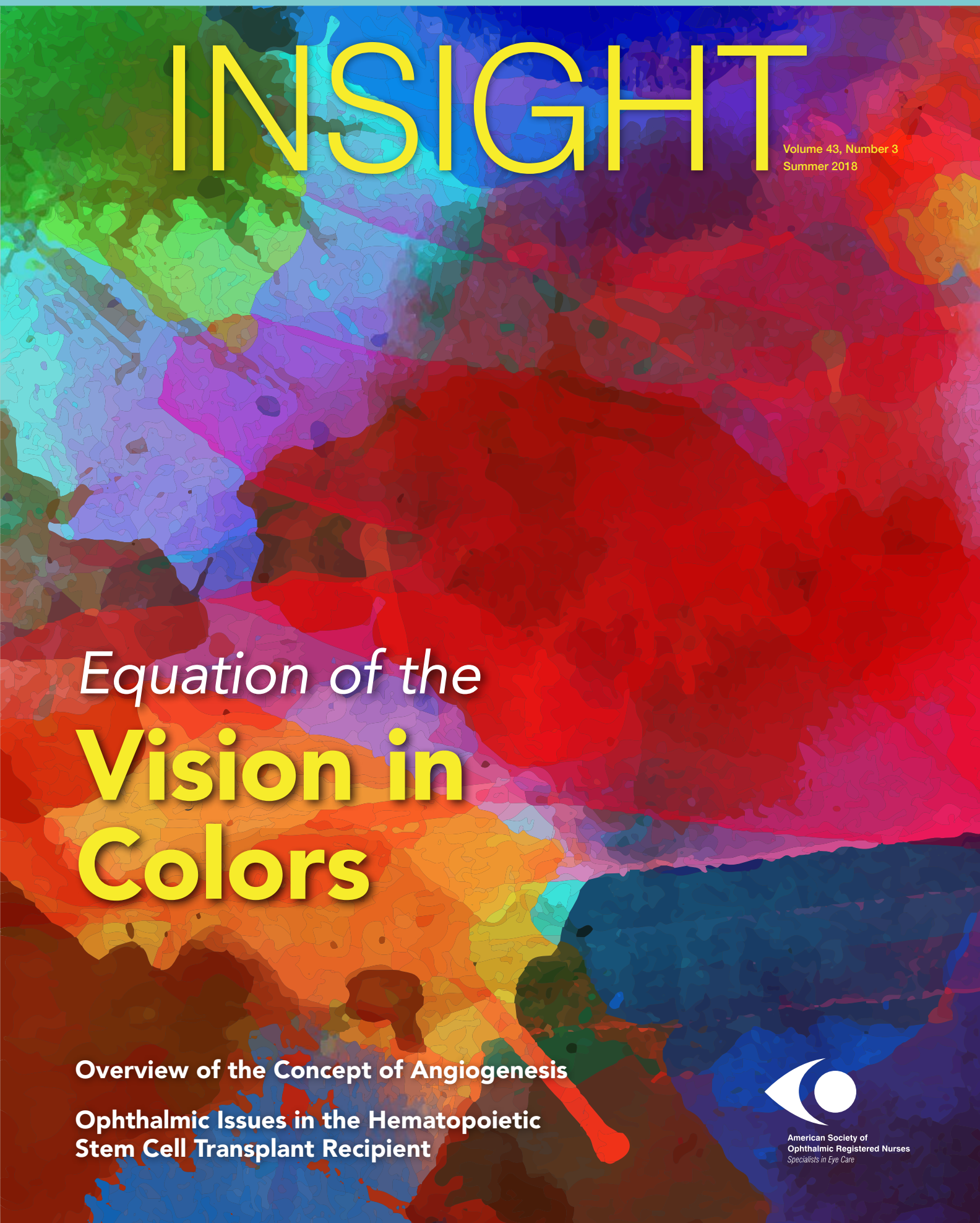
Journal of the American Society of Ophthalmic Registered Nurses

INSIGHT

Volume 43, Number 3
Summer 2018



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INSIGHT

Volume 43, Number 3, Summer 2018. Insight—Journal of the American Society of Ophthalmic Registered Nurses (ISSN 1060-135X) is published quarterly (four issues per volume, one volume per year) by the American Society of Ophthalmic Registered Nurses, 655 Beach Street, San Francisco, CA, 94109.

SUBSCRIBER SERVICES: Domestic individual, $69; domestic student/resident, $35; domestic institution, $109; international individual, $79; international student/resident, $39; international institution, $119. Prices subject to change without notice. Printed in USA.

PUBLISHER
American Society of Ophthalmic Registered Nurses
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San Francisco, CA, 94109
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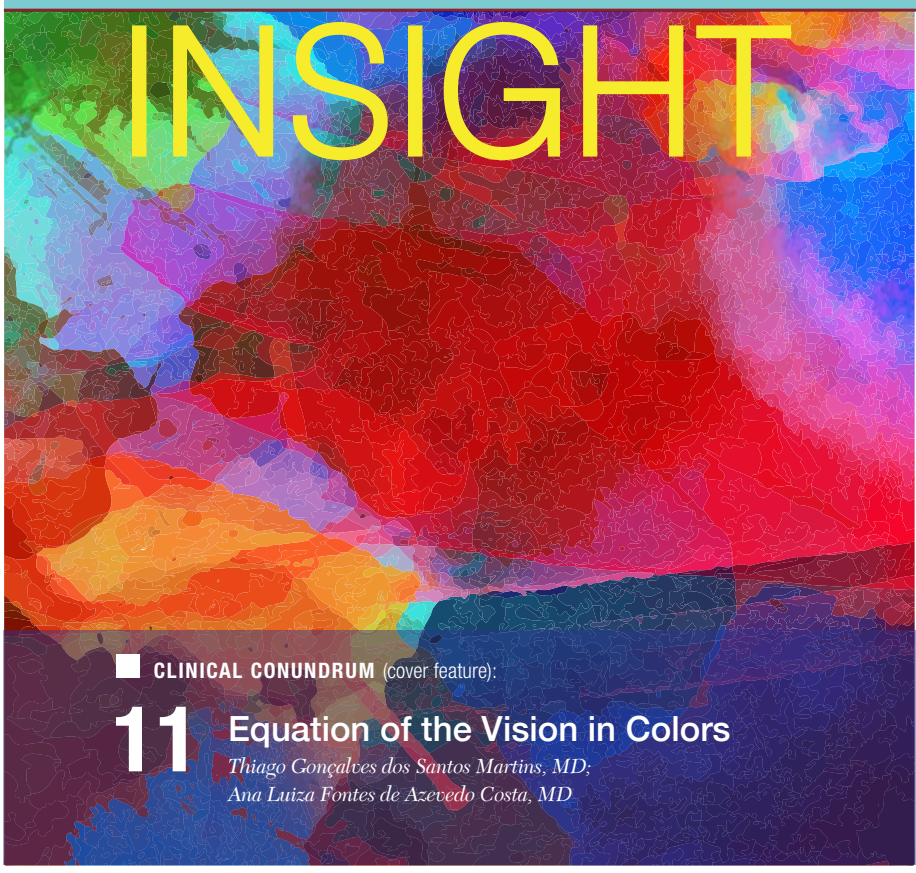

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INSIGHT

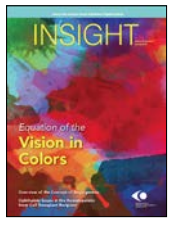
Contents *(continued)*

Additional Services

Indexed or abstracted in the Cumulative Index to Nursing & Allied Health Literature (CINAHL).

Correction:

In the Spring 2018 issue (Volume 43 Number 3), the Eye Wonder article 'Transportation and Vision Loss: Where Are We Now?' was written by Adele Crudden, PhD. This was noted in the table of contents and should be noted on the title page of the article, too. We apologize for any confusion.



Grow with Insight and learn more about angiogenesis on page 5.

PRESIDENT'S MESSAGE

The Value of ASORN Continuing Education

THE QUALITY OF OPHTHALMIC PATIENT CARE depends a great deal on the competency and leadership skills of the ophthalmic nurse. Each of us must be a strong, competent, knowledgeable, and consistent leader. Regardless of our specific titles or positions, we are challenged each day with numerous opportunities to lead. We must be visible, credible, and act with courage in the face of these challenges. And we must inspire competence, strength, and courage with our patients and fellow colleagues. To accomplish this, we have a professional responsibility to stay abreast of new regulations, refined techniques and technologies, and the latest evidence-based practice.

ASORN continuing education programs can help. The 2018 ASORN educational activities include innovative courses that are increasingly valuable at a time when shrinking budgets, mounting regulations, and uncertainty in reimbursements are a reality. As healthcare continues to change and evolve, continuing education is a great way to keep current with the latest developments in patient care and nursing practice. In addition, continuing education is a requirement in many states for re-licensure, and certification. Patients trust nurses to keep them safe and to be their advocates when they are unable to advocate for themselves. For the 16th year in a row, Americans' rating of the honesty and ethical standards finds nurses once again at the top of the list (http://news.gallup.com). Look to ASORN continuing education activities to help you keep current, serve as patient advocates, and provide safe, quality care to our ophthalmic patients.

The mission of ASORN is to foster excellence in ophthalmic patient care while supporting the ophthalmic team through individual development, education, and evidence-based practice. Seize this opportunity to participate in some of the exciting and relevant continuing education programs:

INSIGHT JOURNAL ARTICLES – Each quarter, the ASORN online journal provides many interesting articles, features, and at least one continuing education activity. To complete the continuing education activity and earn credits, look on EyeCareCE to complete the requirements for successful completion. In addition, EyeCareCE offers many other educational offerings for the ophthalmic provider. A huge thank you to EyeCareCE for providing a FREE course to ASORN members during the month of May 2018 in honor or Nurse's Week.

LIVE MEETINGS – There are numerous traditional live seminars provided by ASORN each year. There is still time to register for the upcoming two live 2018 programs which will provide skills and knowledge to enhance the care of patients in daily practice settings:

Austin, Texas: Combined Ophthalmic Symposium August 24-25, 2018
Chicago, Illinois: ASORN Annual Meeting – "Looking Toward the Future" October 26-27, 2018

WEBINARS – Five webinars are to be presented live in 2018, and available as recorded webinars for a period of time. Attending the live webinar allows the learner to ask questions of and interact with the speaker. Recording the webinar allows for more flexibility for the learner to attend. The ASORN Board of Directors has worked hard to find sponsorships for the webinar series, so these are FREE to members.

