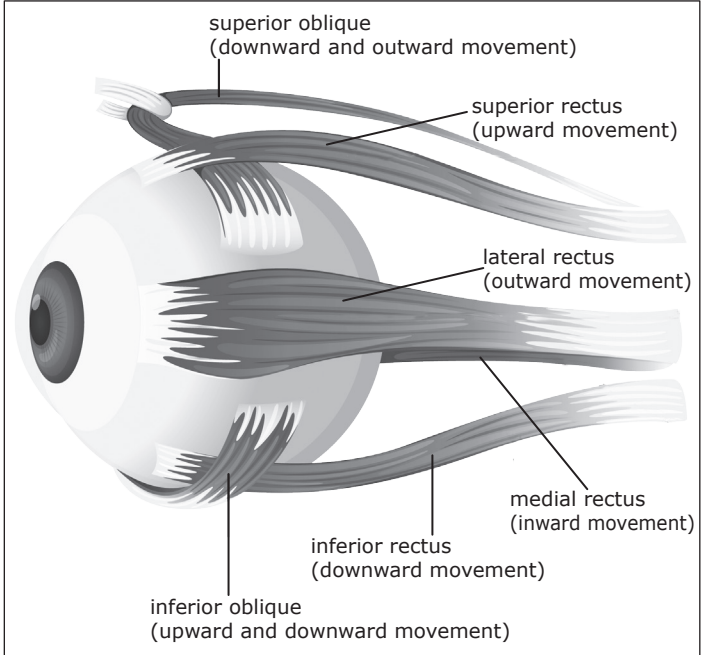
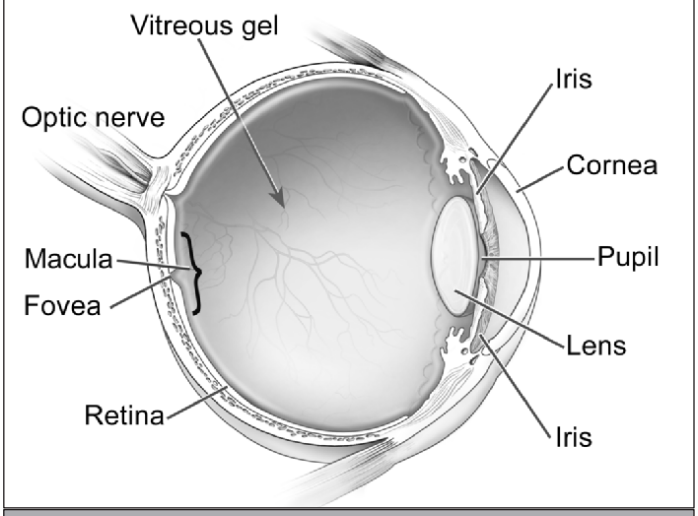


Figure 2. Parts of the Eye



The cornea has a high concentration of nerve fibers that make it very sensitive to touch or anything that might enter the eye such as small particles of dust.

Together, the iris, choroid, and ciliary body make up the uveal tract.[1] The iris is the colored part of the eye. It is a circular membrane between the cornea and the lens. In the center of the iris is the black circle called the pupil. The pupil allows light to enter the eye. The iris controls the amount of light that enters the eye by increasing or decreasing the size of the pupil. In bright light, the pupil constricts, while in dim light the pupil dilates, enabling the right amount of light to enter the eye making vision clear.

The lens of the eye is a transparent structure suspended behind the iris. The lens focuses light onto the retina by changing its shape, as necessary, assuring a clear visual image is provided to the retina.[1] Cataracts are changes in the lens of the eye. The lens becomes progressively opaque (i.e., cloudy), reducing the clarity of vision. Cataract surgery in most cases involves the removal of the content of the capsule (natural lens of the eye) and implanting an intraocular lens (an artificial lens).

The choroid is located between the sclera and retina.[1] The

choroid contains blood vessels that provide nutrients to the retina. The ciliary body is connected to the sclera. A part of the ciliary body secretes aqueous humor, a clear liquid that nourishes the front part of the inner eye.

There are two main compartments in the eye called chambers. The anterior (meaning front) chamber is formed by the inner side of the cornea on the front and the iris in the back.[1] The posterior (meaning back) chamber is behind the iris and in front of the lens and the retina.[1] The aqueous humor is formed in the posterior chamber and flows through the pupil to the front of the eye before it drains from the eye. This drainage occurs through channels known as the trabecular meshwork.[1]

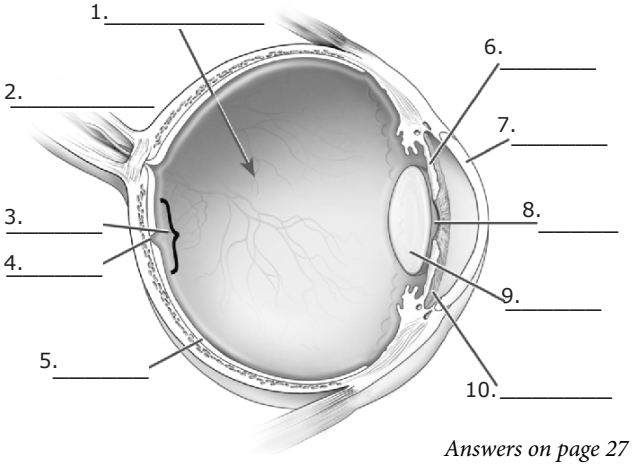
The largest chamber of the eye lies between the back of the lens and the retina. This is called the vitreous chamber.[1] The vitreous is a clear gel that fills the space between the lens and the retina.

The inner portion of the eye contains the retina with the optic nerve. The retina is a light-sensitive tissue at the back of the eye. The retina contains receptors that receive light through the lens and convert it to neural signals that are sent to the brain to form visual images.[1]

The optic nerve is a bundle of more than one million nerve fibers which send these signals from the retina to the brain.[1] See **Figure 2** (on page 3) for a visual description of the parts of the eye discussed above.

Test Your Knowledge #1

Label the Parts of the Eye.



Answers on page 27

The eyelids and eyelashes help protect the eye.[1] Both the eyelids and the eyelashes protect the eye from things like dust and foreign debris. The eyelids also contain various sebaceous (oil/fat secreting) and sweat glands that contribute to the layers of tear film (aqueous, or watery layer and lipid, or fatty layer).

The nerves of the eye are part of the autonomic nervous system. It has two divisions, sympathetic and parasympathetic. Parasympathetic signals cause the pupil to constrict (meaning narrow). When the pupil narrows it is called miosis. Sympathetic signals have the opposite effect. They cause the pupil to dilate (meaning expand). When the pupil expands it is called mydriasis. This is important because some eye medications act through these systems and cause the pupil to narrow or expand.

Ophthalmic Dosage Forms and Medication Administration

Ophthalmic medications are drugs administered into the eye. Ophthalmic drug dosage forms include ointments, gels, solutions, and suspensions. Common sense might suggest the ointment dosage form, which has a similar consistency to petroleum jelly, would be preferred, as it would lengthen the amount of time the product is in contact with the eye. However, many medications are not effectively released from the ophthalmic ointments, so not enough of the drug reaches the eye to achieve the desired therapeutic response.[2] Gels contain large molecules that attach to the eye to extend the contact time with the eye and increase the availability of medications to the eye. Additionally, dosage forms like ointments or gels may temporarily blur the patient's vision because of their thick consistency, which may aggravate patients. Applying these medications before bed may increase their tolerability, as the patient will not notice the blurred vision. Suspensions are a liquid dosage form with solid drug particles dispersed throughout the liquid. Suspensions are preferred products because the drug particles within suspensions have increased time in contact with the eye that leads to a longer-lasting effect than solution. The pH of tears is neutral (7.4). Accordingly, neutral pH is optimal for eye drops. However, tears can buffer products instilled into the eye, so the eye can tolerate products with a pH range from 4.5 to 11.5.[3]

Patients frequently complain of pain associated with

the administration of eye medications. This is because the cornea contains a high concentration of nerve fibers. If patients complain of pain associated with the administration of eye medications, they should be encouraged to look away from the dropper tip, either to the right or the left. The goal is to instill the drop onto the "white" of the eye versus the cornea. On the other hand, patients who indicate they cannot tell if their drops have been instilled should be directed to look at the dropper tip which will make it more likely that the patient feels the drop. If this approach is unsuccessful, solution eye drops can also be refrigerated. The cool temperature assists patients in knowing the medication has been administered successfully into the eye.

Frequently prescriptions are written for two drops of medication to be administered at the prescribed time interval (e.g., once or twice daily). Tear (also called lacrimal) volume is 6-10 microliters. The eye can hold up to 30 microliters but typical drop volume is 40-70 microliters. In essence the volume of one drop is more than the eye can hold, which results in medication running down the cheek after administration. Placing two drops simultaneously will achieve no added benefit since the eye cannot absorb that much liquid at one time. If two drops of medication are prescribed, patients should be instructed to separate the drops by at least five minutes.

Figure 3. How To Dispense Eye Drops

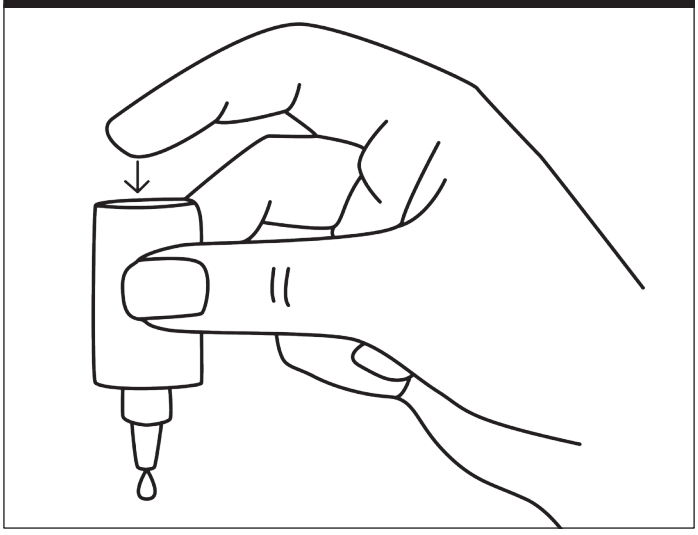
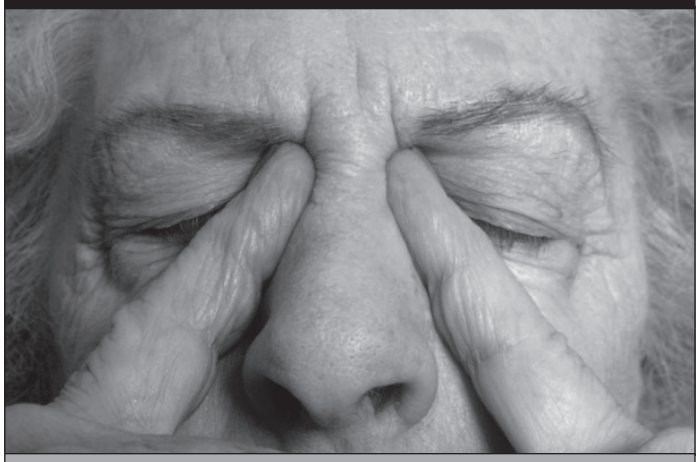


Figure 4. Punctal Occlusion



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In addition to factors influencing the amount of medication remaining in contact with the eye, patients are often frustrated by squeezing too much medication from the dropper bottle and "wasting" medicine. To avoid this, patients should be instructed to hold the neck of the bottle between their thumb and middle finger and their index finger on the bottom of the bottle. Use the index finger to lightly depress the bottom of the bottle to release one drop into the eye, as shown in **Figure 3**.

