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Reshaping Eye Care:
Innovative Pharmaceutical Options for Presbyopia

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Reshaping Eye Care: Innovative Pharmaceutical Options for Presbyopia

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Content Source

This continuing education (CE) activity captures content from a live symposium.

Activity Description

This supplement summarizes a discussion on diagnosing and classifying patients with presbyopia, understanding the mechanism of action of pharmaceutical therapies, and matching patients with the best treatment.

Target Audience

This certified CE activity is designed for optometrists.

Learning Objectives

Upon completion of this activity, the participant should be able to:

- **Summarize** the clinical/behavioral symptoms, visual acuity, and near vision correction that characterize mild, moderate, and advanced levels of presbyopia
- **Discuss** the optics of the pinhole effect and how it improves functional vision
- **Describe** the mechanism of action and evaluate the latest clinical evidence for pilocarpine-based miotic agents for the treatment of presbyopia
- **Review** patient-specific factors that may influence treatment outcomes, with a focus on the prevalence of dry eye in presbyopic patients
- **Execute** strategies to identify patients with presbyopia who may benefit from pharmacological therapies

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PRETEST QUESTIONS

Please complete prior to accessing the material and submit with Posttest/Activity Evaluation/Satisfaction Measures for credit.

1. Please rate your confidence in your ability to diagnose and treat patients with presbyopia (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).

a. 1
b. 2
c. 3
d. 4
e. 5

2. According to quality-of-life surveys, which of the following statements is TRUE?

a. The loss of near vision has the most significant impact on quality of life in comparison to other age-related ailments
b. The loss of near vision has a significant impact on quality of life in comparison to other age-related ailments, though not as much as arthritis
c. The loss of near vision has the least significant impact on quality of life in comparison to other age-related ailments
d. The loss of near vision does not significantly impact quality of life

3. All of the following represent nonsurgical solutions to presbyopia, EXCEPT:

a. Progressive lenses
b. Eye drops that modulate pupil size
c. Multifocal contact lenses
d. Corneal inlays

4. A 62-year-old patient presents to your office for exam. His near visual acuity measures J10 and he has complete inability to read at near and intermediate distance without aid. What severity of presbyopia does this patient have?

a. Mild presbyopia
b. Moderate presbyopia
c. Advanced presbyopia
d. No presbyopia

5. You are evaluating a 45-year-old patient in your office. She notes increasing difficulty with near tasks and desires a pharmaceutical solution. She is reluctant to wear bifocals. You recommend a miotic eye drop to aid with her presbyopia. She asks about the most common side effect. What do you answer?

a. Headache
b. Visual impairment
c. Conjunctivitis
d. Cataract formation

6. A 46-year-old man presents to your office for a routine eye exam. He notes blurry near vision and needing increased light to see a menu. His eye exam is unremarkable and you note emmetropia with +1.50 add OU. All of the following are reasonable treatment options for this patient, EXCEPT:

a. OTC reading glasses
b. Progressive glasses
c. Pilocarpine eye drops
d. Dorzolamide eye drops

7. What is the estimated annual economic loss globally due to uncorrected presbyopia?

a. $1 to $5 billion
b. $6 to $10 billion
c. $11 to $25 billion
d. $50 to $75 billion

8. A 48-year-old presbyopic patient presents to your office for evaluation. He is increasingly frustrated by his loss of near vision and desires a solution. He measures plano at distance with a +1.50 near correction. All of the following are reasonable options for this patient's presbyopia, EXCEPT:

a. Single vision spectacles
b. Multifocal contacts
c. Pupil-modulation drops
d. Intense pulsed light therapy

9. A 54-year-old patient presents to your office for evaluation. He notes decreased near vision only in dim light, and is having increasing difficulty reading his dashboard when driving at night. According to the American Optometric Association classification, how would his presbyopia be characterized?

a. Incipient
b. Absolute
c. Nocturnal
d. Functional

10. Which of the following statements about the pinhole effect and the iris is TRUE?

a. A smaller pinhole at the iris plane can improve depth of field without compromising peripheral vision
b. A larger pinhole at the iris plane can improve depth of field without compromising peripheral vision
c. A smaller pinhole at the iris plane can worsen depth of field but improve peripheral vision
d. A larger pinhole at the iris plane can worsen depth of field but improve peripheral vision

11. Which of the following describes the mechanism of action of pilocarpine?

a. Cholinomimetic drug
b. Adrenergic drug
c. Aqueous suppressant drug
d. All of the above

12. What is the approximate time of onset for 1.25% pilocarpine HCl?

a. ~1 hour
b. ~30 minutes
c. ~15 minutes
d. ~2 hour

13. A 45-year-old presbyopic patient presents to your office. He is interested in a nonsurgical option to treat his presbyopia. Which of the following is a reasonable option?

a. Pilocarpine drop
b. Dorzolamide drop
c. Latanoprost drop
d. Timolol drop

14. Which of the following represents an ophthalmic finding that might impact your decision to prescribe presbyopia-correcting drops?

a. History of allergic conjunctivitis
b. History of retinal tears and presence of lattice degeneration
c. Diagnosis of glaucoma
d. Presence of cataract

Reshaping Eye Care: Innovative Pharmaceutical Options for Presbyopia

This has been an exciting time in optometry with the approval of the first presbyopia-correcting eye drop in 2021. It has a novel mechanism of action, ie, inducing miosis to improve near vision without compromising distance vision, for treating a condition that most of us have previously treated with glasses or contact lenses. As a community, we're very familiar with glasses and contact lenses as management strategies. We are less familiar with how presbyopia-correcting eye drops affect the optical system and, therefore, their effect on functional vision. With several such pharmaceutical options for presbyopia in the pipeline, this treatment modality will likely persist in presbyopia care. Notably, evidence from the clinical trials suggests reasonable duration of therapeutic effect and mild adverse events. Therefore, these eye drops can be a flexible, adjunct option for most patients. Since the commercialization of pilocarpine 1.25% for prebyopia, it has become clear that identifying the right patients is critical for optimizing the success of this medication. A panel of optometrists who understands the intricacies of presbyopia-correcting drops will discuss strategies for incorporating this treatment into our practices.

— Mark T. Dunbar, OD, FAAO, Program Chair

PREVALENCE AND STRATIFICATION OF PRESBYOPIA

Jaclyn Garlich, OD, FAAO: We know how common it is to encounter patients with presbyopia. Globally, there are 1.8 billion people with presbyopia.[1] Of those, 826 million have impaired near vision due to inadequate or no vision correction, ie, 45% need presbyopia correction. While near vision impairment due to no vision correction tends to be an issue predominantly in developing countries, it does contribute to an estimated $11 to $25 billion annual economic loss due to uncorrected presbyopia.[2] Similar to patients with dry eye, patients with presbyopia encounter work productivity issues. We may not realize the burden because we are accustomed to treating patients with presbyopia.