PUBLICATIONS – Although no longer available for continuing education credits, these publications continue to be outstanding resources for the ophthalmic nurse:

- *Ophthalmic Procedures in the Office and Clinic*
- *Ophthalmic Procedures ion the OR* and ASC
- *Care and Handling of the Ophthalmic Microsurgical Instruments*

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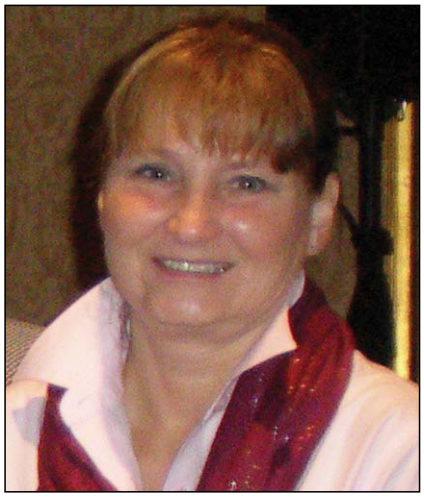

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VIEWPOINT

Spotlight on Ambulatory Care – Opportunities for Ophthalmic Nurses

ENORMOUS CHANGES ARE OCCURRING in the health care landscape that impact ophthalmic nurses, especially those in ambulatory care. These include payment reform and a shift toward value, the digital transformation and ever-growing use of technology, an increasingly aged and diverse population, and health care delivery that is moving from hospitals to the ambulatory care environment. While there is evidence of nurse value in the acute care settings, there is a paucity of metrics for ambulatory care nurse sensitive measurement (Mastal, Matlock & Start, 2016). Among the public there is continually high trust of nurses yet many don't understand what nurses do (Buresh & Gordon, 2013). For ophthalmic nurses specifically, clinicians and nurses of other specialties don't fully understand ophthalmic nursing practice (Marsden, 2014; Clouse, 2015). Without a clear understanding of the scope, capabilities, and outcomes of registered nurses work, their role and value in innovative future care models will be limited.

Over 3 million registered nurses (RNs) serve as the foundation of health care in the United States. Of these, 18% work in ambulatory care (Bureau of Labor Statistics, 2016). Ambulatory care nursing is a complex and multifaceted specialty of nurses who work independently and collaboratively in the design and provision of care across multiple settings that include clinics, offices, ambulatory care surgery centers, telehealth service environments, and patients' homes (American Academy of Ambulatory Care Nursing [AAACN], 2017). In 2010, 48.3 million ambulatory surgery procedures were performed in the United States and 16% of these were eye operations (Hall, Schwartzman, Zhang, & Liu, 2017). During this same year, approximately 55 million visits were made to office-based ophthalmologists for a variety of acute, chronic, and preventive ophthalmic care needs (Centers for Disease Control, 2010). These are among sites and opportunities for ophthalmic nursing practice leadership and innovation.

In their call-to-action report, the National Academies of Sciences, Engineering, and Medicine (2016) describe the critical impact eyesight has on individual's health and well-being in daily communication, education, employment, and personal independence. They indicate no reliable data exist on the number of people affected by all causes of vision issues but estimate 6.42 million have uncorrectable impairment. The consequences of vision impairment in adults include falls, injuries, social isolation, depression and impacts to other chronic conditions while children experience developmental, social and education challenges. Public awareness to the importance of good eye and vision health, early identification of problems and access to quality care, and enhancement of the health and functioning of those with vision impairments are among report recommendations. Ophthalmic RNs in the outpatient arena often serve as the primary contact with and advocate for patients, families and communities and can bring great value in these areas.

Implications for ambulatory care nurses, such as ophthalmic nurses practicing in the outpatient arena, include the need for leaders to understand ambulatory care nursing, support top of license nurse practice, and ensure effective, safe, and efficient care for populations and individuals (AAACN, 2017). Nurses, including ophthalmic nurses, must also partake in meaningful development, utilization, and benchmarking of ambulatory care nurse sensitive data to quantify their value. A summary report, with exemplars, outlines some of the important ambulatory care nurse sensitive structure, process, and outcome measures (Start, Matlock, & Mastal, 2016). Metric examples include staffing and skill mix, pain assessment and follow-up, RN demographics (degrees and certification), ambulatory surgery adverse outcomes, and readmissions.

The Institute of Medicine (IOM) Future of Nursing report (2010) called for nurses to practice to the full extent of their education and training, and to be full partners with physicians in the re-designing health care in the United States. Despite the trend toward ambulatory care, the RN workforce has declined in the ambulatory care

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Kathleen Mertens, DNP, MPH, RN

Marina Roizenblatt, MD; Julia Sein, MD; Peter L. Gehlbach, MD, PhD

CONTINUING EDUCATION

Overview of the Concept of Angiogenesis

ACCREDITATION:

This continuing education activity is provided by ASORN.

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DISCLOSURE:

The authors, planners and content reviewers have disclosed that they do not have a conflicting relationship of a financial, professional, or personal nature related to this activity.

There is no commercial or non-commercial company support for this CNE activity.

LEARNING OBJECTIVES:

1. Describe the vasculogenesis, angiogenesis, and arteriogenesis processes
2. Discuss the role of angiogenetic factors in select ocular diseases
3. Define the role of the ophthalmic nurse in management of common eye diseases caused by ocular angiogenesis

SUCCESSFUL COMPLETION

1.00 Nursing contact hour may be earned for this learner paced activity. Successful completion includes reading the article, completing an evaluation, taking an online post-test, and achieving a passing score of 80% or higher.

An email will be sent when the test is posted. To take the examination for continuing education credits, go to www.EyeCareCE.org. The expiration date for this activity is 3/31/2021 and will also be stated within the course description posted on EyeCareCE.

Three mechanisms mediating vascular formation and the subsequent remodeling process are vasculogenesis, angiogenesis, and arteriogenesis. During angiogenesis, new blood vessel formation and growth from pre-existing vessels is induced by a complex biochemical pathway occurring in developing tissues. This process takes place predominantly during the embryonic period and is generally quiescent in the adult organism. When it is present in adult tissue, it is generally related to pathologic conditions, such as hypoxia or inflammation.

Many proteins are directly or indirectly involved in coordinating the interactions between positive and negative regulators of angiogenesis. At any given time, a dynamic balance of pro-angiogenic and anti-angiogenic regulators determine whether angiogenesis will occur. Insufficient, excessive, or aberrant angiogenesis serves as a final common pathway to the pathogenesis of some of the most prevalent eye diseases worldwide. These include but are not limited to diabetic retinopathy, exudative age-related macular degeneration, corneal neovascularization, retinopathy of prematurity, retinal vein occlusion, neovascular glaucoma, and sickle cell retinopathy.

Therefore, all levels of the health-care provider system that deals with prevalent causes of blindness will benefit from a working understanding of angiogenesis. As vital members of the health-care team, nurses facilitate patient referrals to specialized eye care, educate patients and their families about the pathophysiology of their disease, assist in evaluation and treatment, and help ensure patient compliance.

Introduction

The morphological and functional characteristics of the blood vessel network are continuously changing during development. The three main mechanisms that mediate vascular formation and remodeling processes are vasculogenesis, angiogenesis, and arteriogenesis (Lutty et al., 2010; Semenza, 2007). In development, the blood vessels form during embryogenesis by vasculogenesis and angiogenesis, followed by arteriogenesis (Risau, 1997). Although these three processes might play similar roles in blood vessel network expansion, they are triggered by different mechanisms (Shi et al., 2017).

Classically, the concept of vasculogenesis describes the new blood vessel formation occurring predominantly during the stages of embryonic development, when angiogenic progenitor cells migrate to sites of vascularization (Diaz-Flores et al., 2017). "Angiogenesis" is defined as the process of new blood vessel formation and growth from other

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pre-existing vasculature that is induced by localized biochemical stimuli originating in the growing tissues (Falcon, Chintharlapalli, Uhlik, & Pytowski, 2016; Hillen & Griffioen, 2007). Finally, arteriogenesis is the remodeling and maturation of an existing vessel to increase its luminal diameter in response to increased blood flow, so that the initial vascular plexus becomes an adult vasculature (Heil, Eitenmuller, Schmitz-Rixen, & Schaper, 2006).

In order to guarantee tissue homeostasis through controlled growth and development, angiogenesis requires endothelial cell sprouting, proliferation, and migration, together with capillary tube formation. This process is essentially physiologic during the embryonic period for normal tissue growth, remodeling, and regeneration (Shi et al., 2017). It is generally quiescent in the adult organism, when angiogenesis usually occurs due to pathologic conditions, such as stress, regeneration, inflammation, organization of thrombi, collateral circulation development, and neoplasia (Diaz-Flores et al., 2017).

When blood supply is insufficient to supply local tissue demand for oxygen and nutrients, angiogenic factors are activated (Krock, Skuli, & Simon, 2011). Insufficient, excessive, or aberrant angiogenesis is involved in the pathogenesis of some of the most prevalent eye diseases worldwide, such as diabetic retinopathy, age-related macular degeneration (AMD), retinopathy of prematurity (ROP), retinal venous occlusion, and sickle cell retinopathy (Carmeliet & Jain, 2011; Ferguson & Apte, 2008).

Consequently, health care providers at all levels who care for patients diagnosed with prevalent causes of blindness may benefit from a basic understanding of the angiogenesis process. Patients can also benefit from such an understanding, insofar as a working knowledge of ocular neovascularization helps them learn about their diagnosis, understand their treatment choices, and make sense of treatment limitations. In this context, nurses are vital members of the health team and therefore should be trained to refer patients to specialized eye care whenever necessary, educate patients and their families about their disease, assist in evaluation and visual treatments, and ensure patient compliance.

Pathogenesis Overview

Angiogenesis is a complex process in which dynamic cascades of relevant signals and proteins serve as positive and negative regulators of blood vessel growth and formation (Campochiaro, 2004). Among the many negative regulators are thrombospondin, angiostatin, endostatin, molecules down-regulating vascular endothelial growth factor (VEGF), and pigment epithelium-derived factor. Angiogenesis stimulators include VEGF,

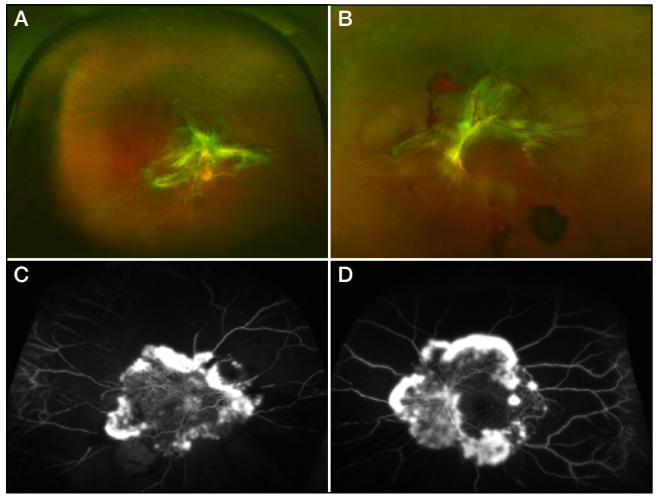

Figure 1. A and B: Color photographs of right and left eyes, respectively, with severe proliferative diabetic retinopathy associated with ischemic retina and retinal neovascularization. C and D: The corresponding late-phase fluorescein angiography images, showing diffuse vascular leakage.

fibroblast growth factor, angiopoietins, transforming growth factor, hepatocyte growth factor, connective tissue growth factor, and interleukin-8 (Conway, Collen, & Carmeliet, 2001; Witmer, Vrensen, Van Noorden, & Schlingemann, 2003), among others.