Ophthalmic medications may drain through a passage way in the corner of the eye called the nasolacrimal duct. If this occurs, the drug may be absorbed into the systemic circulation (i.e., distributed throughout the body via the blood stream) instead of only being absorbed locally (i.e., in the eye). For some medications (e.g., phenylephrine), systemic absorption can result in side effects such as an increase in blood pressure or heart rate. In order to reduce systemic absorption of ophthalmic medications, patients should be instructed to place their finger over the corner of their eye for 1-2 minutes following medication administration. This process is known as punctal occlusion. **Figure 4** shows an example of punctal occlusion. **Table 1** (on page 6) provides an overview of helpful patient tips on ophthalmic drop administration.

Table 1. Helpful Patient Tips

IF PATIENT…	ADVISE PATIENT TO…
complains of blurred vision	apply ointment or gel before bedtime to minimize noticing the blurred vision
complains of pain when administering eye drops	look away from the dropper tip, either to the right or the left, to instill the drop on the "white" of the eye
cannot tell if drops have been instilled	look at the dropper tip to increase the likelihood of feeling the drop OR refrigerate the eye drop bottle, so they can feel the cool temperature when administering (do not freeze suspensions)
has prescription for two drops of medication to be administered	separate drops by at least five minutes
often "wastes" medication by squeezing too much from the dropper bottle	hold the bottle using their thumb and middle finger and lightly depress the bottom of the bottle to release one drop

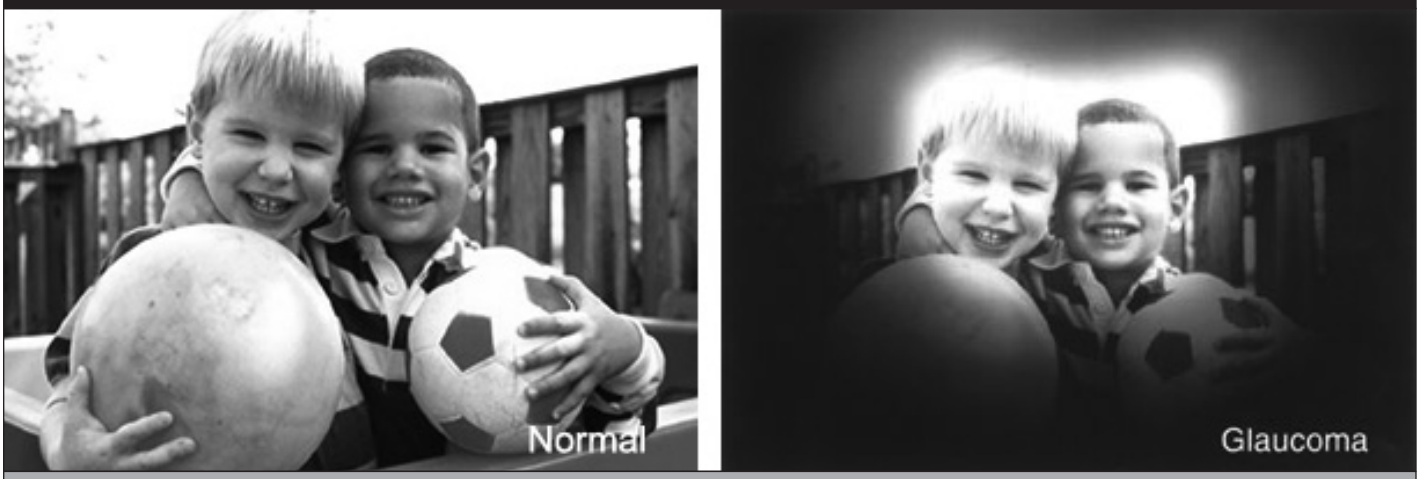
Ophthalmic Medications for Disorders of the Eye

Glaucoma/Ocular Hypertension

Glaucoma is the most common eye disorder, and a leading cause of irreversible blindness worldwide. The estimated number of cases worldwide is 60 million, and is expected to increase to 76 million in 2020 and 111 million in 2040.[4] In the United States (US), an estimated three million Americans are living with glaucoma but only half know they have it. Glaucoma is a nonspecific term used for a group of diseases that can irreversibly damage the optic nerve. This damage to the optic nerve can lead to vision loss. Increased pressure in the eye (called intraocular pressure or IOP) is the most common risk factor for the development of glaucoma. Generally, the higher the IOP, the greater the risk for developing glaucoma. Increasing age, African American race, and family history are risk factors for glaucoma.[1]

As mentioned previously, the ciliary body of the eye produces aqueous humor. The production and flow of aqueous humor from the posterior to the anterior chamber creates the IOP of the eye. IOP is measured by a test known as tonometry. Tonometry involves flattening a small central area of the cornea with air or a small plastic

Figure 5. Field of Vision with Glaucoma



Courtesy: National Eye Institute, National Institutes of Health (NEI/NIH). Available at: https://nei.nih.gov/health/examples/

cone. Generally, an IOP of 10-20 mmHg is considered normal. IOP consistently higher than 22 mmHg should cause suspicion of glaucoma. Increased IOP puts pressure on the optic nerve in the back of the eye. This increased pressure results in vision loss, beginning with a reduction in peripheral (side) vision. (**Figure 5** on page 6) A definite diagnosis of glaucoma cannot be made based on increased IOP alone, as there must be evidence of vision loss .[5]

A condition called ocular hypertension has been defined as an IOP exceeding 21 mmHg, without evidence of vision loss. Similar medications may be used to treat both ocular hypertension and glaucoma.

Open-Angle Glaucoma

Primary open-angle glaucoma (POAG) occurs in approximately 2% of people older than 40 years of age in the US.[1,2] Patients with POAG have less aqueous humor flowing out of the anterior chamber of the eye which results in a buildup of aqueous humor and a higher IOP. POAG occurs due to damage of the drainage canals comprising the trabecular meshwork.

POAG usually develops gradually and the condition is asymptomatic (without symptoms) initially. The best way to detect early loss of vision is through a visual field test. **Figure 6** depicts a visual field test, used to determine loss of peripheral vision.

Patients place their chin on a rest and look into a half-globe. They are instructed to press a button when they can see a beam of light within the globe. Visual field changes occur due to changes in the optic disc, allowing for the differentiation of glaucoma versus ocular hypertension. Patients with normal visual fields and an IOP of 24mmHg or higher have a 10% likelihood of developing glaucoma within five years.[5]

Figure 6. Visual Field Test

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Angle Closure Glaucoma

A second type of glaucoma is known as angle-closure glaucoma. Angle-closure glaucoma accounts for about 10% of all glaucoma cases. This condition occurs due to physical blockage of the channels that allow aqueous humor to exit the eye.[1]

Angle-closure glaucoma is a medical emergency. Symptoms include blurry vision or sudden vision loss. There also may be the appearance of haloes around lights and pain that is often severe. Medications are generally used to treat angle-closure glaucoma, although surgical procedures may be needed to manage the condition.

Table 2 (on page 8) provides a summary of eye conditions associated with increased intraocular pressure.

Treatment of Glaucoma And Ocular Hypertension

There are various therapeutic agents used for the treatment of POAG or ocular hypertension. First-line agents generally include beta-adrenergic blockers (commonly referred to as beta-blockers) or prostaglandin analogues. An overview of treatment options is included in **Table 3** (on page 10).

Beta-Adrenergic Blockers

Ophthalmic beta-adrenergic blockers reduce the production of aqueous humor. Beta-blockers have been associated with a 20% to 35% reduction in IOP.[6-14] Most agents, except betaxolol, block beta 1- and beta 2-adrenergic receptors (non-selective). Betaxolol is a selective beta 1-adrenergic blocker. Beta 1 adrenergic receptors are primarily in the heart and beta 2 adrenergic receptors are primarily in the lungs. As a result, betaxolol may result in less adverse effects on lung function than non-selective beta-adrenergic blockers in patients with lung disease.

Timolol (Timoptic)

Timolol was the first commercially marketed beta-adrenergic blocker and is often considered the gold standard against which other medications are compared for safety and efficacy. Timolol is available in concentrations of 0.25% and 0.5%. Timolol is usually administered twice daily.

Timolol has been associated with a reduction of resting heart rate (by about 5-10 beats/minute), worsening of heart failure, and shortness of breath.[15,16] Therefore, timolol should be used with caution in patients with a slow resting heart rate or lung disease.

Timoptic XE is a unique gel-forming solution administered once daily. It is similar in effect to twice daily administration of timolol.[17]

Levobunolol (Betagan)

Levobunolol is approved for either once or twice daily administration. Levobunolol 0.5% and 1% are comparable to timolol in lowering IOP. The rates of adverse reactions, including decreases in heart rate, are also similar to that for timolol.[7,18]

Metipranolol (OptiPranolol)

Metipranolol 0.1% to 0.6%, is comparable to timolol 0.25% to 0.5% in reducing IOP.[8,9] Metipranolol is more likely to cause stinging or burning on administration and has been associated with a condition known as granulomatous anterior uveitis (painful inflammation of the eye).[19,20] As a result of these side effects, metipranolol is used less often than other beta-adrenergic blockers.

Carteolol (Ocupress)

Carteolol, is a unique beta-adrenergic blocking agent that theoretically should have less negative impact on lung and heart function. However, no clinical differences have been seen when the lung and heart function effects of carteolol were compared with those of timolol. Carteolol 1% and timolol 0.25% administered twice daily are equally effective in reducing IOP.[11-13]

Betaxolol (Betoptic)

As previously noted, betaxolol is a selective beta 1-adrenergic blocker. Betaxolol is slightly less effective than timolol in IOP reduction, and more patients tend to need additional medications along with betaxolol than with other beta-adrenergic blockers.[21-24]

Prostaglandin Analogs

Prostaglandins are fatty acids involved in numerous body functions. Latanoprost (Xalatan), travoprost (Travatan Z), bimatoprost (Lumigan), and tafluprost (Zioptan) are all prostaglandin analogs, meaning they behave like prostaglandins in the body. Tafluprost is a preservative-free formulation supplied in single-use containers.[25] The prostaglandin analogs (PGAs) often are prescribed as first-line agents for the treatment of POAG because they are at least as effective as the beta-blockers, can be

Table 2. Summary of Glaucoma and Ocular Hypertension

CONDITION	NOTES
Glaucoma	Diagnosis includes: • IOP consistently higher than 22mmHg • WITH evidence of vision loss
Primary Open-Angle Glaucoma (POAG)	• Caused by degeneration of drainage canals, resulting in higher IOP • Develops gradually and is asymptomatic • Visual field test used to detect early vision loss
Angle-Closure Glaucoma	• Caused by physical blockage of channels allowing aqueous humor to exit the eye • Medical emergency • Symptoms: blurry vision, sudden vision loss, haloes around lights, severe pain
Ocular Hypertension	Diagnosis includes: • IOP exceeding 21 mmHg • WITHOUT evidence of vision loss

administered once a day, and are not associated with many systemic (whole body) adverse effects.

Latanoprost (Xalatan)

Latanoprost is approved for the initial treatment of POAG or ocular hypertension.[26] When administered once daily, latanoprost is at least as effective as timolol in decreasing IOP. When the effectiveness of latanoprost 0.005% once daily was compared with timolol 0.5% twice daily, the IOP-lowering effects of latanoprost were superior to those of timolol.[27,28] Latanoprost should be dosed once daily in the evening. The IOP-lowering effects of latanoprost might actually be reduced when the drug is administered more frequently.

Systemic side effects are minimal with latanoprost, but local reactions (e.g., iris pigmentation [change in eye color]; eyelid skin darkening; eyelash lengthening) are relatively common. Latanoprost can gradually increase the amount of brown pigment in the iris. This pigment change occurs in 7% to 22% of patients and is most noticeable in those with green-brown, blue/gray-brown, or yellow-brown eyes.[26] The onset of increased iris pigmentation usually is noticeable within the first year of treatment and can be permanent. The nature and severity of adverse events are not affected by the increased pigmentation of the iris.