In the United States alone, 128 million individuals are presbyopic, of which 83% to 89% are older than 45 years.[2,3] What's striking is that almost 31 million patients are buying OTC readers. I can only assume that these patients are not getting their annual eye exams. As they continue to hear about presbyopia-correcting eye drops, they may become interested enough to come into our offices and inquire about them. This could be a potentially large influx of patients and a practice-growing opportunity. However, we have yet to see this happen. We'll discuss more about why this may be.

In a survey of 797 patients aged 40 to 55 years, 46% and 96% reported having at least one daily activity being either extremely or somewhat impacted by presbyopia, respectively.[4] We've all heard complaints from patients needing to increase the font size on their phone, requiring more light to see well, and not transitioning rapidly from near to distance vision, etc. It is extremely inconvenient at best.

Dr. Dunbar: Some of these patients have not needed glasses until they become presbyopic. Having to use readers then becomes a significant adjustment and an obvious harbinger of aging. It makes sense that they want solutions that have as minimal an impact on their daily routine and lives as possible.

Dr. Garlich: That's a good point. Certainly, those patients that are plano in the distance but need near vision correction are very frustrated and feel more impacted.

In a survey of 1,000 people with presbyopia, loss of near vision was ranked as having the most significant impact on their quality of life, above age-related conditions such as arthritis, hearing loss, and even dry eye.[5] This makes sense because presbyopia affects so many of the activities we perform for significant periods of time every day, ie, using our phones and computer screens. Presbyopia is no longer a problem we can simply correct with an add power. It is, and has been for a few years, impacting patients' quality of life.

Currently, we have several nonsurgical and surgical options to treat presbyopia. In the nonsurgical category, we have single vision, bifocal/trifocal, or progressive lens glasses; soft multifocal, monovision, gas permeable, or scleral contact lenses; and pupil-modulating or combination pupil-modulating and ciliary body-contracting eye drops. Pilocarpine 1.25% is currently available and more eye drops are in the works. All these nonsurgical options are well-suited for patients who are not looking for permanent, significant alterations to their vision. For those who do, there are corneal inlays, excimer laser for monovision or multifocal ablations, and a whole host of IOL technologies.

Derek N. Cunningham, OD, FAAO: We have a 6-month waiting list at our practice for patients who want refractive lens exchange. They are between 40 to 50 years old and have 20/20 distance vision with glasses or contacts. It demonstrates the incredible demand for near vision correction.

Dr. Garlich: Absolutely. Almost all of us instinctively stratify patients by matching their age to their add power. The American

Optometric Association has a more detailed classification for patients with presbyopia, including incipient, functional, absolute, premature, and nocturnal presbyopia.[6] Incipient presbyopes have compromised near vision but may be able to work around this by increasing the font on their phone or seeking better lighting, ie, they may not feel that they require near vision correction. The functional presbyope is one who experiences visual difficulties. Absolute presbyopia is when no accommodative ability remains and is a progression from functional presbyopia. When these stages are reached at an earlier-than-expected age, it is termed premature presbyopia. We sometimes see this in latent hyperopes. Finally, nocturnal presbyopia arises from a decrease in accommodation under dim lighting.

More recently, presbyopia was categorized by severity, ie, mild, moderate, or advanced, based on the clinical/behavioral symptoms, visual acuity, and required add power (Table).

Dr. Cunningham: As an aside, our surgical colleagues refer to presbyopia as dysfunctional lens syndrome. This term was coined by Drs. Daniel S. Durrie, Jason E. Stahl, and George O. Waring IV who proposed a grading scale of dysfunctionality in 2016.[7] The concept is primarily useful for surgeons when trying to determine whether patients are better suited to corneal or lenticular surgical procedures for vison correction.

THE OPTICS OF THE PINHOLE EFFECT

Dr. Cunningham: The research I perform outside of my surgical practice focuses on understanding how the optical system and optical phenomena can impact functional vision. It may feel like the optics of the pinhole effect are more complex than what we remember, but it's important that we become experts in this area because it will influence the way we individualize presbyopia treatments.

We always liken the eye to a camera. With a camera, a smaller pinhole increases the depth of field.[9] In the eye, miosis or pupillary constriction increases the depth of focus, without restricting peripheral vision.[10] Remember, the pupil can constrict or dilate in response to more than just the ambient light level. Parasympathetic or sympathetic nervous system input, age, iris color, state of arousal, the task the patient may be performing, and their concentration level will also have an impact. This is one of the reasons why patients with presbyopia-correcting IOLs may have 20/25 VA but complain about having blurry vision in their everyday life. We measure their vision with a high-contrast,

TABLE. CLASSIFICATION OF PRESBYOPIA BY SEVERITY[8]

	Mild presbyopia	Moderate presbyopia	Advanced presbyopia
Near add required	< +1.25 D	> +1.25 D to +2.00 D	> +2.00 D
DNCVA (Photopic)	20/25-20/40	>20/40-20/80	>20/80
Jaeger equivalent (photopic)	<J3	J4-J9	>J9
DCNVA (mesopic)	20/25-20/50	>20/50-20-100	>20/100
Jaeger equivalent (mesopic)	≤J5	J6-10	>J10
Behavioral/ clinical findings	Holding objects farther away, difficulty in very dim lighting	Turning up lights in most settings, require aids in almost all circumstances	Inability to read at near and intermediate distance without aid
Typical age	40-47 years	>47-55 years	>55 years
Refractive error	Hyperopes earlier and more impacted	Hyperopes earlier and more impacted	No difference between myopes and hyperopes