VEGF has been identified as a critical regulator of ocular angiogenesis, and this has led to the development of a number of approved therapies for ocular neovascularization (Campochiaro, Aiello, & Rosenfeld, 2016; Rubio & Adamis, 2016). Given the exceedingly high volume of anti-VEGF injections now administered worldwide, it is critical for the effective provision of care in health systems that nursing and other health professionals participate fully in the provision of comprehensive and cost-effective care in their communities (Austeng, Morken, Bolme, Follestad, & Halsteinli, 2016; Emsfors, Christensson, & Elgan, 2017; Randolph, 2014).

Ocular Diseases

Ocular angiogenesis is involved in the pathogenesis of diabetic retinopathy, exudative AMD, corneal neovascularization, corneal graft rejection, ROP, retinal vein occlusion, neovascular glaucoma, and sickle cell retinopathy. It is important to emphasize that these eye diseases represent the main causes of blindness worldwide (Dombrow & Adelman, 2011). As the all-important first point of contact for patients experiencing a perceived change in vision, nurses are often responsible for providing prompt access to care.

Diabetic Retinopathy

During the initial nonproliferative stage, diabetic retinopathy is characterized by microvascular degeneration that may progress to a proliferative phase if untreated (Lai & Lo, 2013). Ocular

diabetic complications are usually asymptomatic in early stages, and most can be prevented or minimized with adequate disease control. In this regard, specialized care providers, such as nurse educators, can teach patients how to diminish or eliminate risk factors for disease progression and to recognize clinical deterioration that requires care.

Chronic hyperglycemia induces biochemical changes in endothelial cells, leading to their degeneration and subsequent hypoxia due to insufficient vascular supply to retinal tissue. This environment increases VEGF release, along with release of many other angiogenic factors, resulting in the proliferative phase characterized by neovascularization (see Figure 1) (Crawford, Alfaro, Kerrison, & Jablon, 2009; Liu, Wang, Sun, & Chen, 2017). Unfortunately, the enhanced production of pro-angiogenic growth factors leads almost exclusively to pathologic preretinal neovascularization, and little revascularization of ischemic retina occurs (Duh, Sun, & Stitt, 2017). A further consequence is diabetic macular edema. Both angiogenesis and inflammation are involved in the pathogenesis of retinal disease in this setting (Romero-Aroca et al., 2016).

Exudative AMD

Diabetic retinopathy and AMD cause a disproportionate burden to the health-care system. At present they are considered the most prevalent retinal diseases affecting quality of life (Bressler, 2004; Song & Wong, 2014). Patients diagnosed with AMD have an upregulation of genes that promote retinal pigment epithelium changes together with an increase in VEGF expression that supports pathological angiogenesis (Ambati, Ambati, Yoo, Ianchulev, & Adamis, 2003). AMD causes significant visual impairment and necessitates frequent therapeutic injections of anti-VEGF agents. Anti-VEGF injection therapy is the gold standard in managing the resulting choroidal neovascularization in the exudative stage. However, some patients suffer worsening eye disease, despite anti-VEGF treatment, suggesting that other vascular mediators may also contribute to the disease pathogenesis (Cabral et al., 2017). The high cost of multiple anti-VEGF injections for AMD control is another reason nurses and other health-care professionals, as well as patients, need a broad understanding of anti-angiogenic therapy.

Corneal Neovascularization and Graft Rejection

The normal cornea enjoys a unique immune-privileged status because it lacks the lymphatics or blood vessels that would allow direct access to immune effector cells. However, pathologic response to tissue damage, resulting from ocular inflammation or immune-mediated graft rejection, might lead to the formation of blood and lymphatic "neovessels" within the normally avascular corneal stroma. This in turn results in lipid exudation, inflammation, opacity, and scarring (Benayoun et al., 2013; Dohlman et al., 2015; Emami-Naeini et al., 2014).

Immune-mediated corneal transplant rejection occurs when there is pathological lymphangiogenesis combined with hemangiogenesis, two closely linked processes. The influx of vascular cells into the stroma is the major route for disrupting corneal immune privilege. As a result, corneal antigens access lymph nodes, and this in turn leads to induction of adaptive immune responses, with a subsequent higher rate of graft rejection (Benayoun et al., 2013; Patel & Dana, 2009). Management of corneal graft rejection is based on early detection and aggressive corticosteroid therapy (Panda, Vanathi, Kumar, Dash, & Priya, 2007). Early detection is a great opportunity for nursing and other health team members to make a prognostic difference for their patients.

Retinopathy of Prematurity

ROP is a retinal vasoproliferative disease characterized by delayed physiological retinal vascular development that may lead to a pathologic vitreous and retinal neovascularization. The pathology is considered a leading cause of childhood blindness, significantly affecting the future quality of life and longterm healthcare costs of preterm infants exposed to high concentrations of oxygen (Wang, 2016).

The superficial and deep layers of the retinal vasculature are developmentally coordinated by gradients of growth factors. During the gestational period, the primitive retina remains avascular until the fourth month. Until then, it obtains nutrients from the hyaloid vasculature. Thereafter, prominent vasculogenesis and angiogenesis lead to hyaloid artery invasion of the nerve fiber layer. Disorganized vascular growth into the vitreous and at the border of the avascular retina occurs in infants who develop ROP (Suelves & Shulman, 2016). This can progress into tractional retinal detachment, which ultimately results in irreversible vision loss if not treated in a timely manner. In this situation, nurses can ensure that infants born prematurely have early access to specialized eye care for early diagnosis and prompt treatment, which correlate with a better visual prognosis.

Retinal Vein Occlusion

Pathological angiogenesis contributes to the visual consequences of both branch retinal vein occlusion and central retinal vein occlusion. These are prevalent diseases defined by a disrupted retinal blood supply and a high risk of subsequent visual impairment due to retinal edema and neovascularization. Vitreous concentrations of proteins related to hypoxia, angiogenesis, and inflammation are significantly elevated prior to clinical evidence of neovascular changes and enhanced vascular permeability

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leading to leakage of fluid into the macula. In recent years, anti-inflammatory and anti-angiogenic therapeutic approaches have been used to mitigate this disease pathway and to improve vision (Ehlken et al., 2015; Pielen et al., 2013). The presence of retinal vasculopathy in the absence of typical predisposing factors, especially in young people, is a warning sign that further systemic evaluation to rule out underlying hypercoagulability or hyperviscosity syndrome is warranted (Bressler, 2004). In this regard, nurse providers have an opportunity to impact the care of retinal vein occlusion patients and ensure appropriate follow-up.

Neovascular Glaucoma

Neovascular glaucoma is a potentially devastating form of secondary angle-closure glaucoma that usually occurs as a consequence of either a delayed diagnosis or an insufficient treatment of ocular ischemic diseases, such as proliferative diabetic retinopathy, ischemic central retinal vein occlusion, and ocular ischemic syndrome (Hayreh, 2007). Eye ischemia promotes gradual neovascularization over the trabecular meshwork and iris, which results in a fibrovascular membrane. The subsequent contraction of this membrane pulls peripheral iris into the angle, leading to further angle closure. The new vessels' growth is mediated by pro-angiogenic factors, which diffuse into the anterior chamber. Recent studies have demonstrated a significant association between increased ocular VEGF levels and pathological conditions that involve neovascularization or inflammation, such as neovascular glaucoma (Simha, Braganza, Abraham, Samuel, & Lindsley, 2009). In this setting, a number of studies have investigated the use of topical, intracameral, or intravitreal administration anti-VEGF as a therapeutic option. Neovascular glaucoma might be considered a severe complication in the setting of inadequate clinical control of prevalent retinal diseases, and its prognosis is often poor, resulting in visual loss and uncontrollable pain. Therefore, it is important for patients, nurses, and providers to understand this disease and its pathogenesis(Andres-Guerrero et al., 2017).

Sickle Cell Retinopathy

Sickle cell disease is the most prevalent genetic blood disorder. A specific hemoglobin mutation causes the sickled erythrocyte morphology that is responsible for defective oxygen transport as well as for the direct microvascular occlusion that affects the retina. The end stage is tissue hypoxia, a pro-angiogenic state, and anomalous neovascularization (Brittain & Parise, 2007; Scott, 2016). Proliferative sickle cell retinopathy is considered the most common cause of irreversible vision loss in patients with sickle cell disease (Jee et al., 2017). Laser photocoagulation is commonly used to prevent visual loss secondary to vitreous hemorrhage and retinal detachment (Myint, Sahoo, Moe, & Ni, 2015). The role of anti-VEGF therapy is being defined.

Conclusion

A large number of known and unknown factors are involved in the complex angiogenesis cascade. Novel factors have been identified over the past decade, better elucidating the molecular mechanism responsible for the pathogenesis of prevalent neovascular diseases, including but not limited to diabetic retinopathy, exudative AMD, corneal graft rejection, corneal neovascularization, ROP, retinal vein occlusion, neovascular glaucoma, and sickle cell retinopathy.

All levels of the multidisciplinary healthcare team serving patients diagnosed with prevalent causes of blindness should have a working understanding of related disease pathophysiology in order to establish an early diagnosis, educate, and care for their patients. Therefore, nurse care providers and clinical educators can best serve their patients with the most common causes of blindness by understanding ocular angiogenesis of common eye diseases and their often treatable complications.

The authors have no financial or conflicting interests to disclose.

Acknowledgments

MR: Lemann Foundation, Instituto de Visão-IPEPO, São Paulo, Brazil.

PG: Research to Prevent Blindness, New York, New York, USA, and gifts by the J. Willard and Alice S. Marriott Foundation, the Gale Trust, Mr. Herb Ehlers, Mr. Bill Wilbur, Mr. & Mrs. Rajandre Shaw, Ms. Helen Nassif, Mary Keck and Mr. Ronald Stiff.