Latanoprost can be used with other classes of IOP-reducing medications. Latanoprost has additive effects when administered with beta-blockers (e.g., timolol), carbonic-anhydrase inhibitors (e.g., dorzolamide), and alpha 2-adrenergic agonists (e.g., brimonidine, apraclonidine). Latanoprost is a good ophthalmic agent to add for patients who are unable to lower their IOP enough with single-agent therapy. The effectiveness of latanoprost when used once a day alone or in addition to other IOP-lowering drugs and its low risk of side effects make it one of the most common, if not the most common, treatment option for POAG and ocular hypertension.[27-32]

Unopened bottles of latanoprost should be stored in the refrigerator. Opened bottles may be stored at room temperature for up to six weeks.[26]

Travoprost (Travatan Z)

Travoprost (Travatan Z) is suggested for use in patients who cannot tolerate or fail to respond to other agents. However, travoprost is used as a first-line agent in clinical practice because it is more effective than timolol and at least as effective as latanoprost.[33] Travoprost appears to be slightly more effective in African American patients.[34]

The side-effect profile of travoprost is similar to that for latanoprost, including increased iris pigmentation and eyelash changes.[33-35] Eye irritation may be less with travoprost because it is free of the preservative benzalkonium chloride (BAK), though it is not completely preservative free.

Bimatoprost (Lumigan)

Bimatoprost is another prostaglandin analogue used as first-line therapy. Bimatoprost administered once or twice daily has been shown more effective than timolol twice daily. Once daily bimatoprost has also been shown more effective than latanoprost once daily. Changes in iris pigmentation appear to occur at a lower rate in patients treated with bimatoprost than those treated with latanoprost (1% versus 7%). The overall side effect profile of bimatoprost appears to be similar to that for latanoprost and travoprost.[36-38]

In addition to use for POAG or ocular hypertension, the FDA approved the cosmetic use of bimatoprost solution under the trade name Latisse. Latisse solution is applied with an applicator to the base of the upper eyelashes to produce eyelash lengthening, thickening, and darkening. Results are generally seen after 8 to 16 weeks of use.[39]

Tafluprost (Zioptan)

Tafluprost (Zioptan) is a preservative-free product used for the reduction of elevated IOP and ocular hypertension. Tafluprost once daily in the evening is as effective as latanoprost once daily in the evening and timolol 0.5% twice daily and has demonstrated additive efficacy when administered with tafluprost.[40-42] The fact that tafluprost does not include preservatives may make it more tolerable for patients who are sensitive to the preservatives found in other prostaglandin analogues. The adverse effect profile is similar to other PGAs.[40-44]

Unopened foil pouches of tafluprost should be stored in the refrigerator. Single-use containers may be stored in the opened foil pouch for 28 days at room temperature.[25]

Table 3. Common Topical Agents Used in the Treatment of Open-Angle Glaucoma[25, 26, 35, 38, 46, 49-51]			
GENERIC	STRENGTH	USUAL DOSAGE	COMMENTS
betaxolol (Betoptic [solution], Betoptic S [suspension])	0.25% (suspension) 0.5% (solution)	1 drop BID 1 drop BID	Shake suspension well before use. Twice daily dosage enhances compliance.
carteolol (Ocupress)	1%	1 drop BID	Effective with few side effects. Twice daily dosage enhances compliance.
levobunolol (Betagan)	0.25%, 0.5%	1 drop daily or BID	Effective with few ocular side effects. Once or twice daily dosage enhances compliance.
metipranolol (OptiPranolol)	0.3%	1 drop BID	Effective with few side effects. Twice daily dosage enhances compliance.
timolol (Timoptic, Betimol, Istalol)	0.25%, 0.5% 0.5% (Istalol) 0.25%, 0.5% preservative-free (Timoptic Ocudose)	1 drop BID 1 drop daily in morning (Istalol)	Effective with few ocular side effects. Twice daily dosage enhances compliance (except with Istalol).
timolol Gel Forming Solution (Timoptic XE, Timolol GFS)	0.25%, 0.5%	1 drop daily	Once-daily timolol formulation.
apraclonidine (Iopidine)	0.5%, 1%	1 drop preoperatively and postoperatively or 1 drop BID to TID	May be used pre-operatively and post-operatively for the prevention of increased IOP after laser surgery.
brimonidine (Alphagan)	0.15%, 0.2%	1 drop BID to TID	Effective long-term monotherapy or add-on therapy.
brimonidine (Alphagan P)	0.1%, 0.15%	1 drop BID to TID	Contains PURITE preservative. PURITE improves eye penetration and use of lower concentrations.
brinzolamide (Azopt)	1%	1 drop TID	Shake suspension well before use.
dorzolamide (Trusopt)	2%	1 drop TID	Effective long-term monotherapy or add-on therapy.
latanoprost (Xalatan)	0.005%	1 drop once a day at bedtime	May cause increased pigmentation of the iris and eyelid. Store unopened bottles in refrigerator. Opened bottles may be stored at room temperature up to 6 weeks.
travoprost (Travatan Z)	0.004%	1 drop once a day at bedtime	May cause increased pigmentation of the iris and eyelid. May be more effective than latanoprost.
bimatoprost (Lumigan)	0.01%, 0.03%	1 drop once a day at bedtime	May cause increased pigmentation of the iris and eyelid. May be more effective than latanoprost.
tafluprost (Zioptan)	0.0015% Preservative-free dropperette	1 drop once a day at bedtime	May cause increased pigmentation of the iris and eyelid. Store unopened foiled pouches in refrigerator. Single-use container may be stored in the opened foil pouch for 28 days at room temperature.
pilocarpine (Isopto Carpine)	1%, 2%, 4% 4% (gel/ointment)	1–2 drops TID or QID ½ inch in cul-de-sac daily at bedtime	Long-term proven effectiveness.
brimonidine tartrate 0.2%/timolol 0.5% (Combigan)	0.2%/0.5%	1 drop BID	Combination products may improve adherence.
dorzolamide 2%/timolol 0.5% (Cosopt)	2%/0.5% 2%/0.5% preservative-free (Cosopt PF)	1 drop BID	Combination products may improve adherence.
brinzolamide 1%/brimonidine 0.2% (Simbrinza)	1%/0.2%	1 drop TID	Shake suspension well before use. Combination products may improve adherence.
BID= twice daily; TID= three times a day; QID= four times a day; GFS= gel forming solution; IOP= intraocular pressure			

Alpha 2-Adrenergic Agonists

Apraclonidine (Iopidine) and brimonidine (Alphagan) are selective alpha 2-adrenergic agonists. These medications are similar to clonidine, which is used for reducing blood pressure. Apha 2-adrenergic agonists appear to lower IOP by decreasing the production of aqueous humor and by increasing aqueous outflow.[45]

Brimonidine is an alternative first-line agent in the treatment of POAG. It may also be used as add-on therapy if patients need more than one medication to reach their goal IOP. The 0.5% apraclonidine solution is indicated for short-term therapy in patients on maximally tolerated medical therapy, prior to surgical intervention.

Long-term IOP control should be monitored closely in patients taking alpha 2-adrenergic agonists because these drugs may lose their effectiveness after the patient has used the drug for an extended length of time (this is called tachyphylaxis). Common ocular side effects include burning, stinging, blurring, and an allergic-like reaction consisting of redness, itchiness and edema (swelling) of the eyelid and conjunctiva.[45,46]

Although ocular side effects are less common with brimonidine than with apraclonidine, side effects outside of the eye (e.g., dry nose and mouth, mild reduction in blood pressure, decreased pulse, and lethargy) are more common with brimonidine.[46] Alpha 2-adrenergic agonists should be used with caution in patients with heart disease, depression, and kidney or liver dysfunction.[45,46] Brimonidine (Alphagan P) is available with Purite as a preservative, which improves drug delivery into the eye, allowing use of a lower drug concentration.[46]

Topical Carbonic Anhydrase Inhibitors

Carbonic anhydrase is found in high concentrations in the ciliary body and retina of the eye. Carbonic anhydrase inhibitors (CAIs) lower IOP by decreasing the production of aqueous humor.

Although oral CAIs have been used for many years in the treatment of elevated IOPs, they have been replaced by the topical ophthalmic CAIs (i.e., eye drops) dorzolamide (Trusopt) and brinzolamide (Azopt), which are safer and better tolerated. Topical CAIs are excellent alternatives to beta-blockers in the initial management of elevated IOPs, and are effective as add-on agents. Brinzolamide 1% three times daily reduces IOP comparably to that achieved with dorzolamide 2% three times daily and to betaxolol 0.5% twice daily, but slightly less than timolol 0.5% twice daily. IOP is reduced by approximately 20%. Brinzolamide and dorzolamide are approved for three times daily dosing; however, twice daily dosing may be adequate. Dorzolamide provides additional IOP-lowering effects when added to existing beta-blocker therapy.[47,48] An ophthalmic solution containing a combination of dorzolamide hydrochloride and timolol maleate is marketed as Cosopt and a combination of brinzolamide and brimonidine is marketed as Simbrinza.[49]

The topical CAIs are well tolerated with few systemic side effects. The most common adverse effects reported with dorzolamide are burning, stinging, or discomfort of the eye, allergic reactions, and bitter taste. The bitter taste can be masked by chewing gum or sucking on hard candy. Brinzolamide causes less burning and stinging of the eyes than dorzolamide, because its pH is more neutral. Dorzolamide and brinzolamide are sulfa drugs that might cause allergic reactions in patients with a sulfa allergy. These drugs should not be used in patients with kidney or liver dysfunction.[50-52] Patients should be educated to tightly cap the bottle after each use, because the medication may crystallize on the tip of the dropper resulting in irritation of the eye after the medication is administered.

Cholinergic Agents

Pilocarpine (Isopto Carpine)

Pilocarpine historically was an initial treatment of choice, but with the introduction and widespread use of newer agents, pilocarpine has fallen out of favor. Pilocarpine increases the flow of aqueous humor out of the eye. It is routinely used in combination with beta-blockers or other agents in the short-term treatment of angle-closure glaucoma.

Combination Therapy

In general, drugs with different pharmacologic actions have at least partially additive effects in lowering IOP in the treatment of glaucoma. Drugs with similar pharmacologic actions (i.e., from the same pharmacologic class) should not be combined because adverse effects are more likely and only small increases in effectiveness are likely to be seen.

Timolol and other beta-adrenergic blocking drugs have additive IOP-lowering effects when used in combination with miotic agents, prostaglandin analogs, alpha 2-agonists, and CAIs. For example, the IOP-lowering effect is greater when timolol is used in combination with pilocarpine, dorzolamide, brimonidine, and travoprost.[34] Likewise, latanoprost has additive effects when administered with timolol, dorzolamide, and alpha2-adrenergic agonists.[28-32, 53-58] The trend toward the development of fixed-combination products offers many advantages in the treatment of POAG. These advantages include improved adherence (taking medications properly) because of a reduction in the number of dosages.

There are two beta-adrenergic blocker combination products currently on the market, timolol/dorzolamide (Cosopt) and brimonidine/timolol (Combigan). The IOP-lowering effects of timolol/dorzolamide (Cosopt) are comparable to or greater than those of latanoprost monotherapy (taken alone).[51] Brinzolamide and brimonidine are combined and available as Simbrinza.[49]

Hyperosmotic Agents

Hyperosmotic agents (**Table 4**) are used in the treatment of angle-closure glaucoma. These medications are given intravenously or orally and act by causing a reduction in total body fluid, including aqueous humor. [59]

Intravenously administered drugs provide a faster, somewhat greater effect than oral agents. Palatability (taste) may be a problem with oral agents and can be improved by serving these agents over crushed ice or with lemon juice or cola flavoring.

Orally, 50% glycerin is the usual drug of choice and is administered in dosages of 1 to 1.5 g/kg.[60] Isosorbide is an alternative, especially in diabetic patients because it is not metabolized (broken down) to provide calories.[61] Intravenously, mannitol is the drug of choice. It is administered in doses of 1 to 2 g/kg and is not metabolized to provide calories.