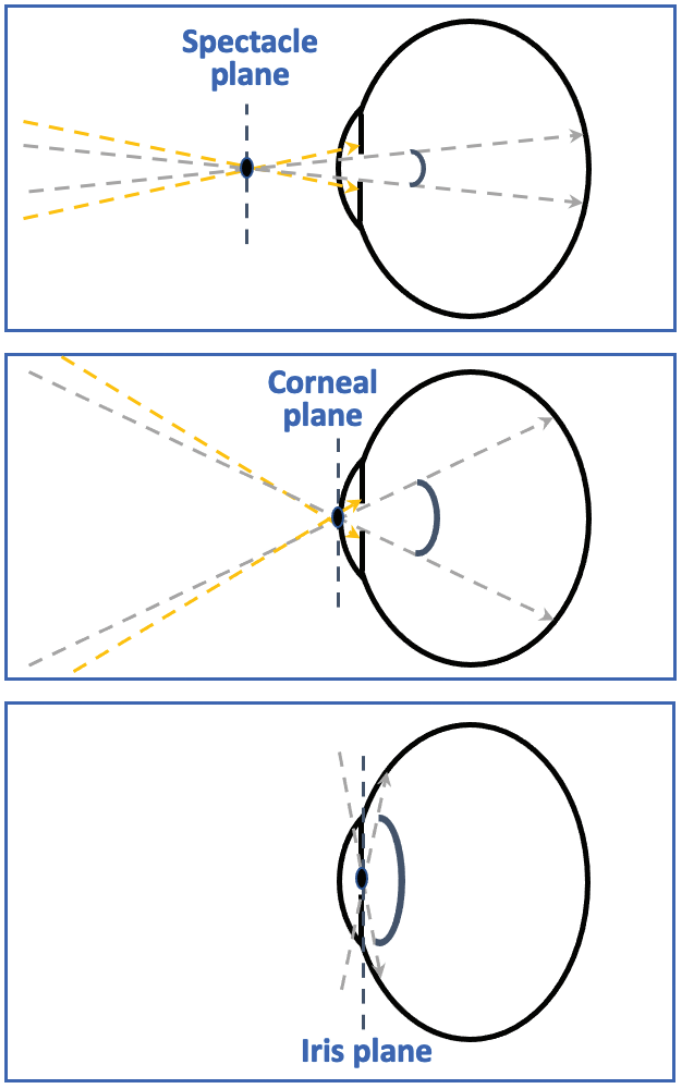

Figure 1. Pinhole placement affects the field of vision. A pinhole at the iris plane extends depth of focus without restricting peripheral vision.

black-on-white chart in a brightly lit room, which does not mimic the real-life situations they encounter throughout the day.

When the pupil is dilated, more light enters the eye which theoretically improves image quality. However, the eye is not a perfect imaging system, and the higher-order corneal aberrations are also amplified in this situation. We see the same degradation in image quality in cameras with larger apertures. If the pupil is constricted, we limit the amount of light entering the eye, but we also see interference fringes. A pinhole, when executed perfectly, only allows parallel light rays. This is exactly what happens with the pinhole occluder that temporarily bypasses the refractive errors in the optical system.

The question then arises: What is the perfect plane to place a pinhole in the eye? If we place it at the spectacle plane, it reduces the field of vision (Figure 1). Placing it at the corneal plane, eg, some corneal inlays, has a relative increase in the field of vision, but some peripheral vision is still lost. A pinhole at the iris plane places the nodal point, where light rays cross over, at the same plane as where the natural pinhole exists. Glasses and even contact lenses have a vertex distance, which changes the properties of the optical system. By placing a pinhole at the iris plane, we work within the optical system that is already present. Depth of focus is extended without affecting peripheral vision, producing excellent near and distance vision. This, of course, assumes that other factors such as higher-order aberrations, patient-specific factors, and lighting conditions are trivial and, usually, they are not.

There is no single pupil diameter that can uniformly increase the depth of focus in all patients as pupil size naturally varies between individuals and can also change depending on the environment. However, a study by Xu et al deduced that the optimal pupil size range may be 40% to 50% of an individual's natural pupil size (Figure 2).[11] In their model, under photopic, mesopic, or scotopic conditions, progressive pupil constriction results in continued improvement of near vision.[11] The magnitude of improvement in image quality varies with lighting because, under mesopic and scotopic lighting, the natural pupil size must substantially increase to deliver the same degree of light that overcomes the retina contrast barrier and provides functional vision. This pupillary effect is also why patients with presbyopia-correcting IOLs, specifically those with diffractive optics, experience significant reduction in their visual capabilities and performance in lower lighting conditions.

With distance vision, the model demonstrates a slight improvement in image quality that remains mostly stable under all lighting conditions.[11] However, when pupil constriction falls below 40% of the natural pupil size, image quality becomes less optimal. In fact, under mesopic and scotopic lighting, distance vision deteriorates significantly as pupil constriction falls below 30% of the natural pupil size. Therefore, a 40% to 50% reduction in pupil size represents a range within which near vision is improved and the quality of distance vision is not sacrificed, under all lighting conditions.

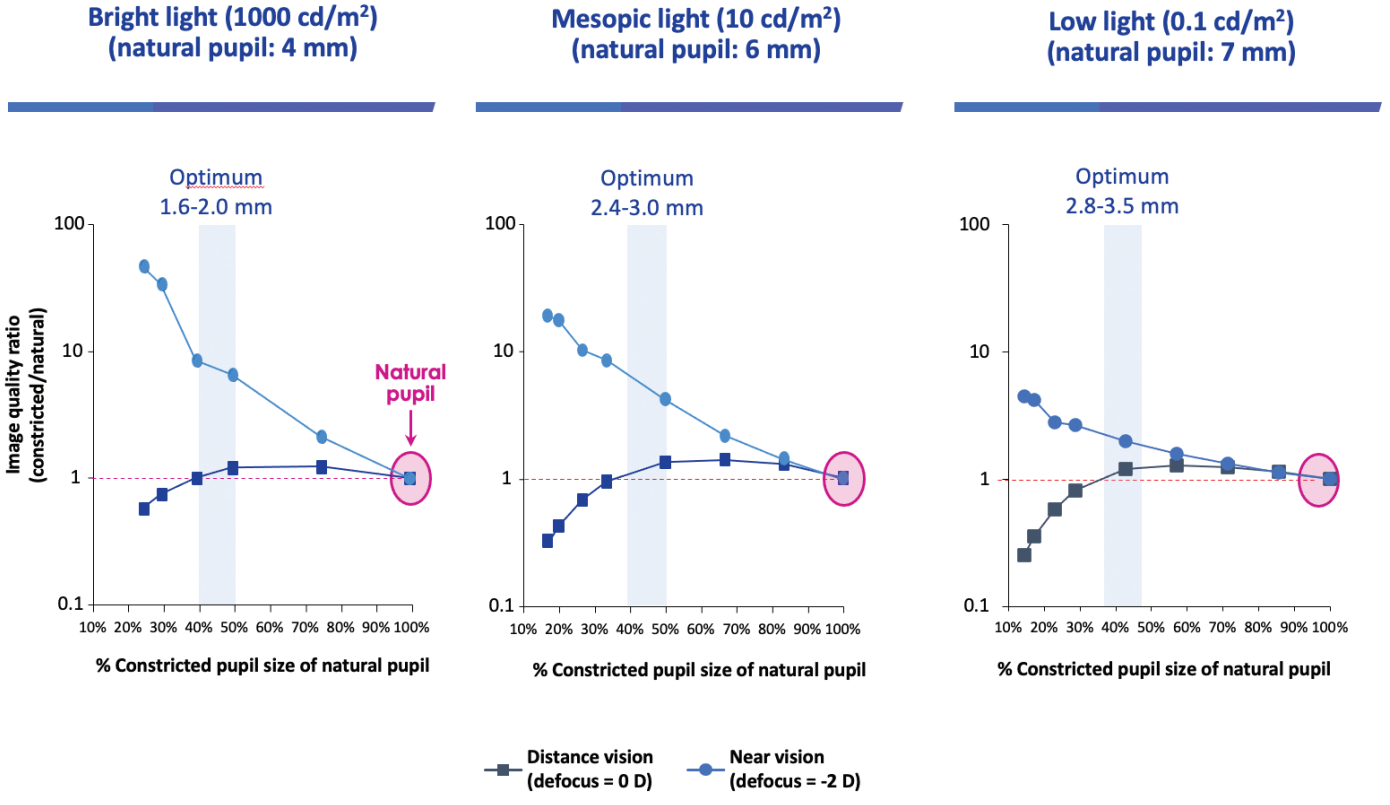

Figure 2. Image quality of near and distance vision under different lighting conditions and with different levels of pupil constriction. Adapted from Xu et al. *Optom Vis Sci.* 2016;93(11):1409-1419.[10]