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POST-TEST QUESTIONS

1. Which of the following is not a trigger for vascular formation?
- A. Angiogenesis
- B. Arteriogenesis
- C. Vasculogenesis
- D. Epitheliogenesis

2. Which of the following is a critical regulator of ocular angiogenesis?
- A. GRF
- B. ILGF
- C. VEGF
- D. PDGF

3. The remodeling and maturation of an existing vessel is known as:
- A. Angiogenesis
- B. Arteriogenesis
- C. Vasculogenesis
- D. Epithelialization

4. Which of the following is not an anti-angiogenetic factor?
- A. Integrin
- B. Endostatin
- C. Angiostatin
- D. Thrombospondin

5. The following changes occur in chronic hyperglycemia except:
- A. Hypoxia
- B. Macular edema
- C. Neovascularization
- D. Revascularization

6. Gestational primitive retina vascularization starts at:
- A. Three months
- B. Four months
- C. Five months
- D. Six months

7. How can nurses promote eye health in infants?
- A. Ensure early access to specialized eye care
- B. Perform eye examinations on all infants at birth
- C. Educate parents on common eye diseases in infants
- D. Administer eye drops to infants during hospitalization

8. Proliferative diabetic retinopathy (PDR) and ischemic central vein occlusion (CRVO) may cause the following condition:
- A. Retinal dystrophy
- B. Pigmentary glaucoma
- C. Neovascular glaucoma
- D. Central serous chorioretinopathy (CSCR)

9. In neovascular glaucoma, angle closure occurs due to the following:
- A. Gradual revascularization and edema around the angle
- B. Rapid revascularization and edema around the angle
- C. Relaxation of the membrane pulling the iris into the angle
- D. Contraction of the membrane pulling the iris into the angle

10. Sue Smith, a certified registered ophthalmic nurse, instructs a new graduate nurse working in the eye clinic that in order to educate, evaluate, and ensure patient compliance, nurses should have:
- A. Completed orientation to the eye clinic
- B. A passion for the specialty of ophthalmic nursing
- C. A working understanding of ocular disease pathophysiology
- D. Taken continuing education courses in eye anatomy and diseases

ASORN members and other eye care professionals now have an online source for continuing education and training: EyeCareCE. The site is the collaborative effort of five organizations. Together, the International Joint Commission on Allied Health Personnel in Ophthalmology (IJCAHPO), the American Society of Ophthalmic Registered Nurses (ASORN), the Association of Technical Personnel in Ophthalmology (ATPO), the Canadian Society of Ophthalmic Medical Personnel (CSOMP), the American Academy of Ophthalmic Executives (AAOE), the Contact Lens Society of America (CLSA), and the Ophthalmic Photographer's Society (OPS), teamed to produce a comprehensive online training resource for eye care professionals. ASORN is proud to participate in this online educational partnership.

Equation of the Vision in Colors

Thiago Gonçalves dos Santos Martins, MD; Ana Luiza Fontes de Azevedo Costa, MD

CLINICAL CONUNDRUM

THE PROCESS OF COLOR perception occurs when light excites the photosensitive molecules of the retinal photoreceptors (rods and cones), which initiates the decoding of the information present in light rays. The rods perceive movement and shades of grey, while cones provide a much more detailed vision, including color. From the rods and cones, the visual information is directed to the thalamus and the cerebral cortex, whereupon color perception occurs (Backhaus, 1998; Feynman, Leighton, & Sands, 2010).

Vision in Colors

In the distant past, mammals were small, nocturnal animals whose retinas were predominantly composed of rods, resulting in practically colorless vision. With evolution, mammals began to acquire diurnal habits and developed color vision to better survive among predators. Subsequently, mammals were able to see colorful fruits in the trees or predators hidden inside the vegetation (Luo, 2007).

Primates, like other mammals, have a single rod type. But while most mammals have only two types of cones, primates have three. Cones in the retina are present in different proportions and are sensitive to different frequencies (Zele & Cao, 2015), and this explains why different species of animals see the world differently even though they are in the same environment, receiving the same luminous stimuli.

Humans have three types of cones, primarily responsible for the frequencies of red, green, and blue vision. The different mixtures of the three primary colors from all the possible colors perceived by humans (Rodrigues, 2003). However, the proportion of cones in each retina is not the same in all humans, and in some cases, complete absence of one or more of the cones may occur, characterizing color vision deficiencies, also known as color blindness (Deeb & Kohl, 2003)leading to gene deletions or the formation of red-green hybrid genes that explain the majority of the common red-green color vision deficiencies. Gene expression studies suggest that only the two most proximal genes of the array are expressed in the retina. The severity of the color vision defect is roughly related to the difference in absorption maxima of the photopigments encoded by the first two genes of the array. A single amino acid polymorphism (Ser180Ala.

Light on the cones causes chemical reactions that produce electrical stimuli in the brain, interpreted as color. When the three types of cones are stimulated in different proportions, these

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Equation of the Vision in Colors

Continued from page 11

stimuli together are interpreted in the brain as just one color. When the three types of cones are stimulated equally, this produces the sensation of white light. When stimulated together, but with different intensities, the sensation of all colors may occur (Deeb & Kohl, 2003).

Deepening Our Understanding of Color Perception

Because color is a sensation, it will always be difficult to construct explanatory models. Based on physical and biological data, we are studying an equation that explains the interpretation of colors, which would vary not only with the stimulus of the environment, but also with intrinsic factors of the observer (such as number of cones, nerve connections, and others factors). Each axis of this graph would have a vector force exerted by the number of cones (A, B, C) the person possesses and by the degree of stimuli received from the environment (a, b, c), resulting in a color interpreted by the brain (X). Thus, we have an equation for how the brain interprets colors: X = a.A + b.B + c.C (see Figure 1). All force is a vector quantity that has a value and a direction. The number of cones and the environment stimuli are variables to this vector force.

In the human eye, the same environmental stimulus (a, b, c) applied to the cones and their nerve connections (A, B, C) can produce different vector intensities in the three-dimensional light spectrum. The same stimuli can produce the sensation of color X in one person, and in another, the sensation of color Y.

Some color blind people lack certain cones and connections (A, B, or C), but they still have one or two vector forces when

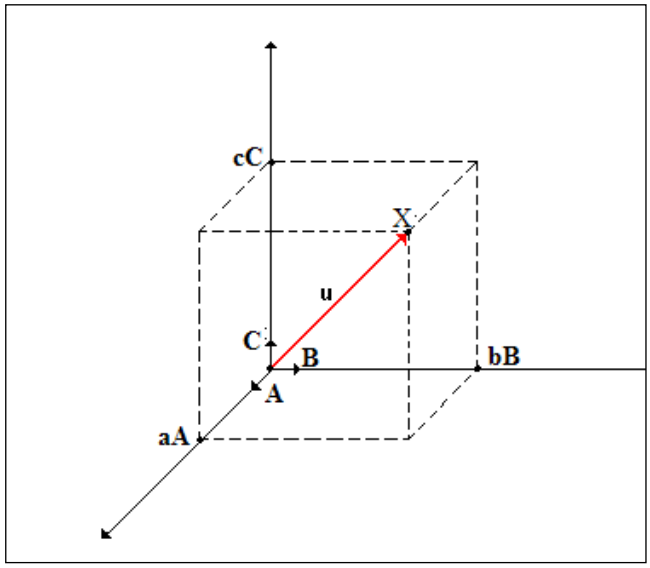

Figure 1. Graphical representation of the color equation.

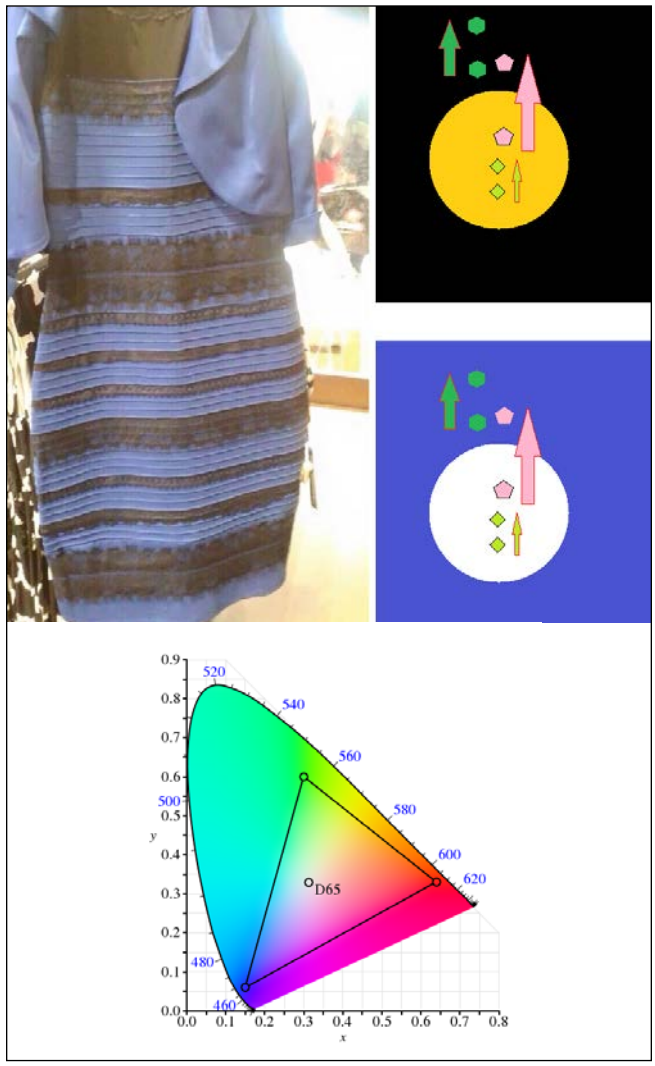

Figure 2. Filter strip photo, which different people perceive as having different colors, and graphical representation of the three groups of people in relation to the "zone of chromatic confusion."

walking through a three-dimensional spectrum of colors. Although they do not see the same colors as other people, with different external stimuli (a, b, c) they end up having a spectra of different colors and consequently are able to differentiate between two objects of different colors.

We can test the equation using a photo taken with a filter, which causes different people to observe distinct colors due to different numbers of cones and nerve connections (A, B, C) (see Figure 2). One group of people observing this picture describe the colors as white and gold; a second group, as blue and black; and a third group, as white and gold at certain times of the day and blue and black at other times of the day.