Primary side effects of hyperosmotic agents include headache, nausea, vomiting, increased urination, and dehydration. It is important that the patient not be allowed to drink because this will counteract the effects of these agents.

Corticosteroids

Corticosteroids (**Table 5**) are hormones produced naturally in the body or synthetically (man-made). While they are involved in various functions, the primary use of corticosteroids in eye disorders is to treat inflammation inside of the eye.

Corticosteroid preparations are divided into three classes: high, medium, and low potency. **Table 5** is a list of commercially available products in the US.

You will note some medications, e.g., prednisolone, are listed in high and intermediate potency categories. This is because the salt form as well as the concentration determine the potency. Acetate salts of fluorometholone and prednisolone have the greatest anti-inflammatory potency.[62-64] The most prescribed corticosteroid is prednisolone acetate 1%, based on its potency as well as the availability of generic alternatives reducing the cost to patients.

Patients who receive ophthalmic corticosteroid preparations should be counseled to shake suspension formulations prior to administration. All patients who receive ophthalmic corticosteroid products for periods of up to four weeks or longer should be instructed to have their IOP checked. This is because ophthalmic corticosteroids may increase intraocular pressure which could be problematic for patients with intraocular hypertension or glaucoma. About 5% of the population will experience an increase greater than 16 mmHg.

Table 4: Hyperosmotic Agents

GENERIC	MODE OF ADMINISTRATION	STRENGTH	DOSAGE
Mannitol	IV	5%, 10%, 15%, 20%	1–2 g/kg
Glycerin	PO	50%	1–1.5 g/kg
Isosorbide	PO	45%	1.5–2 g/kg

IV = intravenous; PO = by mouth

Remember, normal intraocular pressure is 10-20 mmHg. About 30% of the population will experience an increase between 6 and 15 mmHg, possibly posing a visual threat.[65-67] The balance of the population, about 65%, will experience an increase of less than 5 mmHg. Given there is no predictive test for the genetic predisposition toward increased intraocular pressure, checks are recommended for all patients.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Five ophthalmic nonsteroidal anti-inflammatory drugs (**NSAIDs, Table 6**) are currently available for use in the US: flurbiprofen, ketorolac, diclofenac, bromfenac, and nepafenac. These medications are approved for use in four categories: (1) pain and inflammation associated with cataract surgery; (2) pain associated with corneal surgery; (3) inhibition of pupil constriction during surgery; and (4) seasonal allergic conjunctivitis.[68-76] NSAIDs are also being evaluated for use in other conditions including macular edema (fluid collection in the retina causing vision to be less clear). **Table 6** (on page 15) contains information regarding the indications for use and doses of ophthalmic NSAIDs.

Common Eye Infections

Antibiotics

Sties (also known as hordeolum) are infections of the hair follicles or sebaceous (oil secreting) glands of the eyelids.[1] A stye is commonly caused by gram-positive bacteria that are found on the skin, including *Staphylococcus aureus*.[1] Initial treatment may include hot, moist compresses. Over-the-counter products should not be recommended because they are ineffective. An eye doctor (ophthalmologist, optometrist) should evaluate sties that do not respond to warm compresses within a few days. Treatment may need to include antibiotics effective against the organisms commonly causing the infection, such as sodium sulfacetamide.

Conjunctivitis (often called pink eye), a common external eye problem that involves inflammation of the conjunctiva, is usually associated with symptoms of a red eye.[1] There may sometimes be discharge from the eye that is either watery or pus-like. Other symptoms of conjunctivitis include itching, stinging, or a scratching sensation similar to what one would experience if sand

Table 5. Corticosteroids

GENERIC NAME/STRENGTH	TRADE NAME
High Potency	
fluorometholone acetate 0.1%	Flarex
prednisolone acetate 1%	Pred Forte
rimexolone 1%	Vexol
Intermediate Potency	
dexamethasone alcohol 0.1%	Maxidex
difluprednate 0.05%	Durezol
fluorometholone 0.1%	FML
fluorometholone 0.25%	FML Forte
loteprednol 0.2%	Lotemax
loteprednol 0.5%	Alrex
prednisolone acetate 0.12%	Pred Mild
prednisolone sodium phosphate 0.125%	Inflamase Mild
prednisolone sodium phosphate 1%	Inflamase Forte
Low Potency	
dexamethasone 0.05%	Decadron, Maxidex
dexamethasone 0.1%	Decadron, Maxidex
medrysone 1%	HMS

was blown into the eyes. Patients with pain or a reduction in vision should be referred to an eye doctor immediately, because these are symptoms of other more serious eye disease.

Conjunctivitis is most commonly caused by bacteria, viruses, or allergies. Most cases of bacterial conjunctivitis are caused by bacteria such as *Staphylococcus*, *aureus, Streptococcus pneumonia, Haemophilus influenzae* or *Moraxella catarrhalis*, although a number of other organisms may be responsible.[1] The infection usually starts in one eye and is spread to the other by the hands. It also may be spread to other persons, so it is important not to share towels or wash cloths and to seek treatment.

Broad-spectrum antibiotics (meaning the drugs are active against multiple different types of organisms) are frequently used to prevent eye infections that could occur during eye procedures. These medications are commonly administered just before and for a few days after certain

Test Your Knowledge #2
Identify the Prescription Error

You are a technician entering prescriptions into the computer at a community pharmacy. Identify the prescribing error in each of the following prescriptions.

John Smith, M.D.
111 1st Ave.
Nowhere, USA

Lic: A11111
DEA: AA1111111
NPI: 111111111

Name: Jane Doe DOB: June 25, 1950

Address: 222 2nd Ave. Nowhere, USA **Date:** June 25, 2017

Travoprost 0.004%
Instill 1 drop in both eyes three times daily for glaucoma
Dispense 1 bottle

Refills 5 Void After June 24, 2018

John Smith
Signature

John Smith, M.D.
111 1st Ave.
Nowhere, USA

Lic: A11111
DEA: AA1111111
NPI: 111111111

Name: Jane Doe DOB: June 25, 1950

Address: 222 2nd Ave. Nowhere, USA **Date:** June 25, 2017

Cosopt 2%/0.5% gel
Place 1 inch strip of gel into both eyes twice daily for glaucoma
Dispense 1 bottle

Refills 5 Void After June 24, 2018

John Smith
Signature

Answers on page 27

surgical procedures (e.g., cataract removal). **Table 7** (on page 17) contains commonly prescribed ophthalmic antibiotic preparations.

Some antibiotics are combined with corticosteroids to treat eye infections and reduce inflammation. Examples include Blephamide (sulfacetamide plus prednisolone) and Tobradex (tobramycin plus dexamethasone).

Macular Degeneration

Some eye conditions, such as age-related macular degeneration, macular edema following retinal vein occlusion, and diabetic macular edema, can lead to blurred vision and eventually blindness due to abnormally growing vessels in the eye which can become leaky.[77-83] In particular, wet age-related macular degeneration is the leading cause of blindness in Americans of European descent who are 55 years of age and older.[84] One cause of these conditions is increased levels of vascular endothelial growth factor (VEGF).

VEGF Inhibitors

Over the past decade, the development of several new drugs that block the actions of VEGF in the eye (known as VEGF inhibitors) has significantly improved our ability to treat these conditions. Interestingly, VEGF inhibitors are also effective in treating various types of cancer.[79] However, when used as a cancer treatment, the medications are administered intravenously so that they can work throughout the body. By injecting these medications into the eye, they only block VEGF in the eye and rarely produce side effects outside of the eye.

VEGF inhibitors are injected directly into the vitreous of the eye by an ophthalmologist. The injections are typically given once a month over the first few months but may be given less frequently after that (frequency needed to maintain vision improvement varies by patient), particularly if using aflibercept, which has a significantly longer half-life (i.e., how long it takes for half the drug to be eliminated after administration) than the other VEGF inhibitors available.[79-83,85] Other treatments that may be

Table 6. Nonsteroidal Anti-Inflammatory Agents[76]

OPHTHALMIC INDICATION	RECOMMENDED OPTIONS
Pain & inflammation associated with cataract surgery	diclofenac (Voltaren) 0.1% 4 times daily
	ketorolac 0.4% (Acular LS) 4 times daily
	bromfenac 0.09% (Bromday) once or 2 times daily
	ketorolac 0.45% (Acuvail) 2 times daily
	nepafenac 0.3% (Ilevro) once daily
	bromfenac 0.07% (Prolensa) once daily
Cost consideration:	diclofenac (Voltaren) 0.1% 4 times daily
	ketorolac 0.5% (Acular) 4 times daily
Adherence concerns:	bromfenac 0.09% (Bromday) once daily
	ketorolac 0.45% (Acuvail) 2 times daily
	nepafenac 0.3% (Ilevro) once daily
	bromfenac 0.07% (Prolensa) once daily
Pain associated with corneal refractive surgery	ketorolac 0.5% 4 times daily
Inhibition of intraoperative miosis	flurbiprofen 0.03%
	ketorolac 0.5%
Seasonal allergic conjunctivitis	diclofenac 0.1% 4 times daily

Test Your Knowledge #3

Patient Case: Mary

Mary is an 81-year-old African American woman who is seeing her optometrist for a routine eye exam. Before her appointment she fills out a questionnaire related to eye disorders. This questionnaire revealed the following information:

She is far-sighted and has worn glasses for approximately 50 years.

She had surgery to remove a cataract eight years ago.

Both her grandmother and grandfather on her father's side of the family suffered from glaucoma.

Her only medical condition is high cholesterol and she takes atorvastatin to treat this.

During the appointment, her optometrist finds that her vision has not worsened since her last visit but does note that she has ocular hypertension, with an intra-ocular pressure of 25 mmHg. She is referred to an ophthalmologist who diagnoses her with primary open-angle glaucoma.

Question 1: Based on this case, identify four risk factors for glaucoma exhibited by Mary.

1) _____
2) _____
3) _____
4) _____

Question 2: Mary's ophthalmologist decides to start her on a topical beta-blocker. Which of the following medications is a topical beta-adrenergic antagonist?

A. Apraclonidine
B. Brinzolamide
C. Timolol
D. Travoprost

Question 3: Which of the following is a possible side effect of the topical beta-blocker that the pharmacist should counsel Mary about?

A. Slight increase in fasting blood glucose
B. Slight increase in resting heart rate (pulse rate)
C. Slight reduction in fasting blood glucose
D. Slight reduction in resting heart rate (pulse rate)

Question 4: Mary returns to her ophthalmologist for a checkup and her intraocular pressure is still higher than her goal and the ophthalmologist would like to make a change to her glaucoma regimen. Assuming she is taking the beta-blocker identified in Question 2, which of the following would be the best choice for Mary?

A. Add betaxolol to her current therapy
B. Add levobunolol to her current therapy
C. Switch her current therapy to Cosopt
D. Switch her current therapy to pilocarpine

Answers on page 27

used for these conditions include corticosteroids or laser therapy.