The visual system is already a dynamic one. How it changes with age and/or surgery will affect the range of options that can successfully be used to treat presbyopia. For example, patients who have previously had radial keratotomy procedures may benefit from pupil constriction in bright light conditions because we reduce the influence of the cornea on their functional vision. However, under low light conditions, the same constricted pupil reduces their functional ability and dilating the pupil would reintroduce the impact of the existing higher-order aberrations. Therefore, pupil constriction is not an entirely viable option for these patients and could become a significant issue depending on their mix of daily activities and hobbies, and the lighting conditions under which these are performed.

As eye care practitioners, appreciating how the optics of the different components in the eye impact functional vision and how the optics change with age or surgery will help us understand how different therapies affect the optical system, identify which patients may benefit from therapies and, more importantly, adequately counsel patients on what they can expect from treatment.

PHARMACEUTICAL THERAPIES FOR PRESBYOPIA

Dr. Dunbar: Some of us have experience with pilocarpine in managing patients with glaucoma, before we started using prostaglandins. Many of these patients had great near vision because of the pinhole effect created by pilocarpine. As a cholinomimetic drug, pilocarpine lowered IOP by affecting trabecular outflow. It also acts as an agonist for muscarinic receptors in the parasympathetic system to contract the ciliary muscle (increases lens sphericity and refractive power) and the iris muscle (miosis increases depth of focus).[12] This is precisely why miotics are a viable option to treat presbyopia. They work at the iris plane to increase depth of focus. We also know that pilocarpine has a relatively short half-life, so the constricted pupil returns to its natural size between 4 to 6 hours, depending on the individual. In the glaucoma era, pilocarpine was dosed four times a day which led to sustained pupil constriction and other undesirable adverse events; however, clinical trials for pilocarpine-based presbyopia treatments use less frequent dosing.

Dr. Cunningham: The pilocarpine concentrations are also lower. In glaucoma, pilocarpine was used at a concentration between 2% to 4%. We had a patient who noticed floaters and flashes in his vision after administering a drop of pilocarpine 1.25% at home. He requested to come to the office immediately. We were able to dilate his pupil without too much difficulty for the retina exam. It did take longer than normal, and the dilation was not maximal, but it could be done.

Dr. Dunbar: An ideal miotic would:

1) Have a good safety and tolerability profile
2) Be comfortable to use so that the patient remains motivated to continue using medication—pilocarpine has a pH of about 4.5, which can sting and burn the ocular surface, so any pilocarpine-based medication should have pH balance
3) Have low blur/not compromise distance visual acuity
4) Induce minimal headaches/brow aches, which was historically seen in patients using pilocarpine as a glaucoma treatment
5) Have a duration of effect between 6 to 8 hours and allow flexible dosing because patients like the option of a treatment that has a decent duration of therapeutic effect but eventually wears off so that it can be used as needed, ie, on a night out, the weekend, for computer work during the workday
6) Have an immediate onset of action
7) Maintain functional vision, which goes beyond 20/20 VA (or J1+) to include the ability of patients to view their devices comfortably and see in dim lighting and at different distances.

We have learned a lot from the recent approval of pilocarpine 1.25%. Some of our preconceptions about pilocarpine partly stemmed from its use in glaucoma management. However, the pilocarpine-based presbyopia therapies, of which there are a few in the pipeline, have tried to maintain the therapeutic effect of the drug while trying to minimize its negative aspects, eg, headaches/brow aches, stinging, and burning.

With pilocarpine 1.25%, the concentration of the drug was chosen specifically because it balanced optimal pupillary constriction, good functional vision, good distance vision, and all under varied lighting levels. The formulation is optimized so that the acidic pilocarpine is able to adapt to the physiological pH of tear film and mitigate issues of discomfort. In the GEMINI 1 and 2 phase 3 clinical trials (N = 750 participants aged 40 to 55 years), pilocarpine 1.25% or placebo was administered bilaterally, once daily, for 30 days.[13,14] Both trials met their primary efficacy endpoint with a significantly greater proportion of patients treated with pilocarpine 1.25% gaining at least 3 lines in mesopic, high-contrast, binocular distance-corrected near visual acuity (DCNVA) at day 30, hour 3, and hour 6, without a loss of distance vision. Specifically, 75% of patients achieved at least a 2-line improvement in mesopic DCNVA, and 93% achieved a photopic DCNVA of 20/40 or better.[13,14] These data suggest that functional vision was relatively well-preserved.

Looking at the response rate of at least a 3-line gain in mesopic DCNVA, there was a rapid onset of therapeutic effect within 15 minutes, which peaked around 40% by 1 hour.[13,14] Around hour 6, the response rate was around 20%, which is still a fairly long duration of effect. Improvements in distance-corrected intermediate visual acuity (DCIVA) lasted up to 10 hours.[13,14] While some patients experienced longer durations of therapeutic effect, others complained that it wore off after 4 or 5 hours. In response to this, the phase 3 VIRGO trial (N = 230 subjects aged 40 to 55 years) evaluated twice-daily pilocarpine 1.25% over a 14-day period.[15] Subjects received the second drop 6 hours after the first was administered. The primary endpoint was met with significantly more patients gaining at least 3 lines of mesopic DCNVA with no more than 1 line loss in corrected distance visual acuity (CDVA) at day 14, hour 9 versus placebo. The twice-daily use of pilocarpine 1.25% has not yet been approved by the FDA.[15]

The GEMINI trials had no treatment emergent serious adverse events. The most common treatment emergent nonserious

adverse events were headache (14.1%) and some visual impairment (4.3%).[13,14] We know from the use of pilocarpine for glaucoma management that it is associated with an increased risk of retinal tears, retinal detachments, and posterior vitreous detachment (PVD).[16-19] The mechanism of action involves pilocarpine-induced forward displacement of the lens and vitreous due to ciliary and iris muscle contraction. While none of the patients in the clinical trial developed retinal detachment, there have been some cases reported since the FDA approval of pilocarpine 1.25%.[20,21] Within a total of 150,000 commercial prescriptions (as of December 2, 2022), 36 retinal detachments have been reported along with some retinal tears and vitreomacular traction (as of September 30, 2022).[22,23] This equates to an approximately 0.02% risk of retinal detachment.