We noticed that it was the photo of the dress (taken with a filter) that caused the discordance in the colors, and not the dress

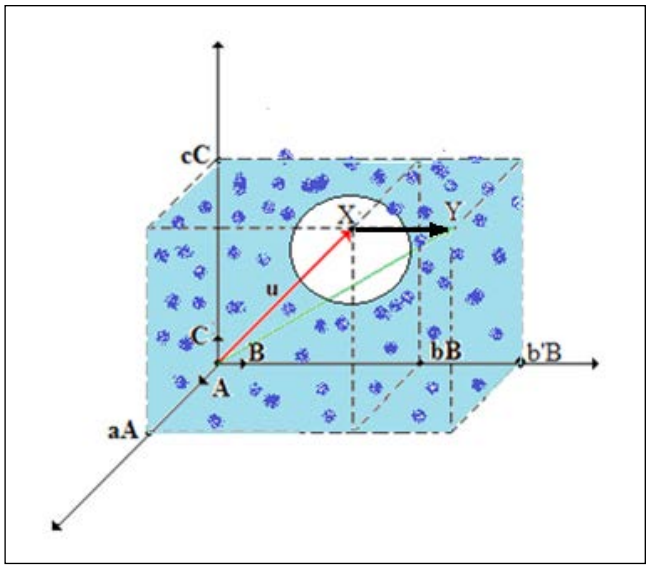

Figure 3. Graphical representation of the change in color perception of the dress in the same person.

itself. The pattern of colors in the dress itself features a color spectrum that causes the entire world population without color vision deficiency to see within the spectrum of blue and black, but the filter of the photo divides the population into three groups by changing the spectrum and placing the first group in the gold and white zone, the second group in the "zone of chromatic confusion" (people who see gold and white, but when they have their cones stimulated, they see blue and black, and after a period of metabolization, they see gold and white again), and the third group that sees only blue and black and do not see gold and white with any environmental stimulus (a, b, c). If a person sees gold and white, it doesn't mean they're color blind. If simply means that he has a different number of cones or different number of connections in the central nerve system.

Thus the same visual stimulus (a, b, c) may not cause the same color sensation in the eyes. For example, let's say a person has just woken up. Their eyes have been closed until now and have not yet been strongly stimulated by the colors of the environment. When looking at the image of the controversial dress, they can see it as gold and white (X). But if they are visually stimulated by color—for example, by staring at a blue photo—then the dress which before was gold and white may now be perceived as black and blue (X → Y) (see Figure 3). Those who see gold and white and then see blue and black are in a threshold zone between the different spectra (a "zone of confusion"); when they receive the stimulus, as with a blue photo, they alter their (a, b, c), which increases their vector force so they are no longer in the zone of confusion. This is because, although they still maintain the same number of cones and connections (A, B, C), they now present different stimuli (a, b, c) due to the color filter created by the opacity of the lens.

Conclusion

Colors are interpreted by the brain in three dimensions as a result of the action of different types of cones and connections (A, B, C) and their respective stimuli (a, b, c). Our equation, X = a.A + b.B + c.C, was derived from this information. Further studies of this equation are needed to explain how we interpret colors in the world.

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Susan Goldstein, MA, RN, BSN, CCRN

Ophthalmic Issues in the Hematopoietic Stem Cell Transplant Recipient

Hematopoietic stem cell transplantation (HSCT) is used to treat a number of malignant / premalignant (i.e., leukemias, lymphoma) and nonmalignant disorders (i.e., inherited metabolic disorders; inherited or acquired immune disorders, including HIV; and inherited red cell disorders, such as sickle cell). Transplants may be autologous, in which the patient's own blood-producing stem cells are harvested and stored, then reinfused following chemotherapy and/ or radiation treatment, or allogeneic, in which the patient receives chemotherapy and/or radiation that destroys the patient's own stem cells, which are then replaced by those of a donor. When donor cells are used, donor and recipient tissue types are matched as closely as possible; however, these transplants bring the risk of complications due to the possibility of antigen reactions between the donor cells and recipient. These reactions can result in the development of graft-versus-host disease (GVHD). GVHD may affect many areas, including the skin, liver, lungs, GI tract, and eyes, and can present significant challenges for post-allogeneic HSCT patients. With the growing population of patients undergoing HSCTs and living longer after transplant, ophthalmic nurses can expect to care for patients who have experienced HSCT.

Case Study

My husband underwent an allogeneic bone marrow transplant from a matched, unrelated donor in August of 2016 for myelodysplastic syndrome. He received a full-strength chemotherapeutic regimen of busulfan and fludarabine prior to transplant, which completely destroyed his own bone marrow, permanently eliminating his immune system and capacity to produce blood cells. After receiving the infusion of donated stem cells, he was hospitalized for three weeks and confined to a germ-free isolation room while the donor cells established themselves in his body. This period of establishment, known as "engraftment," replaced his destroyed marrow with the healthy stem cells of the donor.

The transplant process brought with it many side effects, including ophthalmic effects. His first ocular complaint was dry eye, which began with commencement of the chemotherapeutic regimen and worsened at the time of engraftment. He also experienced transient visual acuity changes. With a baseline myopia of –2.75, he was unable to read the signs posted in his hospital room without corrective lenses. After transplant, he was startled to wake up one day and find himself able to read the smallest print on these signs effortlessly. This passed within a few days and he returned to baseline. A few days later he developed a new presbyopia and required reading glasses for the first time in his life.

My husband was discharged from the hospital in mid-September. He was on multiple medications, including strong immunosuppressive drugs to prevent the donor immune cells from attacking his body's own tissues. These drugs were tapered off gradually throughout the fall and winter. His dry eye worsened significantly during this time. Notably, his new-onset presbyopia simultaneously improved to a point of complete resolution.

To address the dry eye, he was seen by a local ophthalmologist, who developed a treatment plan of artificial tears and lubricant eye drops, followed by cyclosporine drops if necessary. If these measures did not resolve the condition, he would be a candidate for punctal plugs.

Fortunately, at the same time we realized that with the cold, dry winter, the relative humidity in our house had become extremely low, less than 12%. Using a whole-house humidification system to bring the house to a healthy 45% humidity level helped improve my husband's ocular symptoms until he only occasionally used artificial tears and lubricants.

A multitude of factors may have contributed to his ocular conditions. The chemotherapy regimen had included fludarabine, an agent with known ocular toxicity (Ding, Herzlich, Bishop, Tuo &

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Ophthalmic Issues in the Hematopoietic Stem Cell Transplant Recipient

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Chan, 2008). For prevention of fungal infections he was receiving voriconazole, known to cause visual acuity changes (Walsh et al., 2002). The tapering of tacrolimus and corticosteroids, used for immunosuppression and prevention of GVHD, is a known contributor to the development of dry eye (Ogawa et al., 2001). Additionally, the environmental factor of low relative humidity may have aggravated the dryness.

Ophthalmic Conditions Experienced by HSCT Patients

Cataracts and dry eye syndrome are the two most common ophthalmic complications following HSCT (Clark, Savani, Mohty, & Savani, 2016). HSCT patients can also suffer from conjunctivitis, corneal ulcers, elevations in intraocular pressure, macular or optic disc edema, and transient or permanent visual acuity changes (Tabbara et al., 2009). These conditions can arise from pre-transplant chemotherapy or radiation, immunosuppression, corticosteroid use, cytomegalovirus retinitis, or ocular zoster reactivation (Walton & Reed, 1999). They may also be a symptom of GVHD.

GVHD in the HSCT Patient

A major complication of allogeneic transplant, GVHD is a condition in which transplanted immune cells from the donor (the "graft") attack the tissues of the recipient (the "host"). GVHD may be experienced as an acute or a chronic event, with the acute phase traditionally identified as the first 100 days post-transplant, though symptoms and phases can sometimes overlap (Garnett, Apperley, & Pavlů 2013). Either form of the disease has the potential to affect multiple body systems, including the lungs, skin, and eyes (Munir & Aylward, 2017). GVHD is a significant cause of post-transplant morbidity and mortality.

While the first observed manifestation of GVHD often involves the skin, it can also manifest as an ophthalmic disorder. Ocular GVHD is estimated to affect 40%–60% of all HSCT patients (Clark et al., 2016). The median time from HSCT to onset of ocular chronic GVHD is 293 days (Shikari, Amparo, Saboo, & Dana, 2015).

Ocular GVHD can cause dry eye through scarring and fibrotic damage to the eyelids, conjunctiva, lacrimal glands, and cornea (Kim, Yoo, Kim, Joo, & Na, 2017). GVHD can similarly damage the meibomian glands, inhibiting the production of lipids and altering tear chemistry. This can result in reduced tear evaporation times, contributing to an increase in eye dryness and corneal damage (Engel et al., 2015).

Cataracts in the HSCT Patient

The causal relationship between total body irradiation (TBI) and cataract development is well described (Nassar, Tabbara, & Aljurf, 2013). There is a high risk of cataracts in post-HSCT patients who have received TBI (40%–70%) and/or a prolonged course of corticosteroids (45%) (Fred Hutchinson Cancer Research Center, 2017), with cataract development occurring three to five years following transplant (Clark et al., 2016). As the use of TBI has decreased in favor of improved chemotherapy regimens, the overall incidence of cataract in HSCT patients has declined (Najima et al., 2011). Current guidelines recommendation slit-lamp ocular fundus examinations one year after transplant and annually thereafter.

Dry Eye in the HSCT Patient

Estimates of the prevalence of dry eye following HSCT range from 40% to 75% (Clark et al., 2016), with a median time of 171 days from time of transplant to time of dry eye diagnosis (Na & Kim, 2012). However, a 2017 study showed that dry eye was present among 53% of HSCT recipients prior to transplant, leading to the recommendation that patients receive a pre-transplant ocular surface assessment (Giannaccare et al., 2017). Dry eye may be caused by chemotherapy, TBI, or by post-transplant medications. It can also be a symptom of GVHD.

Since HSCT patients are confined for lengthy periods to hospital rooms and indoor environments, it is important to recognize that conditions of low relative humidity can aggravate eye dryness. Exposure to a low-humidity (5%) environment for only one hour has been observed to produce changes in tear chemistry similar to those of patients with known dry eye (Abusharha & Pearce, 2013). When possible, indoor relative humidity levels should be kept within an optimal 40%–50% range. Keep in mind that the use of room humidifiers by immunocompromised patients may be contraindicated due to the risk of mold or bacterial contamination. When this is the case, there is an even greater need to be diligent in the use of ophthalmic lubrication and moisturizing agents.