Four VEGF inhibitors are currently available to treat eye disorders.[79] Pegaptanib (Macugen) was the first to market. However, it is approved only for treatment of age-related macular degeneration and not often used due to the development of more effective VEGF inhibitors, ranibizumab (Lucentis), aflibercept (Eylea for eye disorders) and bevacizumab (Avastin).[77-83] Both ranibizumab and aflibercept are FDA-approved to treat age-related macular degeneration, macular edema following retinal vein occlusion, and diabetic macular edema or diabetic retinopathy with diabetic macular edema.[79] While aflibercept is also available under a different brand name (Zaltrap) and approved to treat cancer, bevacizumab is the only one of the four medications that only carries approval for cancer treatments such as metastatic colorectal cancer. Even though it is not approved to treat eye disorders, bevacizumab is commonly used for this purpose because it is available at a lower cost than ranibizumab or aflibercept.[77-83]

Since the medication is used in much larger volumes to treat cancer, bevacizumab is generally reconstituted and then repackaged into smaller single-use vials in a pharmacy prior to ophthalmic use. Ranibizumab, aflibercept, and bevacizumab are all quite effective and lead to significant improvements in vision when given

Table 7. Antibiotics		
GENERIC NAME	TRADE NAME	STRENGTH/DOSAGE FORM
ciprofloxacin	Ciloxan	0.3%; solution, ointment
gentamicin		0.3%; solution, ointment
moxifloxacin	Vigamox	0.5%; solution
neomycin, polymyxin, gramicidin (or bacitracin)	Neosporin	neomycin 1.75mg, polymyxin 10,000 units, gramicidin 0.025 mg/mL; solution, ointment
ofloxacin		0.3%; solution, ointment
polymyxin, trimethoprim	Polytrim	Polymyxin 10,000 units plus trimethoprim1mg/mL; solution, ointment
sulfacetamide		10%; solution, ointment
tobramycin		0.3%; solution, ointment

OPHTHALMIC MEDICATION COMPOUNDING EXAMPLES

From time to time non-ophthalmic medications are compounded to be used as an ophthalmic treatment for various conditions or to fortify (e.g., increase the concentration of or make fortified) commercially available ophthalmic products. One such situation is the compounding of antibiotics to treat bacterial corneal ulcers.

Example:
A physician wants to use a 35 mg/mL cefazolin ocular solution to treat a bacterial corneal ulcer. This product is not commercially available so it will have to be compounded in the pharmacy. Describe a way this product could be made.

Answer:
Ophthalmic cefazolin solutions can be compounded using cefazolin powder for reconstitution and artificial tear solution. To produce a 35mg/mL solution, 525 mg of cefazolin could be added to 15 mL of artificial tears. One way to produce this solution would be to reconstitute 525 mg of cefazolin with 2 mL of normal saline. After removing 2 mL from the bottle of artificial tears, this reconstituted 525 mg of cefazolin could be added to the bottle of artificial tears to replace the 2 mL removed, producing the desired 35 mg/mL ocular cefazolin solution.

to patients for these disorders. Overall, these injections are well-tolerated. Possible side effects include eye pain, conjunctival hemorrhage (bleeding), and increased IOP, among others.[79] However, several studies have raised concerns that bevacizumab may produce more adverse effects, than ranibizumab or aflibercept, which have been studied in more large scale trials for eye conditions than bevacizumab.[86-94] Of particular concern is the greater risk of infection if sterility is compromised during repackaging. Rare, but serious, potential side effects of the VEGF inhibitors include endophthalmitis (inflammation of the internal eye) and retinal detachment.[79]

Dry Eyes

Human tears play an important role in the health of the eye in that they lubricate and protect the eye, as well as remove debris.[95-96] However, environmental factors, underlying medical conditions, medication side effects, or various other causes may lead to intermittently (occasional) or chronically (constant) dry eyes. This condition often leads to irritation and temporary blurring of vision. Dry eye disease affects many patients, with prevalence ranging from approximately 5-35%, depending on age.[97] It is more common in older individuals and females.[98-99] Occasionally, severe chronic dry eye disease can lead to more eye damage if left untreated.[95]

Medications may be used to alleviate symptoms of dry eyes and reduce the risk of eye surface damage.[95] Additionally, though not discussed in this module, discontinuation

of medications or alteration of environmental factors contributing to the symptoms, treatment of underlying medical conditions, or procedures performed by an ophthalmologist may be needed to alleviate dry eyes. Non-pharmacologic (non-medication) measures that may be recommended include: increasing dietary intake of omega-3 fatty acids (or alternatively, taking fish oil supplements); avoiding dry, dusty or windy conditions; using a humidifier in the house; applying a warm compress to the eye; avoiding cigarette smoke; and reducing the amount of time spent looking at electronic screens.[96]

Artificial Tears

The most common medications used to treat dry eye disease are artificial tear substitutes.[97] Tear substitutes lubricate the eye to provide temporary relief. They may be used for dry eye disease of varying levels of severity, though it is important for patients to understand that artificial tear substitutes do not treat underlying causes of dry eyes so patients with severe or chronic dry eyes may still need additional treatment from an ophthalmologist.

Many brands of artificial tear substitutes are available over-the-counter as drops, gels, or ointments, with no single product showing clear superiority over others in clinical trials.[96] The effects of ointments tend to last longer; however they tend to cause blurring of vision because of their high viscosity (thickness). Therefore, these are often used before bed to reduce overnight and next-morning symptoms. A once-daily prescription-only ocular insert called Lacrisert is available as well.

These products are very well-tolerated and may be used frequently (as often as every 30 minutes for short-term use) with few side effects.[95,100] However, some patients may notice stinging upon administration.[96] This may be due to differences in pH between the individual patient's eye and the artificial tear substitute.[101] While artificial tear substitutes are formulated to approximately mimic the pH of the eye, both the pH of individual patient's eyes and the pH of specific tear substitutes differ slightly, meaning individual patients may tolerate certain tear substitutes better than others. If the stinging is too bothersome, patients should be counseled to try a different artificial tear product. Finding the ideal formulation may require trial and error. Another change that may help alleviate irritation is to switch to a preservative-free product.[95-96,100]

Preservatives are commonly used to help prevent the growth of micro-organisms (e.g., bacteria) and reduce the risk of contamination of the medication when exposed to the environment. This increases the shelf-life of these medications, allows them to be sold in multi-dose bottles, and reduces the user's risk of infection. However, preservatives increase the risk of eye irritation, so preservative-free formulations may be better tolerated. This is especially true in patients using these medications frequently. Chronic use of more than four doses per day has been shown to worsen symptoms. If patients are dosing this frequently, preservative-free formulations are preferred because side effects from the preservatives are more common as the number of drops used per day increases. Preservative-free products tend to be more expensive as they must be packaged as single-dose units.

Other Options for Dry Eyes

Cyclosporine ophthalmic emulsion (Restasis) is an anti-inflammatory and immunosuppressive medication that may be used for chronic moderate-to-severe dry eye disease caused by chronic inflammation.[79] This medication is quite effective, with one study demonstrating

Test Your Knowledge #4

Match the potential side effect with the most likely medication class to cause it

	Possible Side Effect	Medication Class
	1. Increased intraocular pressure	A. Beta-blockers
	2. Rebound congestion	B. Prostaglandin analogs
	3. Discoloration of the iris of the eye	C. Corticosteroids
	4. Miosis	D. Ophthalmic decongestants
	5. Worsening symptoms of heart failure and pulmonary conditions	E. Parasympathomimetics (e.g., pilocarpine)

Answers on page 27

improvement in 72.1% of patients, including 66.7% of the patients with severe disease.[102] Cyclosporine's approved dose is one drop in each eye every 12 hours,[79] but studies have also demonstrated efficacy with three or four times daily dosing[103] or when reducing to once daily dosing after one year of twice daily dosing.[104] Stinging or burning on administration is the most common side effect, reported in up to 17% of patients.[79] Ophthalmic corticosteroids, which have been previously discussed, may also be used for dry eye symptoms not relieved by artificial tear substitutes.[95]

Allergic Conjunctivitis

Allergic conjunctivitis is an inflammation of the eye (primarily the conjunctiva) caused by an allergic reaction (e.g. seasonal allergies), which often results in itchy, red eyes and watery discharge.[106] While oral medications are often part of the treatment plan to help resolve allergy symptoms, including conjunctivitis, this section will focus on topical medications used for eye symptoms, specifically ophthalmic antihistamines, decongestants, mast-cell stabilizers, or products containing combinations of these drug classes, many of which are available over-the-counter. Other topical medications that may be used to alleviate symptoms of allergic conjunctivitis that have previously been discussed include artificial tears, corticosteroids, and NSAIDs. Non-pharmacologic therapies that may help alleviate symptoms include avoiding exposure to allergens (e.g. pollen, dander, etc.) and applying a cold compress 3-4 times daily.

Ophthalmic Decongestants

Ophthalmic decongestants (also known as vasoconstrictors) act by constricting the blood vessels in the eye, which reduces redness in the eye.[107] These medications are generally well tolerated and produce few

Table 8. Topical Medications for Allergic Conjunctivitis[79,106]

Generic Name	Brand Name	Drug Class	Number of Doses Per Day
naphazoline	Naphcon, Clear Eyes Redness Relief	Decongestant	4-6
oxymetazoline	Visine-LR	Decongestant	4
phenylephrine	Refresh Redness Relief	Decongestant	4
tetrahydrozoline	Visine	Decongestant	4
alcaftadine	Lastacaft	Histamine antagonist	1
emedastine difumarate	Emadine	Histamine antagonist	4
azelastine HCl	Optivar	Histamine antagonist/mast cell stabilizer	2
bepotastine besilate	Bepreve	Histamine antagonist/mast cell stabilizer	2
epinastine HCl	Elestat	Histamine antagonist/mast cell stabilizer	2
ketotifen fumarate	Zaditor, Alaway	Histamine antagonist/mast cell stabilizer	2
oloptadine HCl 0.1%	Patanol	Histamine antagonist/mast cell stabilizer	2
oloptadine HCl 0.2%	Pataday	Histamine antagonist/mast cell stabilizer	1
cromolyn sodium	Crolom	Mast cell stabilizer	4-6
lodoxamide tromethamine	Alomide	Mast cell stabilizer	4
nedocromil sodium	Alocril	Mast cell stabilizer	2
pemirolast potassium	Alamast	Mast cell stabilizer	4
nephazoline and antazoline	Vasocon-A	Decongestant and antihistamine	4
naphazoline and pheniramine	Naphcon-A, Opcon-A, Visine-A	Decongestant and antihistamine	4

side effects with short-term use. While these medications do not typically cause adverse effects outside of the eye, high dose or frequent use may increase the risk of such effects, including increased blood pressure, among others.[105] Additionally, prolonged use of these medications may actually cause increased dilation of the blood vessels and worsened symptoms when the decongestant is discontinued (called rebound congestion). As a result, these ophthalmic decongestants should not be used for more than 72 hours.[79] If symptoms are not improved within 72 hours of use, the patient should consider seeing a doctor. Additionally, these medications are not safe for use in patients with angle-closure glaucoma as they may worsen the condition.

Four ophthalmic decongestants are available over-the-counter: phenylephrine, naphazoline, tetrahydrozoline, and oxymetazoline.[105] These medications are available alone or in combination with antihistamines or mast cell stabilizers. The decongestants have short durations of action and may need to be dosed 4-6 times per day. **Table 8** (on page 19) provides additional information regarding available products.

Ophthalmic Antihistamines

Histamine is an important component of our body's immune response to allergens. Ophthalmic antihistamines block histamine receptors, which reduces inflammation.[79] These medications are well-tolerated and may be used for prolonged periods of time, if needed.[105] Common side effects include burning, stinging or discomfort upon administration, as well as pupil dilation.

Several different ophthalmic antihistamines are available, either as individual products or in combination with decongestants, and are listed in Table 8. Depending on the product, the recommended dosing ranges from 1-4 times daily.[106] While products containing combinations of antihistamines and decongestants may be more effective, remember that their use is limited to less than 72 hours due to the inclusion of a decongestant. Therefore, products that do not contain a decongestant are preferred for long-term use. Like the decongestants, these medications should not be used in patients with angle-closure glaucoma.

Ophthalmic Mast Cell Stabilizers

Mast cells release histamine and other substances that contribute to immune responses in the body. Mast cell stabilizers prevent mast cell degranulation (breakdown), which is the process by which mast cells release these inflammatory substances, and therefore reduce inflammatory symptoms associated with allergic conjunctivitis.