Jack L. Schaeffer, OD, FAAO: The risk is less than the possibility of developing an ulcer from a contact lens. The other reason that we may have seen the greater incidence of retinal detachments in the real world than what was observed in the clinical trials, could be poor patient screening. In those early days, we should have excluded patients who had an inherently higher risk of retinal detachment, eg, myopes with retinal tears or lattice degeneration.[16,18]

Dr. Dunbar: The next pilocarpine agent in the pipeline is 0.4% pilocarpine (CSF-1). It is a preservative-free, lower concentration formulation in a proprietary multifaceted vehicle with a pH of 6. A study showed that the formulation remained stable for at least 18 months in refrigerated storage and an additional 3 months at room temperature, despite being preservative-free.[24] Longer studies are ongoing. Specifically, the formulation was designed to ensure an effective dose of pilocarpine was administered upon instillation even at a near-neutral pH, at which pilocarpine would typically degrade and bioavailability would be affected.[25,26]

Over 600 participants aged 45 to 64 years were enrolled in the 2-week NEAR 1 and 2 phase 3 trials.[27] CSF-1 was administered bilaterally, twice a day. During week 1, the second dose was administered 2 hours after the first dose and during week 2, the second dose was administered 3 hours after the first dose.[28] In the NEAR 2 trial (N = 304 participants), the primary endpoint was met with a significantly higher proportion of patients receiving CSF-1 gaining at least 3 lines in mesopic DCNVA without losing more than 1 line in CDVA at day 8 and 1 hour after dose one in the study eye versus vehicle (41.6% vs 21.3%, respectively; Figure 3). This difference was significant at all time points tested and the treatment effect was further amplified 1 hour after the second dose was administered. Overall, by hour 5, 46.1% versus 19.3% of participants, respectively, had improved mesopic DCNVA without significant loss of CDVA. The majority of participants receiving CSF-1 achieved at least a 2-line improvement in mesopic DCNVA without losing more than 1 line in CDVA at all time points. The most common treatment emergent adverse events were headache (9.8%), brow ache (2.6%), blurred vision (7.2%), and installation site pain (5.9%). Less than 5% of all treatment emergent adverse events were moderate, with 95.3% of them being mild. There were no serious adverse events.[28] The company completed its New Drug Application filing with the FDA in January 2023.[29]

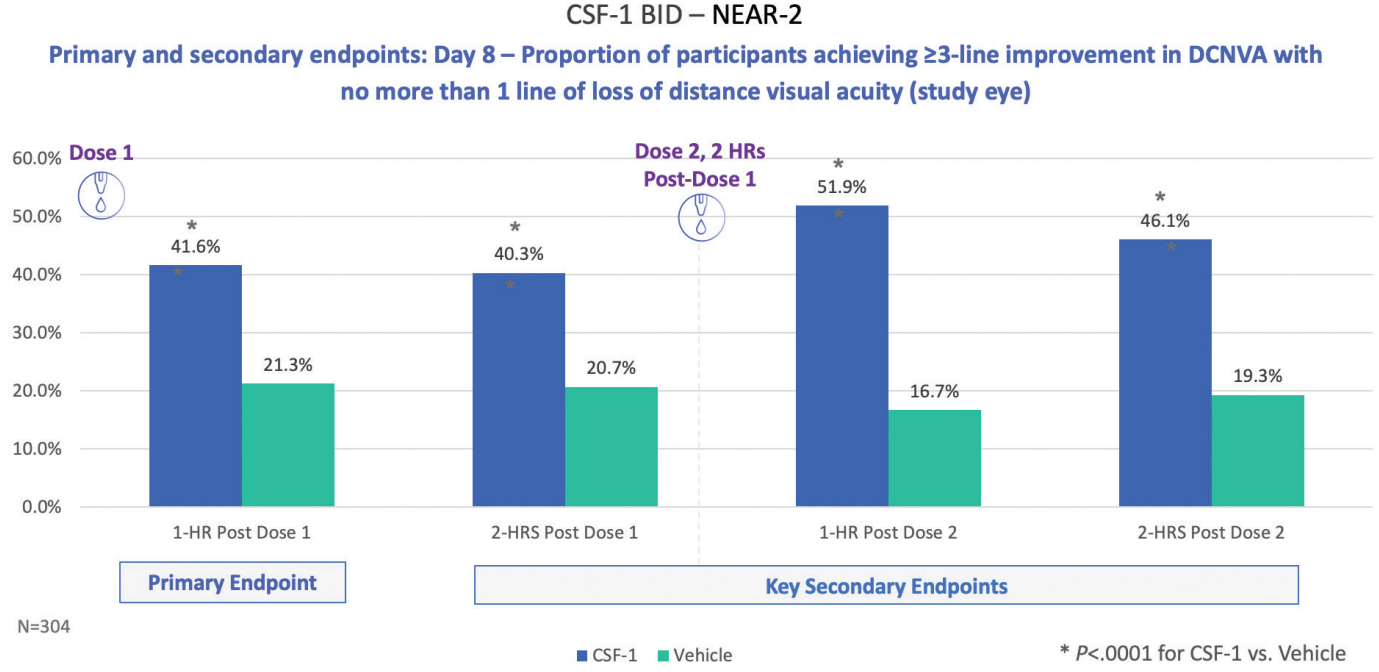

Figure 3. CSF-1 administered twice a day met the primary endpoint of improved near vision without loss of distance vision.[28]

Last but not least, we have microdosing technology with the Optejet dispenser, which is designed to deliver a 6 µL to 8 µL volume of pilocarpine 1% or 2% as a spray that coats the ocular surface.[30] This volume is consistent with tear film capacity and is designed to reduce overexposure to the drug and any preservatives that may irritate the ocular surface.[30] A survey of 100 patients with presbyopia between 40 and 55 years of age reported that four out of five patients preferred this microdosing delivery device over conventional eye drops.[31] The VISION-1 phase 3 trial (N = 84 patients) reported that pilocarpine 2% was superior to placebo in improvement in high-contrast binocular mesopic DCNVA 2 hours after treatment.[30] It was also well-tolerated with less than 3% of patients reporting headaches/brow aches. All adverse events were mild and transient.[30] Similar results were recently reported in the VISION-2 trial (N = 140 patients).[32]

Dr. Cunningham: These results seem promising, but I do wonder whether the mechanism of delivery will induce anxiety, similar to what is experienced by patients using noncontact tonometers.