Treatment and management of dry eye syndrome among HSCT patients has often taken a stepwise approach, beginning with artificial tears (Blackburn, Mueller, & Ramasubramanian, 2017). "Next step" recommendations have included use of cyclosporine, tacrolimus, or autologous serum eye drops for management of dry eye (Sanz-Marco, Udaondo, Garcia-Delpech, Vazquez, & Diaz-Llopis, 2013; Na & Kim, 2012). More advanced treatments include punctal plugs and humidity goggles. Finally, scleral

TABLE 1

Ophthalmic Follow-up Recommendations for Allogeneic HSCT Patients

Intervention	Visual acuity testing	Dry eye / ocular surface assessment	Slit-lamp ocular fundus examination	Evaluation of ocular clinical symptoms
Evaluating for	GVHD, medication toxicities	DES, keratoconjunctivitis sicca, ocular GVHD	Cataracts, retinal microvasculopathy	DES, GVHD, medication toxicities
Recommended time interval	Pre-HSCT 6 months post-HSCT (Clark, Savani, Mohty & Savani, 2016; Majhail et al., 2012) 1 year post-HSCT (Clark, Savani, Mohty & Savani, 2016; Majhail et al., 2012) Annually thereafter (Clark, Savani, Mohty & Savani, 2016; Majhail et al., 2012) and as needed	Pre-HSCT (Giannaccare et al., 2017) 6 months post-HSCT 1 year post-HSCT and as needed	1 year post-HSCT (Fred Hutchinson Cancer Research Center, 2017; Majhail et al., 2012) Annually thereafter (Fred Hutchinson Cancer Research Center, 2017)	At each visit *and* as needed

Note: GHVD = graft-vs.-host disease; DES = dry eye syndrome. Adapted from "What Do We Need to Know About Allogeneic Hematopoietic Stem Cell Transplant Survivors?" by C. Clark, M. Savani, M. Mohty, and B. Savani, 2016, Bone Marrow Transplantation, 51(8), 1025–1031; *Long-term follow-up after hematopoietic stem cell transplant: General guidelines for referring physicians*, Fred Hutchinson Cancer Research Center, 2017, retrieved from https://www.fredhutch.org/content/dam/public/Treatment-Suport/Long-Term-Follow-Up/LTFU_HSCT_guidelines_physicians.pdf; "Recommended Screening and Preventive Practices for Long-term Survivors After Hematopoietic Cell Transplantation," by N. Majhail, J. Rizzo, S. Lee, M. Aljurf, Y. Atsuta, C. Bonfim, … A. Tichelli, 2012, Bone Marrow Transplantation, 47(3), 337–341; and "Ocular Surface Analysis in Hematological Patients Before and After Allogeneic Hematopoietic Stem Cell Transplantation: Implication for Daily Clinical Practice," by G. Giannaccare, F. Bonifazi, M. Sessa, E. Dan, M. Arpinati, M., M. Fresina, ... E. C. Campos, 2017, *Eye,* 31(10), 1417–1426.

lenses and the prosthetic replacement of the ocular surface ecosystem (PROSE) device (BostonSight) have shown great effectiveness in treatment of severe cases of dry eye due to ocular GVHD (Ridges, Agranat, Hatch, & Jacobs, 2014; Magro et al., 2017). With the publication of the Dry Eye Workshop criteria in 2017, the ophthalmic nurse can anticipate a more protocol-based approach to dry eye management in this patient population (Jones et al., 2017). Transplant centers vary in their recommendations for post-transplant ophthalmic evaluation. A summary of published recommendations can be found in Table 1.

Implications for Nursing Practice and the Ophthalmic Team

Ophthalmic nurses have many opportunities to make valuable contributions in the care of these complicated patients, beginning with obtaining a complete history focusing on vision and medical conditions. A thorough medical history of the transplant patient includes:

- *Documentation of the disease necessitating transplantation*
- *The type or transplant (autologous or allogeneic)*: Autologous transplantation, in which the patient's own stem cells are removed and stored, then reinfused following chemotherapy or radiation therapy, carries with it a lower incidence of complications, including ophthalmic complications, than allogeneic transplantation, in which the patient receives stem cells from a donor.
- *The type of donor (whether related or unrelated) and the tissue antigen match status*: Donor cells that are more closely matched to the patient's own tissue type carry less risk of complications than incompletely or partially matched cells.
- *Days since transplantation*: The post-transplant period has traditionally been divided into early and late phases, with patients generally at greater risk of complications during the first 100 days as the immune system is still in the early stages of recovery.
- *Preparatory ("conditioning") regimen type*: chemotherapy and/or radiation; chemotherapeutic agent(s) used.
- *Strength of conditioning regimen*: Myeloablative conditioning aims to completely destroy the patient's own bone marrow in preparation for transplant. Reduced-intensity conditioning (RIC), used for patients unlikely to tolerate the effects of full-strength myeloablative conditioning, aims to reduce the number of patient's own bone marrow cells prior to transplant.
- *Cytomegalovirus (CMV) status*: A patient previously infected with CMV can undergo reactivation of the virus following transplant, with CMV retinitis as a possible manifestation. CMV retinitis begins with blurred vision which, if left untreated, has a high risk of advancing to total loss of vision (Ljungman, Hakki, & Boeckh, 2011). These patients must be more closely monitored for visual changes.

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Ophthalmic Issues in the Hematopoietic Stem Cell Transplant Recipient

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TABLE 2

Allogeneic HSCT Medications and Reported Ocular/Ophthalmic Effects

Medication	Purpose	Ocular/ophthalmic effects	Source
Cyclosporine	Immunosuppression	Retinal toxic blindness (rare)	López-Jiménez et al., 1997
Tacrolimus	Immunosuppression	Bilateral vision loss (rare) (Not an ophthalmic effect: Tacrolimus can cause posterior reversible encephalopathy, a neurological syndrome that may cause reversible vision changes including total vision loss.)	Apuri, Carlin, Bass, Nguyen, & Greene, 2014
Voriconazole	Antifungal	Loss of visual acuity Visual hallucinations Reversible vision disturbances	Walsh et al., 2002 Eiden et al., 2007
Corticosteroids	Treatment of GVHD	Cataracts Increased intraocular pressure Central serous retinopathy	Nassar, Tabbara & Aljurf, 2013
Busulfan	Conditioning	Cataracts (rare)	Al-Tweigeri, Nabholtz, & Mackey, 1996 Klein & Burns, 2008
Cyclophosphamide (Cytoxan)	Conditioning	Dry eye (keratoconjunctivitis sicca) Conjunctivitis Blurred vision	Al-Tweigeri, Nabholtz, & Mackey, 1996 Klein & Burns, 2008
Fludarabine	Conditioning	Visual changes Visual field deficits Photophobia Hallucinations Complete loss of vision	Ding et al., 2008
Radiation (TBI)	Conditioning	Cataracts Retinopathy	Al-Tweigeri, Nabholtz, & Mackey, 1996
Methotrexate	During and after transplant for prevention and treatment of GVHD, especially steroid-refractory	Conjunctivitis Increased lacrimation Blurred vision Photophobia Ocular pain	Huang, 2005 Giaccone, 2005 Klein & Burns, 2008

Note: TBI = total body irradiation; GVHD = graft-vs.-host disease.

A current medication history is extremely important as well. HSCT patients are on multiple medications, including immunosuppressives, antibiotics, antivirals, and antifungals, for months, years, or in some cases permanently. Particularly in the early post-transplant phase prior to Day 100, medications and doses change frequently. See Table 2 for a description of common medications used in allogeneic HSCT with their reported ocular/ophthalmic effects.

An allergy history is important since the immune systems of allogeneic HSCT patients are destroyed during transplant. They will acquire the immune profile of their donors, possibly including any allergies their donors have. The nurse should be aware that the patient may develop new drug allergies or ocular allergies after transplant (Tabbara et al., 2009), with symptoms that may mimic those of GVHD; as Au (2007) suggests, differentiating GVHD from newly-developed drug allergy "may be difficult and occasionally impossible." Likewise, distinguishing between GVHD and uncomplicated dry eye depends on patient history (Denny, 2013). The ophthalmic nurse needs to be mindful of the details of a patient's transplant history. For example, it is important to ask post-HSCT patients with dry eye whether they are also experiencing problems with dry mouth or skin; their answers can help determine whether GVHD is present.

The ophthalmic nurse with an expanded understanding of stem cell transplantation will add value to the patient encounter and the facilitation of holistic patient care. An understanding of the multiplicity of factors affecting this unique patient population will be helpful in guiding the ophthalmic nurse in patient assessment and education. Education should focus on the following:

- The need for testing, evaluation, and treatment of dry eye, and the risks of untreated dry eye (e.g., corneal ulceration and scarring);
- Risk of cataracts as a late effect of HSCT, particularly in patients receiving TBI or long-term steroid use, and the time frame for monitoring;
- Importance of visual acuity screening and the possibility of transient or permanent acuity changes; and,
- Information about HSCT medications known to cause visual acuity changes, cataracts, or dry eye.

Patients should be encouraged to report ocular symptoms and vision changes, no matter how small they seem. These issues may be overshadowed by other complications or may be perceived as minor relative to the life-threatening disease and transplant process itself (Denny, 2013). Ongoing management can be particularly challenging in a setting where the patient is already dealing with many other health conditions and demands. As Shikari et al. (2015) point out, there are "extraordinary difficulties for the ophthalmologist to follow-up patients with GVHD. These are in many cases extremely ill individuals who are usually followed up in oncology or internal medicine departments, and usually have a variety of systemic manifestations resulting in frequent hospitalization or mortality, which may lead to variable follow-ups to an eye clinic" (p. 246). Keeping this in mind, assure the patient that you will be flexible in response to their changing needs and capabilities.

A nurse with understanding of the transplant experience can earn the confidence of patients and their families. A familiarity with the details of the transplant process is important; also important is an understanding of the isolation and restrictions under which they live during the lengthy hospital stay and subsequent at-home recovery. Their loss of immunity requires many environmental and lifestyle changes. During and immediately after transplant, patients are unable to leave the controlled environment and filtered atmosphere of a closed hospital isolation room. Upon returning home, patients are unable to return to work and may live under protective restrictions; for example, they may be unable to have contact with children who attend school or day-care, visit public environments such as shopping centers or movie theaters, fly or use public transportation, eat in restaurants, have contact with pets or houseplants, eat raw fruits and vegetables, drink well water, use mist humidifiers or wood-burning fireplaces, and swim in lakes, hot tubs, or swimming pools. Understandably, these restrictions can create a sense of hypervigilance, isolation, and fear. As patients' immune systems mature, these restrictions are lifted; however, the stresses of the experience and of dealing with continuing post-treatment effects may remain. With up to 30% of patients experiencing depressive symptoms five years post-transplant (Kuba et al., 2017), HSCT survivors may experience fatigue and depression for months to years. The prospect of unrelieved pain of dry eye or threat of vision loss may be daunting after the multiple physical and emotional challenges these patients have already experienced. A caring and supportive ophthalmic nurse can guide patients toward positive solutions to these concerns.