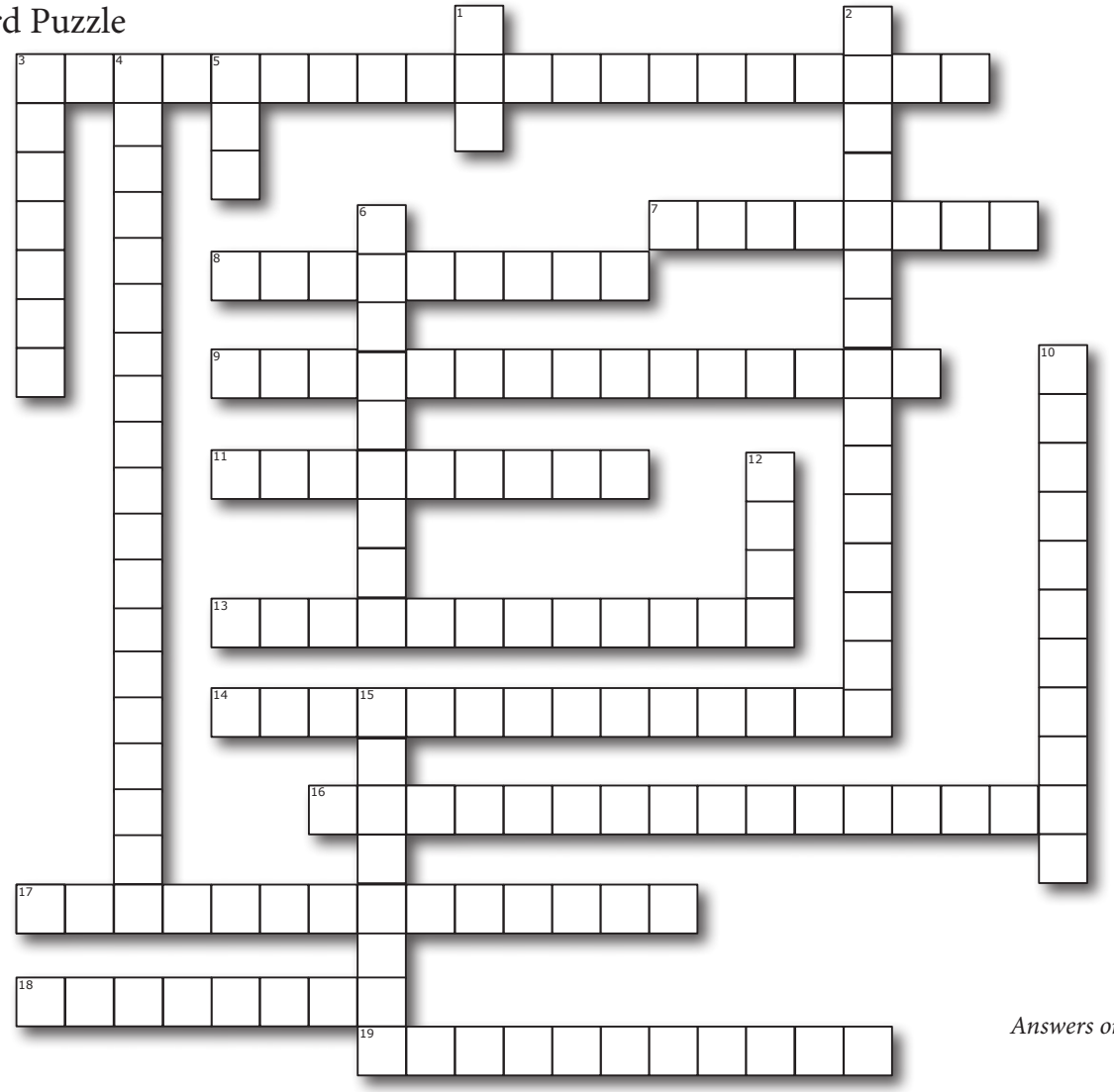
While cromolyn, nedocromil, pemirolast and lodoxamine are considered strictly mast cell stabilizers, several medications display both antihistamine and mast cell stabilizing properties, including ketotifen fumarate, olopatadine, azelastine, epinastine, and alcaftadine.[108-115] There is currently insufficient data to definitively recommend one topical antihistamine or mast cell stabilizer over another.

Conclusion

While dispensed less frequently than certain other drug classes, ophthalmic medications are critically important, particularly when utilized to prevent the loss of vision. Technicians play a key role in assuring the proper procurement, storage, and dispensing of ophthalmic drugs. For non-commercially available products including certain antimicrobials, technicians must assure compounding accuracy and product integrity. Given that many ophthalmic medications are used for chronic conditions such as glaucoma, ocular hypertension, inflammation and allergies, the technician fulfills a key role in supporting the pharmacist to assure appropriate patient compliance.

Test Your Knowledge #5

Crossword Puzzle



Answers on page 27

ACROSS:

3. Travoprost belongs to this class of medications
7. The ophthalmic combination medication containing brimonidine and timolol is marketed under this brand name
8. Generic name for Betoptic
9. Physician specializing in medical or surgical care of the eyes
11. Dilation of the pupils; may be caused by anticholinergic medications
13. Type of glaucoma that is considered a medical emergency
14. Class of medications used for the treatment of age related macular degeneration, which includes pegaptanib, ranibizumab, aflibercept, and bevacizumab
16. Naphazoline and tetrahydrozoline belong to which class of medications that should not be used for more than 72 hours at a time due to the possibility of worsening symptoms
17. External eye problem involving inflammation of the conjunctiva, which may be associated with symptoms of reddened eyes, itching, drainage, stinging, or scratching
18. Brand name of polymyxin-trimethoprim
19. A clear liquid found in the anterior chamber of the eye and may lead to increased intraocular pressure if it is not drained from the eye properly

DOWN:

1. Xalatan solution is primarily prescribed as one drop_____ time(s) daily
2. This class of medications is used for a variety of inflammatory conditions of the eye, but may lead to increased risk of cataract formation
3. Common term for acute bacterial conjunctivitis
4. Defined by intraocular pressure greater than 21 mmHg
5. Timolol ophthalmic solution is primarily prescribed _____ time(s) daily
6. Ophthalmic gentamicin is used to treat which types of ophthalmic infections - bacterial, viral, or fungal?
10. This medication is marketed as Lumigan for increased intraocular pressure and Latisse for inadequate eyelashes
12. Common name for a hordeolum
15. Group of eye disorders that can damage the optic nerve and can lead to blindness

References

1. Riordan-Eva P, Whitcher JP, eds. Vaughan and Ashbury's General Ophthalmology. 18th ed. New York, NY: McGraw-Hill Professional; 2011.
2. Kaur IP, Kanwar M. Ocular preparations: The formulation approach. *Drug Devel Ind Pharm*. 2002;28:473.
3. The University of North Carolina School of Pharmacy Pharmaceutics and Compounding Laboratory. http://pharmlabs.unc.edu/labs/ophthalmics/formulation.htm. Accessed November 2016.
4. Tham YC, Li X, Wong T, et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*. 2014;121(11).
5. American Academy of Ophthalmology. Primary open-angle glaucoma, preferred practice pattern. San Francisco, CA: American Academy of Ophthalmology, 2010. http://www.aao.org/ppp. Accessed August 2016.
6. Rakofsky SI, Mleamed S, Cohen JS, et al. A comparison of the ocular hypotensive efficacy of once-daily and twice-daily levobunolol treatment. *Ophthalmology*. 1989;96:8.
7. Berson FG, Cohen HB, Foerster RJ, et al. Levobunolol compared with timolol for the long-term control of elevated intraocular pressure. *Arch Ophthalmol*. 1985;103:379.
8. Battershill PE, Sorkin EM. Ocular metipranolol: a preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy in glaucoma and ocular hypertension. *Drugs*. 1988;36:601.
9. Mills KB, Wright G. A blind randomised cross-over trial comparing metipranolol 0.3% with timolol 0.25% in open-angle glaucoma: a pilot study. *Br J Ophthalmol*. 1986;70:39.
10. Krieglstein GK, Novack GD, Voepel E, et al. Levobunolol and metipranolol: comparative ocular hypotensive efficacy, safety, and comfort. *Br J Ophthalmol*. 1987;71:250.
11. Scoville B, Mueller B, White BG, et al. A double-masked comparison of carteolol and timolol in ocular hypertension. *Am J Ophthalmol. 1988;105:150.*
12. Stewart WC, Shelds MB, Allen RC, et al. A 3-month comparison of 1% and 2% carteolol and 0.5% timolol in open-angle glaucoma. *Graefes Arch Clin Exp Ophthalmol*. 1991;229:258.
13. Brazier DJ, Smith SE. Ocular and cardiovascular response to topical carteolol 2% and timolol 0.5% in healthy volunteers. *Br J Ophthalmol*. 1988;72:101.
14. Zimmerman TJ, Kaufman HE. Timolol: dose response and duration of action. *Arch Ophthalmol*. 1977;95:605.
15. Britman NA. Cardiac effects of topical timolol. *N Engl J Med*. 1979;300:566.
16. Kim JW, Smith PH. Timolol-induced bradycardia. *Anesth Analg*. 1980;59:301.
17. Shedden AH et al. Multiclinic, double-masked study of 0.5% Timoptic-XE once daily versus 0.5% Timoptic twice daily [Abstract]. *Ophthalmology*. 1993;100(Suppl):111.
18. Berson FG, Epstein DL, Partamian LG. Levobunolol: a beta-adrenoreceptor antagonist effective in the long-term treatment of glaucoma. The Levobunolol Study Group. *Ophthalmology*. 1985;92:1271.
19. Akingbehin T, Villada JR, Walley T. Metipranolol-induced adverse reactions: I. The rechallenge study. *Eye* (Lond). 1992;6(Pt 3):277.
20. Akingbehin T, Villada JR. Metipranolol-induced adverse reactions: II. Loss of intraocular pressure control. *Eye* (Lond). 1992;6(Pt 3):280.
21. Levy NS, Boone L, Ellis E. A controlled comparison of betaxolol and timolol with long-term evaluation of safety and efficacy. *Glaucoma*. 1985;7:54.
22. Berry DP Jr, Van Buskirk EV, Shields MB. Betaxolol and timolol: a comparison of efficacy and side effects. *Arch Ophthalmol*. 1984;102:42.
23. Stewart RH, Kimbrough RL, Ward RL. Betaxolol vs. timolol: a six-month double-blind comparison. *Arch Ophthalmol*. 1986;104:46.
24. Allen RC, Hertzmark E, Walker AM, et al. A double-masked comparison of betaxolol vs. timolol in the treatment of open-angle glaucoma. *Am J Ophthalmol*. 1986;101:535.
25. Zioptan [prescribing information]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp.; 2012
26. Xalatan [prescribing information]. New York, NY. Pfizer, Pharmacia and Upjohn Company; 2009.
27. Camras CB, Wax MB, Ritch R, et al. Latanoprost treatment for glaucoma: effects of treating for 1 year and of switching from timolol. United States Latanoprost Study Group. *Am J Ophthalmol*. 1998;126:390.