Dr. Garlich: It seems to be very user-friendly. The company is also undertaking clinical trials evaluating atropine-based medication for children with high myopia and even children can administer the drug via the dispenser.

Dr. Dunbar: I agree that there may be some anxiety associated with this method of delivery, but it will be interesting to see more detailed data from these trials, as they are released. Regardless, if it receives FDA approval, it is going to be another tool that we may be able to offer to our patients.

A PRACTICE-BUILDING OPPORTUNITY

Dr. Schaeffer: Pharmaceutical options for presbyopia are a disruptive technology. We have not previously had miotics specifically formulated to treat presbyopia. It is perhaps not surprising that there has been slow adoption of pilocarpine 1.25%, which is currently the only FDA-approved therapy available. Part of this may be because most of us do not know how to use it, when to use it, and which patients are good candidates.

A suitable age range for these therapies would be similar to what was used in the clinical trials, ie, 40 to 55 years. However, age is not a strict criterion, as some older patients may respond just as well as younger ones. For example, the NEAR 1 and 2 trials enrolled patients up to 64 years of age.[27,28] Next, measure their baseline refraction—are they hyperopes, emmetropes, or myopes? Pilocarpine is known to induce a myopic shift, so this may increase distance visual acuity in baseline hyperopes.[33,34] At the same time, it may increase the risk of additive myopic blur in baseline emmetropes and low myopes.[33,34] Assess their near vision range and make sure you understand their expectations for their range of vision. We can then consider how patient-specific characteristics like profession, hobbies, iris color, history of refractive surgery, presence of ocular surface disease, contact lens wear, and monovision configuration will influence how pilocarpine-based miotics may perform for individual patients. For example, an accountant who spends several hours on the computer may or may not be a good candidate. It depends on several other factors.

Dr. Dunbar: Yes, I have a patient who is an accountant who loves pilocarpine 1.25%, but he is frustrated when it wears off too quickly. He would benefit from a slightly more durable therapeutic effect or the ability to administer a second dose.

Dr. Schaeffer: Right, it's an individualized decision. In the same vein, if you have a run of three or four patients who don't seem to be suited to the therapy, don't be discouraged. It's just a matter of identifying the reasons why it may not have suited them. For example, accommodation and pupil constriction stimulated by pilocarpine is significantly greater in people with light irises than dark irises.[35,36] A patient with blue irises may not like a highly constricted pupil and deem the therapy a failure.

In this sense, patient selection and, specifically, education is important. We need to be able to explain the mechanism of action so that patients have some understanding of how their vision will improve. We then set realistic expectations on their vision gains and, of course, thoroughly counsel them on the side effects. Make sure we understand their needs and expectations from the therapy. If they expect the effect of the drops to last all day, and do this 7 days a week, explain to them why this will not be possible. For most patients, miotics will be an adjunct treatment, used concomitantly with other management strategies such as glasses, contact lenses, or possibly even cataract surgery.

Dr. Cunningham: We thought these pilocarpine eye drops would be a great adjunct after cataract surgery, but the therapeutic response has been variable compared to a 45-year-old hyperope, for instance.

Dr. Schaeffer: Pharmaceutical therapies are also the perfect opportunity to move toward a fee-for-practice model in optometry. Oxymetazoline hydrochloride ophthalmic solution is a prescription eye drop that is used to treat acquired blepharoptosis in adults and is a drug that is sold in-office. Pilocarpine-based eye drops for presbyopia can follow a similar model if we take the time to explain to our patients that the treatment option exists and how it works.

Dan Press, OD, said, about myopia management services: "The mindset for providing myopia management services should be on reducing the rate of progression of myopia and not necessarily on the specific tools used. This mindset shifts the value focus from the expense/specialization of the materials used to the professional services and expertise involved in the care." This could be applied to presbyopia management services as well. While it may not be as comprehensive as myopia management, we are still providing an overall service that includes a comprehensive eye exam, patient

education and counseling, presbyopia treatment, and follow-up in-office/virtual visits. All of this takes time.

A comprehensive eye exam is essential before starting the presbyopia-correcting eye drop journey. Look at the peripheral retina through a well-dilated pupil to make sure patients don't have any high-risk features. Evaluate the vitreoretinal interface. I would recommend that our colleagues not rely solely on widefield imaging. The use of two additive dilating agents allows for a larger pupil to visualize all retinal quadrants. Consider comorbidities such as high myopia, pseudophakia, and partial PVDs. As Dr. Dunbar highlighted, pilocarpine-based eye drops have a small but serious risk of retinal detachment. Checking the eye thoroughly ensures that we increase our chances of success with these eye drops. Again, this is all part of a larger service and could justifiably attract a fee.

Patient counseling for this therapy is key. If a patient has mild lattice degeneration but is very enthusiastic about using these eye drops, you will need to spend time educating him or her about the possible complications and associated signs and symptoms. This patient will also need to be observed more frequently to monitor for retinal changes. On the other hand, if you perform OCT imaging of the macula and notice a vitreal traction on the same enthusiastic patient, you should explain why it may not be a good idea to start therapy. You may even suggest a follow-up in 6 months to reassess his or her candidacy.

Dr. Dunbar: Currently, there is no standard of care for how to assess patients for these eye drops. A macula OCT is not mandated, but most optometrists will have access to OCT imaging. Having discussed the importance of detecting vitreoretinal issues that may place some patients at a higher risk for retinal detachment, some practices may consider making macula OCT part of the screening protocol. However, the risk of retinal detachment is very low.

Dr. Schaeffer: I completely agree. OCT imaging is a value-add.

Dr. Garlich: How would you present the idea of needing to perform a macula OCT to these patients? Do you think that the extra testing and closer monitoring might scare them off from the treatment option?

Dr. Schaeffer: Quite the opposite. Patients who really want the product will feel like they're in safer hands. It's in the way we present it. We have these presbyopia-correcting eye drops and a full service to make sure we give them the best care possible. At our practice, that service includes a dilated eye exam, widefield imaging, macula OCT, follow-up, etc. As long as we explain why these tests are needed and reiterate that the chance of a retinal detachment is very small, I think patients will appreciate that honesty and diligence in care.

Dr. Garlich: Patient education includes talking about the risks and putting things into perspective. For example, the refractive surgeon we work with is comfortable performing LASIK on patients who have atrophic retinal holes. For these patients, the risk of retinal detachment is significantly higher with LASIK than what we've seen with presbyopia-correcting eye drops so far. Some surgeons would not be comfortable performing LASIK in such cases. There will be varied levels of comfort and appetites for risk amongst ophthalmologists and even optometrists who prescribe pilocarpine-based eye drops.