Summary

The allogeneic HSCT survivor faces complex and enduring challenges, including ophthalmic changes, following transplant and recovery. Understanding the unique needs and concerns of this patient population, and the ways in which the ophthalmic nurse can assist in management of these challenges, provides the opportunity to make a significant contribution to the well-being of these patients and their families.

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Samantha J. Owens, RN, MSN, MHA

CASE STUDY

When the Unexpected Happens: Medical Emergencies in Ophthalmology Settings

MEDICAL EMERGENCIES happen across the United States every day, and responding to these situations falls to first responders in a variety of clinical and nonclinical environments. Because ophthalmology clinics are engaged in increasingly technical and invasive procedures in an aging and complex population of patients, clinic staff are more likely to be involved in medical emergencies. Any staff member who could potentially respond to a patient code needs to understand what the resuscitative process entails, their role on the team, and how to effectively communicate inside the team. These responders should have the proper training to respond to a medical emergency, including opportunities to practice reviving patients in a simulated environment and a debrief of the mock code to reinforce their learning.

Introduction

Each year in the United States approximately 600,000 people suffer a cardiac arrest, with an estimated 6% survival rate in community settings and only a 24% survival rate in hospital settings (Becker, Aufderheide, & Graham, 2015). One does not normally anticipate that a cardiac arrest might occur in an ophthalmology office, but patients are presenting with more complex care needs and more comorbidities than in past years, requiring increasingly invasive treatments. One recent study found that among cataract surgical patients, the average age was 72 ± 9 years, 56.6% had a body mass index over 25 kg/m^2, 57% had hypertension, 21.4% had heart disease, 15.9% were diabetic, and only 16.9% had none of these comorbidities (Koolwojk et al., 2015). Treating older, more complex patients raises the odds that staff will participate in a medical emergency.

Types of Medical Emergencies

One of the most common adverse reactions a patient in the eye clinic may experience is a vasovagal response, defined as a sudden interruption or decrease in blood supply to the brain resulting in lightheadedness, or even a loss of consciousness. A vasovagal response may be a single incident, or it can be recurrent and life threatening (Alowedi, Qahtani, Garcia, & Arevalo, 2017). A vasovagal response can occur because of fear or pain, or as a response to an introduced stimulus, such as a drug injection or an IV start. These reactions range in severity from brief incidents that resolve with monitoring to prolonged and life threatening conditions requiring extensive intervention. Having staff trained in the management of a vasovagal response is critical in maintaining a safe medical environment.

Anaphylaxis, a severe, potentially life-threatening reaction to an allergen, is another medical emergency that can occur in an ophthalmology clinic. As treatment options are expanding in the practice of ophthalmology, we are exposing our patients to a wider list of potential allergens (Ha, Kim, Sohn, & Lim, 2014). Anaphylaxis can occur with medications that were previously tolerated by the patient, especially during intravitreal injection or fluorescein angiography. An anaphylactic response requires immediate medical attention to prevent a potential fatal outcome.

A third medical emergency is cardiac arrest, which is rare in the ophthalmology setting. Cardiac arrest occurs without warning when the heart ceases to pump blood through the body due to an electrical arrhythmia, or from a mechanical malfunction in the heart, leading to loss of consciousness and potentially death (American Heart Association, 2015).

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Immediate intervention is critical to restore blood circulation and protect neurological function.

Many ophthalmology offices are considered pre-acute, with a focus on health maintenance and prevention. Staffed by ophthalmology technicians, office staff, and the ophthalmologists, these clinics are equipped only with basic emergency supplies. The staff of these clinics are likely to have little or no experience in managing a sudden cardiac arrest or prolonged resuscitative rescue. Many ophthalmology clinic staff may not even have basic CPR training.

Resuscitation is most successful (doubling the survival rate) when high-quality CPR is initiated within four minutes of arrest (Eisenberg & Mengert, 2001). In all settings, success is best assured when first responder follows "the chain of survival" – garnering the necessary assistance of other responders to give the patient the best chance for a resuscitation. The chain of survival begins with recognizing that the victim is in distress and calling for help. If the patient is in a clinic or hospital, this will mean following the protocol to alert the rapid response team to respond. In the community setting, the response involves calling for local emergency medical services (i.e., dialing 911 in most areas). As soon as help is on the way, the first responder should initiate high-quality CPR, followed promptly by rapid defibrillation and advanced life support (Eisenberg & Mengert, 2001).

The Response Team

For every minute that CPR is delayed, the likelihood of survival decreases by as much as 10% (Hunziker et al., 2011). The first responder takes the critical first steps by engaging the team and beginning CPR. When the response team arrives, the effective first responder will quickly report the patient's situation, what has been done, and what is known about the patient's condition. This information is relayed to the code leader, who in clinical settings may be an emergency medical technician or a physician. The code leader gathers the information and guides the response team to the best outcome. In a surgical setting or inpatient setting the first responder may be a nurse or a physician; however, it is rare in the outpatient clinical setting that a nurse will be employed in the practice. Some outpatient settings that are currently hiring registered nurses are providing advanced diagnostic studies and interventions and also hire nurses to help manage medical emergencies.

The code leader has broad responsibility to the resuscitation team and understands the capabilities of the people on the team. The code environment can become chaotic, and the effective code leader creates and maintains a peaceful atmosphere that is conducive to the resuscitative process. This person elicits information from the team and directs care with succinct directions to other members of the team.

In most clinic settings, there are only a few staff members. So to achieve an optimal outcome in a medical emergency, all staff members should clearly understand their roles in coordinating critical patient needs. Ideally, a nurse will be with the patient, working with the team leader to carry out interventions. If another nurse is available, they may be assigned the role of family liaison to interpret the interventions and anticipate family needs. If a nurse is not present, then the available staff must work within their scope of practice to assist the team leader in getting needed care to the patient in crisis. Nonclinical staff can provide valuable assistance in initiating layman CPR, bringing needed items from the clinic, and controlling the environment.

Communication of the Response Team

Communication is cited as a contributing factor in up to 65% of serious adverse event reports (Meester, Verspuy, Monsieurs, & Van Bogaert, 2013). In medical emergencies, complex conversation occurs under situations of high stress, and the potential for misunderstanding is high. Miscommunication can be caused by numerous factors, involving the environment, lack of preparation, unclear role hierarchy, language/cultural barriers, and gender barriers (Meester et al., 2013).

Miscommunication can lead to issues or disputes that undermine the resuscitative effort in several ways. Code team members may be inexperienced, environmental stress can lead to a breakdown in the communication protocol, or team members may have histories of conflict with other personnel who are responding to the code. The team leader needs to be able to acknowledge these issues and manage the resulting problems.

Communication tools have been studied, designed, and implemented for high-stress work environments. Communication in special situations can be standardized so that each person understands what is expected and has an opportunity

to ask questions with emotions removed. Structured communication, such as the SBAR model (Situation, Background, Assessment, Recommendation), shifts the focus of the conversation to critical pertinent information and offers an opportunity to verify that the information has been understood (Menke, 2009).

The Value of Mock Codes

A successful code team is competent and organized, limiting the amount of time the patient is in distress. Shorter code times decrease the likelihood of death and disability (Prince, Hines, Chyou, & Heegeman, 2014). But in many ophthalmology settings, inpatient or outpatient, medical emergencies are extremely rare; the situation simply does not present itself often enough to train and maintain an effective code team. One solution to this problem is mock code training.

Mock codes provide staff in all medical settings the opportunity to come together and walk through the resuscitative process without the stress of an actual event. Participants have more time to clarify their roles and find answers to questions that all team members may have. By repeatedly going through code simulations, the response team builds technical skills and strengthens trust in other team members, and participants avail themselves of the opportunity to go through difficult scenarios without endangering a single patient.

Mock code training has benefited from advances in simulation technology. Many hospitals offer simulation labs, where practitioners can practice complex or technical interventions with interactive mannequins that can simulate many different medical emergencies, from choking to sudden cardiac death. Mock code training can reveal to the responders the effectiveness of their interventions; for example, showing the rate and depth of cardiac compressions or providing the experience of intubating a patient during a bronchospasm. Frequently, mock codes are videotaped, allowing the response team to review their actions. The virtual events can reveal responders' strengths, as well as areas of weakness that require further learning or more practice. Simulated codes also allow the participants to switch roles, giving individuals a better anticipation of the needs of other team members.

High-Quality CPR

The goal of mock codes is to ensure that teams are performing the highest quality CPR, leading to higher survival and fewer deficits at the time of patient discharge. Ensuring high-quality CPR starts with all staff having training, no matter what title they hold in the medical facility.

There are five main principles of high-quality CPR:

1. Minimize interruptions during compressions
2. Maintain a chest compression rate of 100 to 120 per minute
3. Maintain a chest compression depth of at least 50 mm in adults or one-third the chest dimension in children
4. Ensure full recoil of the chest after each compression
5. Maintain a rate of fewer than 12 breaths per minute, with minimal chest rise

As more evidence is developed to support each intervention, it is important to disseminate new information to all responders, both in and out of medical settings (Meany et al., 2013). Biennial CPR training reinforces the interventions that have been studied, resulting in the best chance of survival.

Situational Awareness

Situational awareness sounds simple, but it can be complex, encompassing cognitive skills, perception, comprehension, and anticipation (Lauria, 2016). Situational awareness includes identifying the patient populations being served at the facility, anticipating potential medical emergencies, and evaluating the level of education and experience of staff. Because medical emergencies can impact the decision-making skills of all staff members, even those with years of resuscitation experience, it can be difficult to maintain situational awareness during these stressful times. There are many types of critical stress that can affect our ability to maintain situational awareness when dealing with medical emergencies:

1. The physical stress on the responder performing interventions during a code
2. Restimulation of memories of past resuscitative efforts
3. Unique situational unknowns – for example, unwitnessed events, unknown patient factors, or family background
4. The threat of a potentially litigious family member
5. Floor politics, such as policy, staffing, and workload issues
6. The demoralizing effect of an additional burden on top of an already full workday

The more practiced responders are at achieving situational awareness during a medical emergency, the more likely they are to bring the event to a successful conclusion.

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Conclusion

Medical emergencies are not common in ophthalmology settings. For example, the odds of a fatal reaction during a fluorescein angiogram is only 1:222,000 (Breidablik, De Pater, Walther, Nopp, & Guttormsen, 2012). Despite the infrequency, medical emergencies in the ophthalmology office can be managed successfully by cultivating response teams trained in situational awareness, high-quality CPR, and structured communication, with practice provided during regularly scheduled mock codes. Every ophthalmology setting must be prepared to manage an emergency until advanced life support equipment and providers can arrive to continue the rescue attempt.