28. Bucci MG. Intraocular pressure-lowering effects of latanoprost monotherapy versus latanoprost or pilocarpine in combination with timolol: a randomized, observer-masked multicenter study in patients with open-angle glaucoma. Italian Latanoprost Study Group. *J Glaucoma*. 1999;8:24.
29. Simmons ST, Earl ML. Three-month comparison of brimonidine and latanoprost as adjunctive therapy in glaucoma and ocular hypertension patients uncontrolled on beta-blockers: tolerance and peak intraocular pressure lowering. *Ophthalmology*. 2002;109:307.
30. Hoyng PF, Rulo AH, Greve EL, et al. The additive intraocular pressure-lowering effects of latanoprost in combined therapy with other ocular hypotensive agents. *Surv Ophthalmol*. 1997;41(Suppl2):S93.
31. Kimal AM., Topalkara A, Gueler C. Additive effect of latanoprost and dorzolamide in patients with elevated intraocular pressure. *Int Ophthalmol*. 1998;22:37.
32. Smith SL, Sine CS, Pruitt CA, et al. The use of latanoprost 0.005% once daily and its effect on intraocular pressure as primary or adjunctive therapy. *J Ocul Pharmacol Ther*. 1999;15:29.
33. Netland PA, Landry TA, Sullivan EK, et al. Travoprost compared with latanoprost and timolol in patients with open-angle glaucoma or ocular hypertension. *Am J Ophthalmol*. 2001;132:472.
34. Goldberg I, Cunha-Vaz J, Jakobsen JE, et al. Comparison of topical travoprost eye drops given once daily and timolol 0.5% given twice daily in patients with open-angle glaucoma or ocular hypertension. *J Glaucoma*. 2001;10:414.
35. Travatan [prescribing information]. Fort Worth, TX: Alcon Pharmaceuticals; 2004.
36. Sherwood M, Brandt JD. Six-month comparison of bimatoprost once-daily and twice daily with timolol twice daily in patients with elevated intraocular pressure. *Surv Ophthalmol*. 2001;45(Suppl 4):S361.
37. Noecker RS, Kirks MS, Choplin NT, et al. A six-month randomized clinical trial comparing the intraocular pressure-lowering efficacy of bimatoprost and latanoprost in patients with ocular hypertension or glaucoma. *Am J Ophthalmol*. 2003;135:55.
38. Lumigan [prescribing information]. Irvine, CA: Allergan; 2010.
39. Latisse (bimatoprost ophthalmic solution) [prescribing information]. Irvine, CA: Allergan; 2009.
40. Uusitalo H, Pillunat LE, Ropo A. Efficacy and safety of tafluprost 0.0015% versus latanoprost 0.005% eye drops in open-angle glaucoma and ocular hypertension: 24-month results of a randomized, double-masked phase III study. *Acta Ophthalmol*. 2010; 88: 12-19.
41. Chabi A, Varma R, Tsai JC, et al. Randomized clinical trial of the efficacy and safety of preservative-free tafluprost and timolol in patients with open-angle glaucoma or ocular hypertension. *Am J Ophthamol*. 2012; 153: 1187-1196.
42. Ergorov E, Ropo A. Adjunctive use of tafluprost with timolol provides additive effects for reduction of intraocular pressure in patients with glaucoma. *Eur J Ophthamol*. 2009; 19: 214-22.
43. Januleviciene I, Derkac I, Grybauskiene L, et al. Effects of preservative-free tafluprost on tear film osmolarity, tolerability, and intraocular pressure in previously treated patients with open-angle glaucoma. *Clin Ophthalmol*. 2012; 6: 103-109.
44. Uusitalo H, Chen E, Pfeiffer N, et al. Switching from a preserved to a preservative-free prostaglandin preparation in topical glaucoma medication. *Acta Ophthamol*. 2010; 88: 329-336.
45. Toris CB, Gleason MD, Camras CB, et al. Effects of brimonidine on aqueous humor dynamics in human eyes. *Arch Ophthalmol*. 1995;113: 1514.
46. Alphagan P [prescribing information]. Irvine, CA: Allergan; 2008.
47. Strahlman E, Tipping R, Vogel R. A double-masked, randomized 1-year study comparing dorzolamide (Trusopt), timolol, and betaxolol. International Dorzolamide Study Group. *Arch Ophthalmol*. 1995;113:1009.
48. Wayman L, Larsson L, Maus L, et al. Comparison of dorzolamide and timolol as suppressors of aqueous humor flow in humans. *Arch Ophthalmol*. 1997;115:1368.
49. Simbrinza [prescribing information]. Fort Worth, Texas; Alcon; 2014.
50. Azopt [prescribing information]. Fort Worth, TX: Alcon Laboratories; 2008.
51. Trusopt [prescribing information]. Whitehouse Station, PA: Merck & Co; 2009.
52. Rosenberg LF, Krupin T, Tan L, et al. Combination of systemic acetazolamide and topical dorzolamide in reducing intraocular pressure and aqueous humor formation. *Ophthalmology*. 1998;105:88.
53. Yüksel N, Altintas O, Karabas L, et al. The short-term effect of adding brimonidine 0.2% to timolol treatment in patients with open-angle glaucoma. *Ophthalmologica*. 1999;213:228.

54. Sorensen SJ, Abel SR. Comparison of the ocular β-blockers. Ann Pharmacother. 1996;30:43.
55. Berson FG, Epstein DL. Separate and combined effects of timolol maleate and acetazolamide in open-angle glaucoma. *Am J Ophthalmol*. 1981;92:788.
56. Strahlman ER, Vogel R, Tipping RW, et al. The use of dorzolamide and pilocarpine as adjunctive therapy to timolol in patients with elevated intraocular pressure. The Dorzolamide Additivity Study Group. *Ophthalmology*. 1996;103:1283.
57. thoe Schwartzenberg GW, Buys YM. Efficacy of brimonidine 0.2% as adjunctive therapy for patients with glaucoma inadequately controlled with otherwise maximal medical therapy. *Ophthalmol*. 1999;106:1616.
58. Orzalesi N, Rossetti L, Bottoli A, et al. The effect of latanoprost, brimonidine, and a fixed combination of timolol and dorzolamide on circadian intraocular pressure in patients with glaucoma or ocular hypertension. *Arch Ophthalmol*. 2003;121:453.
59. Galin MA, Davidson R, Shachter N Ophthalmological use of osmotic therapy. *Am J Ophthalmol*. 1966;62:629.
60. Drance SM. Effect of oral glycerol on intraocular pressure in normal and glaucomatous eyes. *Arch Ophthalmol*. 1964;72:491.
61. Becker B, Kolker AE, Krupin T. Isosorbide: an oral hyperosmotic agent. *Arch Ophthalmol*. 1967;78:147.
62. Leibowitz HM, Kupferman A.. Bioavailability and effectiveness of topically administered corticosteroids. *Trans Am Acad Ophthalmol Otolaryngol*. 1975;79:78.
63. Leibowitz HM, Kupferman A. Anti-inflammatory effectiveness in the cornea of topically administered prednisolone. *Invest Ophthalmol*. 1974;13:757.
64. Kupferman A, Leibowitz HM. Therapeutic effectiveness of fluorometholone in inflammatory keratitis. Arch *Ophthalmol*. 1975;93:1011.
65. Leibowitz HM, Ryan WJ Jr, Kupferman A. Comparative anti-inflammatory efficacy of topical corticosteroids with low glaucoma-inducing potential. *Arch Ophthalmol*. 1992;110:118.
66. Armaly MF. Statistical attributes of the steroid hypertensive response in the clinically normal eye. I. The demonstration of three levels of response. *Invest Ophthalmol*. 1965;4: 187.
67. Becker B, Ballin N. Glaucoma and corticosteroid provocative testing. *Arch Ophthalmol*. 1965;74:621.
68. Goa KL, Chrisp P. Ocular diclofenac: a review of its pharmacology and clinical use in cataract surgery, and potential in other inflammatory ocular conditions. *Drugs Aging*. 1992;2:473.
69. Ocufen [prescribing information]. Hormigueros, PR: Allergan America; 1992.
70. Voltaren Ophthalmic [prescribing information]. Atlanta, GA: *CIBA Vision Ophthalmics*; 1991.
71. Flach AJ, Lavelle CJ, Olander KW, et al. The effect of ketorolac tromethamine solution in reducing postoperative inflammation after cataract extraction and intraocular lens implantation. *Ophthalmology*. 1988;95:1279.
72. Flach AJ, Stegman RC, Graham J, et al. Prophylaxis of aphakic cystoid macular edema without corticosteroids. *Ophthalmology*. 1990;97:1253.
73. Flach AJ, Jampol LM, Weinberg D, et al. Improvement in visual acuity in chronic aphakic and pseudophakic cystoid macular edema after treatment with topical 0.5% ketorolac tromethamine. *Am J Ophthalmol*. 1991;112:514.
74. Tinkelman DG, Rupp G, Kaufman HS, et al. Double-masked, paired-comparison clinical study of ketorolac tromethamine 0.5% ophthalmic solution compared with placebo eyedrops in the treatment of seasonal allergic conjunctivitis. *Surv Ophthalmol*. 1993;38(Suppl):133.
75. Ballas Z, Blumenthal MN, Tinkelman DG, et al. Clinical evaluation of ketorolac tromethamine 0.5% ophthalmic solution for the treatment of seasonal allergic conjunctivitis. *Surv Ophthalmol*. 1993;38(Suppl):141.
76. Wilson SJ, Schutte SM, Abel SR. Comparing the efficacy of ophthalmic NSAIDs in common indications: a literature review to support cost-effective therapy. *Ann Pharmacother*. 2015;49:727.
77. Evoy KE, Abel SR. Ranibizumab: the first vascular endothelial growth factor inhibitor approved for the treatment of diabetic macular edema. *Ann Pharmacother*. 2013;47(6):811-8.
78. Evoy KE, Abel SR. Aflibercept: newly approved for the treatment of macular edema following central retinal vein occlusion. *Ann Pharmacother*. 2013;47(6):819-27.
79. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://online.lexi.com. Accessed 11/5/2016.

80. American Academy of Ophthalmology. Age-Related Macular Degeneration Preferred Practice Pattern 2015. Available at: https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp-2015#CAREPROCESS. Accessed: 11/6/2016.
81. American Academy of Ophthalmology. Diabetic Retinopathy Preferred Practice Pattern 2016. Available at: https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp-updated-2016. Accessed: 11/6/2016.
82. American Academy of Ophthalmology. Retinal Vein Occlusions Preferred Practice Pattern 2015. Available at: https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp-updated-2016. Accessed: 11/6/2016.
83. Mitchell P, Wong TY. Management paradigms for diabetic macular edema. *American Journal of Ophthalmology*. 2014;157(3):505-513.
84. Congdon N, O'Colmain B, Klaver CC, et al. Causes and prevalence of visual impairment among adults in the United States. *Arch Ophthalmol*. 2004;122:477-485.
85. Mukamal R. American Academy of Ophthalmalogy. Avastin, Eylea and Lucentis – What's the Difference? Available at: http://www.aao.org/eye-health/diseases/avastin-eylea-lucentis-difference. Accessed 11/5/2016.
86. Sharma S, Johnson D, Abouammoh M, Hollands S, Brissette A. Rate of serious adverse effects in a series of bevacizumab and ranibizumab injections. *Canadian Journal of Ophthalmology*. 2012;47(3):275-279.
87. Georgopoulos M, Polak K, Prager F, et al: Characteristics of severe intraocular inflammation following intravitreal injection of bevacizumab (Avastin). *Br J Ophthalmol*.2009; 93:457-462
88. Wickremasinghe SS, Michalova K, Gilhotra J, et al: Acute intraocular inflammation after intravitreous injections of bevacizumab for treatment of neovascular age-related macular degeneration. *Ophthalmology*. 2008; 115:1911-1915
89. Yamashiro K, Tsujikawa A, Miyamoto K, et al: Sterile endophthalmitis after intravitreal injection of bevacizumab obtained from a single batch. Retina. 2010; 30:485-490
90. Sato T, Emi K, Ikeda T, et al: Severe intraocular inflammation after intravitreal injection of bevacizumab. *Ophthalmology*. 2010; 117:512-516
91. Ness T, Feltgen N, Agostini H, et al: Toxic vitritis outbreak after intravitreal injection. *Retina*. 2010; 30:332-338
92. Johnson D, Hollands H, Hollands S, Sharma S, et al: Incidence and characteristics of acute intraocular inflammation after intravitreal injection of bevacizumab: a retrospective cohort study. *Can J Ophthalmol*. 2010; 45:239-242
93. Fielden M, Nelson B, Kherani A, et al: Acute intraocular inflammation following intravitreal injection of bevacizumab: a large cluster of cases. *Acta Ophthalmol*. 2011; 89:e664-e665
94. Chong DY, Anand R, Williams PD, et al: Characterization of sterile intraocular inflammatory responses after intravitreal bevacizumab injection. *Retina*. 2010; 30:1432-1440
95. American Academy of Ophthalmology. Dry Eye Syndrome Preferred Practice Pattern 2013. Available at: http://www.aao.org/preferred-practice-pattern/dry-eye-syndrome-ppp--2013. Accessed: 11/6/2016.
96. Marshall LL , Roach JM. Treatment of dry eye disease. *Consult Pharm*. 2016;31:96-106.
97. The International Dry Eye WorkShop Study Group. The epidemiology of dry eye disease: report of the Epidemiology Subcommittee of the International Dry Eye WorkShop (2007). *Ocul Surf*. 2007;5(2):93-107.
98. Moss SE, Klein R, Klein BE. Incidence of dry eye in an older population. *Arch Ophthalmol*. 2004;122:369-373.
99. Schaumberg DA, Sullivan DA, Buring JE, et al. Prevalence of dry eye syndrome among US women. *Am J Ophthalmol*. 2003;136:318-326.
100. American Optometric Association. Care of the patient with ocular surface disorders. 2010. Available at: https://www.aoa.org/documents/CPG-10.pdf. Accessed: 11/6/2016.
101. Tong L, Petznick A, Lee S, et al. Choice of artificial tear formulations for patients with dry eye: where do we start? *Cornea*. 2012;31 Suppl 1:S32-36.
102. Perry HD, Solomon R, Donnenfeld ED, Perry AR, Wittpenn JR, Greenman HE, Savage HE. Evaluation of topical cyclosporine for the treatment of dry eye disease. *Arch Ophthalmol*. 2008;126(8):1046-1050.
103. Dastjerdi MH, Hamrah R, Dana R. High-frequency topical cyclosporine 0.05% in the treatment of severe dry eye refractory to twice a day dosing. *Cornea*. 2009;28:1091-1096.
104. Su MY, Perry HD, Barsam A, et al. The effect of decreasing the dosage of cyclosporine A 0.05% on DED after 1 year of twice-daily therapy. *Cornea*. 2011;30:1098-1104.