Dr. Schaeffer: Yes, this sort of nuanced discussion is exactly the justification for charging a fee. When you consider fee-for-service practice protocols, ask yourself these four questions: What is the value of your services? What are your office overhead costs? What is the quality of care and protection you provide? What is your level of expertise? You are spending time counseling the patient, explaining the technology of the treatment and recommended testing, and monitoring the patient. Don't shy away from instituting a fee-for-service model. You may not wish to charge a fee in the early stages while you're understanding whether these therapies are a good fit for your practice. I would encourage everybody to at least try it out because these therapies will soon become a part of our treatment paradigm for presbyopia.

Dr. Dunbar: When you prescribe the eye drops, have patients use it for at least 1 to 2 weeks rather than abandoning it after one dose. You never know which circumstances will work best for each patient. Remember, this is an adjunct therapy. Have your patients explore what situations or activities benefit from using these eye drops. Some patients may also experience an initial dimming of vision, which eventually goes away, and brow aches. The longer trial period gives them time to understand whether these side effects bother them, if they dissipate over time, or if they get used to it.

Dr. Cunningham: From a functional standpoint, we're altering how patients see. There will be a degree of neural adaptation in all patients. It may take a few hours for some and weeks for others. In addition to dimming vision, most patients will also claim there's a burning sensation; however, as with the dimming, the burning sensation is not persistent. It does go away. We see this in the clinical studies as well.

Photopic vision will be relatively consistent across patients. Mesopic and scotopic vision can vary and that's the result of higher-order aberrations and diffractive optics of whatever task they're performing. If they complain that they cannot read the back of a lottery ticket but computer work is fine, re-educate them on what they can and cannot do with these drops.

Dr. Schaeffer: Make sure you discuss nighttime driving. We know that patients will experience dimming of vision. They may need to hold off on driving or have someone drive them until they feel comfortable driving at night with the drops.

Dr. Garlich: I say the same thing to these patients. I'd also say that to a patient with monovision.

Dr. Cunningham: Conversely, I have had patients who are first responders who love the drops because it makes the flashing lights they are constantly around so much more bearable.

CASE 1: THE INCIPIENT PRESBYOPE

Dr. Garlich: A 46-year-old man presented for his eye exam at my clinic complaining of near vision impairment. His biggest annoyances were that he needed to use a flashlight to read the menu in a restaurant and his friends were making fun of him for the enlarged font size on his phone. His last eye exam was 30 years ago, but he was healthy overall, plano in the distance, no issues of dry eye on screening, and had a normal fundus exam. He only needed near vision correction. This is exactly the type of patient who comes to the clinic having heard about the presbyopia-correcting eye drops or becomes frustrated enough with his near vision to seek treatment. Where would you start?

Dr. Dunbar: I would first talk about OTC reading glasses because they're easy, cheap, and portable. I'd also explain that he'd need to take them on and off, which could become frustrating. That would then lead to the option of progressive glasses. I would then mention that the FDA recently approved a presbyopia-correcting eye drop, which retails for around $80 and lasts between 4 to 6 hours. If that was an option that interested him, I'd offer to prescribe it. I do talk about it with most patients and let them make the decision themselves. It's often received positively.

Dr. Schaeffer: We will, over time, have more options in this treatment category. Once they become available, that influx of patients will come. This patient is the perfect candidate for these drops, and we should practice speaking to them about it.

Dr. Garlich: I have heard concerns from colleagues, particularly practice owners, about whether these drops will cannibalize sales of glasses or contact lenses. As we've discussed, these drops are not a full-time option. They will need to be used with other solutions.

As Dr. Dunbar mentioned, I did offer this patient all the options available to him, ie, reading glasses, progressive lenses, multifocal or monovision contact lenses, and the presbyopia-correcting eye drops. We all routinely go through the first three options with patients, it's just a matter of including that fourth option in the discussion. A well-informed patient is a happy patient.

This patient was prescribed pilocarpine 1.25% and reading glasses. He was a great example of a new patient needing help and being able to receive flexible treatment because he was a good candidate for all of them. Would you institute any changes to the way you follow-up with patients if they are prescribed these eye drops?

Dr. Schaeffer: The follow-up visit is what we need to learn to do. I would recommend that it become part of the treatment protocol. If we've chosen the right patients, we must gauge whether it's working for them and if it's not, whether they're using it as intended. It's a learning process. The uptake of pilocarpine 1.25% has not been nearly as high as initially expected despite impressive clinical data. Part of that, as we discussed, could be that eye care practitioners are unsure of how to use these drops. Another aspect is making sure patients are giving it their best shot. More than 30 million people use readers and many of them would appreciate the flexibility of not being entirely reliant on readers. These eye drops could help them do that.

Dr. Dunbar: If you don't prescribe it, patients will likely get it from another practice and wonder why their optometrist did not offer them the option.

CASE 2: THE PRESBYOPE WITH RETINAL HOLES

Dr. Dunbar: I had a similar case of a 47-year-old man who had 20/20 uncorrected distance visual acuity but needed near vision correction. He also preferred not to wear reading glasses.

However, the dilated fundus exam showed that he had two atrophic retinal holes in the left eye that were inferior temporal. The right eye was unremarkable. We still don't know if this is a true contraindication. I talked with him about the drops and specifically explained that he needed to be cognizant of the signs and symptoms of retinal detachment. If I had prescribed the drops, I would follow-up within 1 to 2 months. The question of follow-up is a much newer consideration with these drops, and we don't have any established rules.

Dr. Schaeffer: With this patient, I would not prescribe the drug. Until we know more, why take that chance?

Dr. Cunningham: If the patient were referred to a retina specialist who reported that the atrophic holes were well-demarcated or heavily pigmented with no chance of retinal detachment, how would we then proceed?

Dr. Dunbar: I would then consider whether they had a PVD and if the posterior hyaloid were intact. You could detect PVD if you saw a Weiss ring, but you would likely need an OCT for the latter. If neither of these posed an issue, you may feel the risk of retinal detachment was low and feel more comfortable prescribing the drops.

The more pharmaceutical therapies for presbyopia become available to us, the more experience we will collectively have with these borderline patients. We may even see key differences between the therapies, so it's important that optometrists become more comfortable talking about it as a treatment option and following up with patients who do use it. The treatment modality is still young, and we have a lot to learn. ■

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RESHAPING EYE CARE: INNOVATIVE PHARMACEUTICAL OPTIONS FOR PRESBYOPIA

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DEMOGRAPHIC INFORMATION

Profession
___ MD/DO
___ OD
___ NP
___ Nurse/APN
___ PA
___ Other

Years in Practice
___ >20
___ 11-20
___ 6-10
___ 1-5
___ <1

Patients Seen Per Week (with the disease targeted in this educational activity)
___ 0
___ 1-15
___ 16-30
___ 31-50
____ >50

Region
___ Midwest
___ Northeast
___ Northwest
___ Southeast
___ Southwest

LEARNING OBJECTIVES

Did the program meet the following educational objectives?	Agree	Neutral	Disagree
Summarize the clinical/behavioral symptoms, visual acuity, and near vision correction that characterize mild, moderate, and advanced levels of presbyopia	_____	_____	_____
Discuss the optics of the pinhole effect and how it improves functional vision	_____	_____	_____
Describe the mechanism of action and evaluate the latest clinical evidence for pilocarpine-based miotic agents for the treatment of presbyopia	_____	_____	_____
Review patient-specific factors that may influence treatment outcomes, with a focus on the prevalence of dry eye in presbyopic patients	_____	_____	_____
Execute strategies to identify patients with presbyopia who may benefit from pharmacological therapies	_____	_____	_____

POSTTEST QUESTIONS

Please complete at the conclusion of the program.