105. Fiscella RG, Jensen MK. Ophthalmic disorders. In: Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care. Krinsky DL, Ferreri SP, Hemstreet B, et al, Eds. 18th ed. Washington, DC; American Pharmacists Association, 2015.
106. American Academy of Ophthalmology. Conjunctivitis Preferred Practice Pattern 2013. Available at: http://www.aao.org/preferred-practice-pattern/conjunctivitis-ppp--2013. Accessed: 11/6/2016.
107. Bielory L, Katelaris CH, Lightman S, Naclerio RM. Treating the ocular component of allergic rhinoconjunctivitis and related eye disorders. *MedGenMed* 2007;9(3):35.
108. American Academy of Allergy, Asthma, and Immunology. AAAA Allergy and Asthma Medication Guide. April 2016. Available at: https://www.aaaai.org/conditions-and-treatments/treatments/drug-guide/eye-medications. Accessed 11/7/2016.
109. Emadine [prescribing information]. Fort Worth, TX: Alcon Laboratories; 1999.
110. Zaditor [prescribing information]. Duluth, GA: CIBA Vision; 1999.
111. Yanni JM, Weimer LK, Sharif NA, et al. Preclinical efficacy of emedastine, a potent selective histamine H1 antagonist for topical ocular use. *J Ocul Pharmacol*. 1994;10:665.
112. Aguilar AJ. Comparative study of clinical efficacy and tolerance in seasonal allergic conjunctivitis management with 0.1% olopatadine hydrochloride versus ketotifen fumarate. *Acta Ophthalmol Scand. Suppl*. 2000;(230):52.
113. Spangler DL, Bensch G, Berdy GJ. Evaluation of the efficacy of olopatadine hydrochloride 0.1% ophthalmic solution and azelastine hydrochloride 0.05% ophthalmic solution in the conjunctival allergen challenge model. *Clin Ther*. 2001;23:1272.
114. McCabe CF, McCabe SE. Comparative efficacy of bepotastine besilate 1.5% ophthalmic solution versus olopatadine hydrochloride 0.2% ophthalmic solution evaluated by patient preference. *Clin Ophthalmol*. 2012;6:1731.
115. Ackerman S, D'Ambrosio F Jr, Geiner JV, et al. A multicenter evaluation of the efficacy and duration of action of alcaftadine 0.25% and olopatadine 0.2% in the conjunctival allergy challenge model. *J Asthma Allergy*. 2013;6:43.

ANSWER KEY: TEST YOUR KNOWLEDGE EXERCISES

Exercise #1:

1. Vitreous gel
2. Optic nerve
3. Macula
4. Fovea
5. Retina
6. Iris
7. Cornea
8. Pupil
9. Lense
10. Iris

Exercise #2:

1. Incorrect administration frequency: Travoprost should be administered once daily instead of three times daily as written on this prescription.

2. Cosopt is a combination product containing dorzolamide and timolol. It is available only as a solution, not as a gel.

Exercise #3:

1. 1) Advanced age
   2) African American ethnicity
   3) Family history of glaucoma
   4) Increased intraocular pressure

2. C

3. D
   Explaination: Beta-blockers reduce resting heart rate when absorbed systemically (throughout the body, as opposed to locally, just in the eye). Small amounts of ocular beta-blockers may be absorbed systemically when administered as an eye drop and cause a modest reduction in resting heart rate (5-8 beats per minute) and should be used cautiously in patients with low heart rates at baseline.

4. C
   Explaination: Answers A and B are both beta-blockers. These would not be the best option because Mary is already taking a beta-blocker and combination therapy for glaucoma should include medications from different drug classes. Answer D would not be the best choice, as pilocarpine is an older medication that has fallen out of favor compared to newer options available. It is more commonly used in patients who cannot tolerate beta-blockers, prostaglandin inhibitors, or carbonic anhydrase inhibitors or as part of combination therapy in patients not controlled on a single drug. Cosopt is a combination product containing timolol and dorzolamide, a carbonic anhydrase inhibitor. Adding a carbonic anhydrase inhibitor would be a reasonable option for a patient who is taking a beta-blocker and needs extra intraocular pressure reduction.

Exercise #4:

1. C
2. D
3. B
4. E
5. A

Exercise #5
Crossword Puzzle Answers:
Across:

3. prostaglandin analogs
7. Combigan
8. betaxolol
9. ophthalmologist
11. mydriasis
13. angle closure
14. VEGF inhibitors
16. vasoconstrictors (also known as decongestants)
17. conjunctivitis
18. Polytrim
19. aqueous humor

Down:

1. one
2. corticosteroids
3. pink eye
4. ocular hypertension
5. two
6. bacterial
10. bimatoprost
12. stye
15. glaucoma

SELF ASSESSMENT QUESTIONS

Note:
If you purchase a paper subscription, but complete the Self-Assessment Test online at pharmacytechtopics.com, you will be required to take the Pre-Test first, then the final test and evaluation. This Pre-Test does not affect your final test results but will be used to evaluate the effectiveness of the continuing education program.

1. **The colored part of the eye that controls the amount of light that enters the eye is called the _____.**
   A. cornea
   B. iris
   C. lens
   D. retina

2. **Which of the following best defines the role of the lens?**
   A. Contains sensory receptors for light transmission
   B. Focuses light onto the retina
   C. Serves as a protective coating
   D. Transmits visual impulses from the retina to the brain

3. **Punctal occlusion is the technique of applying slight pressure with the finger to the inner corner of the eye, closest to the nose, for 1-2 minutes after administering an eye drop. Why should this technique be recommended to patients?**
   A. Punctal occlusion may increase effectiveness by causing more drug to remain in the eye
   B. Punctal occlusion may reduce side effects by reducing the amount of drug absorbed throughout the rest of the body
   C. Punctal occlusion may reduce effectiveness of ophthalmic medications
   D. A and B are correct

4. **Which of the following conditions is considered a medical emergency?**
   A. Acute bacterial conjunctivitis
   B. Angle-closure glaucoma
   C. Cataract
   D. Stye

5. **Which of the following medications is FDA-approved as a therapy to increase eye lash length and thickness, in addition to its use as a treatment for ocular hypertension?**
   A. Bimatoprost
   B. Dorzolamide
   C. Pilocarpine
   D. Timolol

6. **Which of the following medications may be better tolerated by some patients with an intolerance to other prostaglandin inhibitors due to it being supplied in a totally preservative-free formulation?**
   A. Bimatoprost
   B. Latanoprost
   C. Tafluprost
   D. Travoprost

7. **Which class of medications can have the systemic (i.e., effects outside the eye) side effect of bitter taste AND can result in allergic reactions in someone with a sulfa allergy?**
   A. Anti-cholinergic
   B. Beta-adrenergic antagonists
   C. Carbonic anhydrase inhibitors
   D. Prostaglandin analogs

8. **Which of the following answers correctly matches a medication brand name to its appropriate generic name?**
   A. Lumigan – tafluprost
   B. Zioptan - travoprost
   C. Travatan Z - bimatoprost
   D. Xalatan – latanoprost

9. Which of the following topical ophthalmic medications would be the most likely to increase a patient's intraocular pressure by decreasing aqueous humor outflow, which could be problematic for patients with intraocular hypertension or glaucoma?
A. Carbechol
B. Cromolyn
C. Dexamethasone
D. Sulfacetamide

10. Which of the following ophthalmic medications might be used to reduce inflammation following cataract surgery?
A. Brimonidine
B. Olopatadine
C. Pilocarpine
D. Diclofenac

11. _____ is an infection of the hair follicles or sebaceous glands of the eyelids that should be treated with warm, moist compresses and topical antibiotics.
A. A corneal ulcer
B. A stye
C. Conjunctivitis
D. Pinkeye

12. Flurbiprofen 0.03% may be administered before cataract surgery to inhibit miosis (constriction of the pupil) during surgery. Flurbiprofen is a member of which class of medications?
A. Anticholinergic
B. Corticosteroid
C. Non-steroidal anti-inflammatory (NSAID)
D. Prostaglandin Inhibitor

13. Tobradex is a combination product containing tobramycin and dexamethasone. What is the purpose of the two medications included in this product?
A. Block mast cells and block histamine receptors
B. Reduce intraocular pressure and reduce inflammation
C. Relieve common eye symptoms associated with seasonal allergies, including redness and itchiness
D. Treat a bacterial eye infection and reduce inflammation

14. Which of the following conditions is caused by abnormal growth of blood vessels behind the retina and may result in blurred vision or even blindness?
A. Cataracts
B. Corneal ulcers
C. Glaucoma
D. Macular degeneration

15. Which of the following medications is approved for intravenous treatment of metastatic colorectal cancer but also used off-label for the treatment of ocular disorders, such as age-related macular edema?
A. Bevacizumab
B. Bimatoprost
C. Latanoprost
D. Ranibizumab

16. "Fortified" ophthalmic antibiotics (for example fortified gentamicin) may sometimes be used to treat corneal ulcers. Which of the following best describes what the term "fortified" indicates in this situation?
A. The medication has been compounded to achieve higher concentrations than those commercially manufactured
B. The medication has been formulated to have a longer duration of action
C. The medication has been formulated to have a longer shelf-life
D. Two medications have been combined to create a combination medication

17. Many lubricant eye drops (i.e., artificial tear substitutes) are available over-the-counter to relieve irritation from dry eyes. What is the maximum number of times these products should be used in a 24 hour period?

A. 1 time
B. 2 times
C. 3 times
D. None of the above

18. Which of the following classes of ocular medications that may be used for conjunctivitis should be recommended to use for no more than 72 consecutive hours due to the possibility of worsening symptoms with continued use?

A. Antihistamines
B. Antibiotics
C. Corticoteroids
D. Decongestants (vasoconstrictors)

19. _____ is a medication commonly used to treat bacterial conjunctivitis, while _____ is a medication commonly used to treat allergic conjunctivitis.

A. Azelastine, sulfacetamide
B. Sulfacetamide, azelastine
C. Timolol, naphazoline
D. Naphazoline, timolol

20. Which of these agents is an ophthalmic decongestant available over-the-counter?

A. Azelastine
B. Tetrahydrozoline
C. Cromolyn sodium
D. Ketotifen fumarate