1. Based on this activity, please rate your confidence in your ability to diagnose and treat patients with presbyopia (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).

a. 1
b. 2
c. 3
d. 4
e. 5

2. According to quality-of-life surveys, which of the following statements is TRUE?

a. The loss of near vision has the most significant impact on quality of life in comparison to other age-related ailments
b. The loss of near vision has a significant impact on quality of life in comparison to other age-related ailments, though not as much as arthritis
c. The loss of near vision has the least significant impact on quality of life in comparison to other age-related ailments
d. The loss of near vision does not significantly impact quality of life

3. All of the following represent nonsurgical solutions to presbyopia, EXCEPT:

a. Progressive lenses
b. Eye drops that modulate pupil size
c. Multifocal contact lenses
d. Corneal inlays

4. A 62-year-old patient presents to your office for exam. His near visual acuity measures J10 and he has complete inability to read at near and intermediate distance without aid. What severity of presbyopia does this patient have?

a. Mild presbyopia
b. Moderate presbyopia
c. Advanced presbyopia
d. No presbyopia

5. You are evaluating a 45-year-old patient in your office. She notes increasing difficulty with near tasks and desires a pharmaceutical solution. She is reluctant to wear bifocals. You recommend a miotic eye drop to aid with her presbyopia. She asks about the most common side effect. What do you answer?

a. Headache
b. Visual impairment
c. Conjunctivitis
d. Cataract formation

6. A 46-year-old man presents to your office for a routine eye exam. He notes blurry near vision and needing increased light to see a menu. His eye exam is unremarkable and you note emmetropia with +1.50 add OU. All of the following are reasonable treatment options for this patient, EXCEPT:

a. OTC reading glasses
b. Progressive glasses
c. Pilocarpine eye drops
d. Dorzolamide eye drops

7. What is the estimated annual economic loss globally due to uncorrected presbyopia?

a. $1 to $5 billion
b. $6 to $10 billion
c. $11 to $25 billion
d. $50 to $75 billion

8. A 48-year-old presbyopic patient presents to your office for evaluation. He is increasingly frustrated by his loss of near vision and desires a solution. He measures plano at distance with a +1.50 near correction. All of the following are reasonable options for this patient's presbyopia, EXCEPT:

a. Single vision spectacles
b. Multifocal contacts
c. Pupil-modulation drops
d. Intense pulsed light therapy

9. A 54-year-old patient presents to your office for evaluation. He notes decreased near vision only in dim light, and is having increasing difficulty reading his dashboard when driving at night. According to the American Optometric Association classification, how would his presbyopia be characterized?

a. Incipient
b. Absolute
c. Nocturnal
d. Functional

10. Which of the following statements about the pinhole effect and the iris is TRUE?

a. A smaller pinhole at the iris plane can improve depth of field without compromising peripheral vision
b. A larger pinhole at the iris plane can improve depth of field without compromising peripheral vision
c. A smaller pinhole at the iris plane can worsen depth of field but improve peripheral vision
d. A larger pinhole at the iris plane can worsen depth of field but improve peripheral vision

11. Which of the following describes the mechanism of action of pilocarpine?

a. Cholinomimetic drug
b. Adrenergic drug
c. Aqueous suppressant drug
d. All of the above

12. What is the approximate time of onset for 1.25% pilocarpine HCl?

a. ~1 hour
b. ~30 minutes
c. ~15 minutes
d. ~2 hour

13. A 45-year-old presbyopic patient presents to your office. He is interested in a nonsurgical option to treat his presbyopia. Which of the following is a reasonable option?

a. Pilocarpine drop
b. Dorzolamide drop
c. Latanoprost drop
d. Timolol drop

14. Which of the following represents an ophthalmic finding that might impact your decision to prescribe presbyopia-correcting drops?

a. History of allergic conjunctivitis
b. History of retinal tears and presence of lattice degeneration
c. Diagnosis of glaucoma
d. Presence of cataract

ACTIVITY EVALUATION

Your responses to the questions below will help us evaluate this activity. They will provide us with evidence that improvements were made in patient care as a result of this activity.

Rate your knowledge/skill level prior to participating in this course: 5 = High, 1 = Low____

Rate your knowledge/skill level after participating in this course: 5 = High, 1 = Low____

This activity improved my competence in managing patients with this disease/condition/symptom. _____ Yes _____No

Probability of changing practice behavior based on this activity: _____High _____ Low _____No change needed

If you plan to change your practice behavior, what type of changes do you plan to implement? (check all that apply)

Change in pharmaceutical therapy _____
Change in nonpharmaceutical therapy _____
Change in diagnostic testing _____
Choice of treatment/management approach _____
Change in current practice for referral _____
Change in differential diagnosis _____
My practice has been reinforced _____
I do not plan to implement any new changes in practice _____

Please identify any barriers to change (check all that apply):

_____ Cost
_____ Lack of consensus or professional guidelines
_____ Lack of administrative support
_____ Lack of experience
_____ Lack of time to assess/counsel patients
_____ Lack of opportunity (patients)
_____ Reimbursement/insurance issues
_____ Lack of resources (equipment)
_____ Patient compliance issues
_____ No barriers
_____ Other. Please specify: _____

The design of the program was effective for the content conveyed	___ Yes	___ No
The content supported the identified learning objectives	___ Yes	___ No
The content was free of commercial bias	___ Yes	___ No
The content was relative to your practice	___ Yes	___ No
The faculty was effective	___ Yes	___ No
You were satisfied overall with the activity	___ Yes	___ No
You would recommend this program to your colleagues	___ Yes	___ No

Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced through your participation in this activity:

_____ Patient Care
_____ Practice-Based Learning and Improvement
_____ Professionalism
_____ Medical Knowledge
_____ Interpersonal and Communication Skills
_____ System-Based Practice

Additional comments:

_____

_____ I certify that I have participated in this entire activity.

This information will help evaluate this activity; may we contact you by email in 3 months to inquire if you have made changes to your practice based on this activity? If so, please provide your email address below.

_____

_____