Case Study

Situation

A 41-year-old gentleman presented at his optometry provider for his overdue annual dilated eye exam. He had no eye complaints but did state that his vision was blurrier than it had been at the last exam, 18 months previously.

Background

The patient had a medical history of type 2 diabetes and hypertension, and had a BMI of 46. He stated that his health was good overall. He had no difficulty performing his activities of daily living, and his illness did not interfere with any of his extracurricular activities. He never married, and he worked as a night shift supervisor. He was unwilling to miss work, which made it difficult for him to get to the eye doctor. He enjoyed reading and was having difficulty reading for long periods due to his blurred vision. The patient did not have a formally diagnosed ocular disease prior to this visit, with mild refractive correction only.

Assessment

The optometrist noted on exam that the patient had a new nevus and was suspicious for new-onset nonproliferative diabetic retinopathy. This suspicion led the optometrist to refer the patient to a local ophthalmology clinic to undergo baseline fluorescein angiography. The patient arrived in clinic well hydrated and prepared for his exam. His blood pressure was borderline 136/78, and his pulse rate was 72. The patient was on metformin for his diabetes, and he took lisinopril for renal protection; he was not taking any other medications. He seemed in good spirits and was not exhibiting any signs of pre-procedure anxiety.

Evaluation

The patient was consented and dilated per procedure protocol with bilateral eye drops: 1 drop each of proparacaine 0.5%, phenylephrine 2.5%, and tropicamide 1%. The patient had time to dilate and then was brought to the camera for his color fundus photography. The RN then administered fluorescein 10%, 5 mL, in the right antecubital vein without incident. The patient was tolerating the procedure without signs of distress. He denied nausea or itching. The nurse determined that he appeared to be tolerating the procedure well; she discontinued the IV site and left the room.

Within 60 seconds, the photographer called the RN back to the room because the patient's eyes appeared to have rolled back in his head. The nurse re-entered the room and noted that he was still awake, but was not talking and was pale and diaphoretic. A medical emergency was called to the department while the patient was assisted to the floor to prevent falling. The RN administered an EpiPen 0.3 mg in the left deltoid. The patient was not responsive, and no pulse was noted at the carotid, radial, or femoral pulse sites. 911 was notified to send an ambulance with full life support. Cardiopulmonary resuscitation was started immediately, with oxygen being given via bag mask, a new IV site was established with some difficulty, and NS 0.9% was started wide open. The patient was placed on an automated external defibrillator (AED) as soon as it was available, and no shock was indicated. The patient received five rounds of chest compressions before returning to consciousness spontaneously, with stable vital signs (pulse, 62; blood pressure, 110/52). The patient was taken by ambulance to the emergency room for further evaluation, and he made a full recovery in the inpatient setting.

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Jacquelyn Davanzo, BSN, RN; Jose Echegaray, MD; Pauline Funchain, MD; Arun D. Singh, MD

PROFESSIONAL DIRECTIONS

Systemic Surveillance Options Following Uveal Melanoma Prognostication

UVEAL MELANOMA METASTASIS occurs in 25% of patients diagnosed with uveal melanoma and is the leading cause of death in patients with uveal melanoma irrespective of the method of treatment (Kujala, Mäkitie, & Kivelä, 2003). Involvement of the liver is observed in up to 90% of these cases (Kujala, Mäkitie, & Kivelä, 2003; Diener-West et-al., 2005). Specific cytogenetic and molecular markers, such as a total or partial chromosome 3 loss, have proven to be accurate predictors of metastatic disease (Aalto, Eriksson, Seregard, Larsson, & Knuutila, 2001; Trolet et al., 2009). Systematic surveillance plays a key role in metastatic disease.

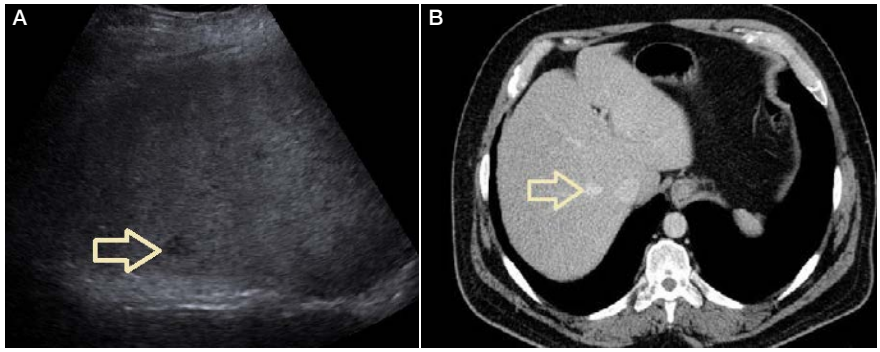

Figure 1. A 62-year-old male was treated with radiation plaque for choroidal melanoma in November 2014 and subsequently. Genetic prognostication showed class 2, high risk for metastasis. Baseline CT scans were negative. Systemic surveillance included ultrasonography of the liver every 3 months for the first year and then every 6 months thereafter. Two years later (October 2016), there were two new hypoechoic right hepatic lobe lesions, measuring 1.2 cm and 1.4 cm (A). For better characterization of the new lesions, CT scans with IV contrast were obtained. CT scan showed a 0.5 cm low-attenuation hepatic lesion that was concerning for metastatic disease (B). Liver biopsy confirmed metastasis.

Staging and Testing

Tumor classification based on genetic expression profiling includes two categories of uveal melanoma with respect to metastases potential, (1) low-risk, class 1, and (2) high-risk, class 2. We have previously reported that the majority of patients (95%) will choose to utilize prognostic testing when offered, with an overall low technical failure rate (4%) (Davanzo, Bellerive, Petrich, & Singh, 2017). Advising systemic surveillance to a patient after cancer diagnosis is essential following baseline scanning to monitor for metastatic spread after treatment. After the prognostic results become available, patients have a variety of options for systemic surveillance that can be tailored to each patient based on prognostication results. In the rare cases in which patients are not eligible for testing (e.g., small tumors), patients refuse testing, or there is a technical failure, patients are advised to undergo standard systemic surveillance.

Systemic Surveillance

Options for systemic surveillance includes observation, liver function testing, and liver imaging, including ultrasonography, computerized tomography (CT) scan of the abdomen/pelvis, or magnetic resonance imaging (MRI) (see Table 1). Observation is often an unrealistic option when patients prefer to have answers and confirmation that they are healthy. However, observation can be an option in patients who are very elderly and/or have several comorbidities. Liver function testing (LFTs) is no longer utilized because it is not an effective predictor of metastatic disease (Diener-West et al., 2004). In a retrospective study of 30 patients with biopsy-confirmed metastatic disease, only four had abnormal LFT results, thus demonstrating that LFTs do not show significant predictive evidence of metastatic disease (Choudhary, Gupta, Bena, Emch, & Singh, 2016).

Ultrasonography of the liver has become the gold standard of systemic surveillance in our practice. This imaging method is minimally invasive, accessible, affordable, and time efficient, and it provides quick results. No contrast is used,

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Systemic Surveillance Options Following Uveal Melanoma Prognostication

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TABLE 1
Systematic Surveillance Imaging

Surveillance type	Advantages	Disadvantages
Observation	Nothing to follow-up for No extra trips No insurance issues No extra cost	No detection of metastases Increased anxiety
Liver function testing	Overall functional status of the liver	Gives no indication of metastasis Time consuming Potential multiple sticks
Ultrasonography	Least invasive Accessible No contrast needed Characterizes lesions that are able to be biopsied Time efficient	Operator dependent for quality imaging Limited by body fat Low resolution False negative results
CT scan	Can image multiple body parts in one scan Higher resolution than ultrasound	May find lesions that are amenable to biopsy IV required for contrast Subject to radiation Limited by kidney function
MRI	Highest sensitivity for detection of lesions Detailed anatomic characterization of lesion	Limited by kidney function Metal implants prohibited Higher cost May find lesions that are not amenable to biopsy

allowing patients with impaired renal function to have access to imaging. Ultrasonography of the liver is restricted in individuals with excess visceral fat; other limitations tend to be operator dependent. Lesion images are adequate for biopsy, if needed. Not all lesions seen on ultrasound are metastatic, but further characterization of new or previously unseen lesions generally requires CT scan or MRI (see Figure 1).

CT scan and MRI are used to obtain a more detailed depiction of lesions that are known and/or are being monitored for growth. CT scans and MRI are used after an ultrasound of the liver has been performed and an abnormality has been noted. CT scan and MRI will also detect incidental lesions or lesions within the liver that are too small to biopsy, thus causing more anxiety for the patient.

Prognostication

Prognostication plays a significant role in recommending systemic surveillance. Knowing whether or not a tumor carries a low or high risk of metastasis is crucial in tailoring systemic surveillance to each individual patient. In patients who have a low risk of metastases (class 1 or disomy of chromosome 3), we recommend our standard surveillance of ultrasonography of the liver every 6 months for at least the first 5 years after primary treatment. This standard surveillance is also applied to patients who do not want or are not eligible for prognostication testing. Patients who are classified as high risk (class 2 or partial/total chromosome 3 loss) are referred to a medical-oncology consultation for more frequent imaging, more intensive imaging, or adjuvant therapy trials, if available.

Conclusion

In conclusion, prognostication testing plays a substantial role in individualizing systemic surveillance for uveal melanoma metastasis. There are several options to choose from, with the standard being ultrasonography of the liver every 6 months for the first 5 years. Based on the patient's risk classification, imaging can be more frequent and invasive. Members of the ophthalmic team need to present systemic surveillance options in a comprehensive, understandable approach to facilitate decision-making processes. Additionally, educating patients and families on follow up tests such as ultrasonography, CT, and MRI contributes to a positive patient experience.

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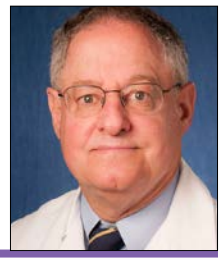

Alan Sugar, MD

PROFESSIONAL DIRECTIONS

Comments on the PROWL Studies of Patient-Reported Outcomes of LASIK

THE PROWL (Patient Reported Outcomes with LASIK) studies developed and validated an online questionnaire that was completed before and after LASIK surgery. Patient satisfaction was very high (96%–99%). There were high rates of glare, starburst, and halos (74%) preoperatively, which diminished postoperatively (41%). New-onset visual symptoms developed in over 40% of survey participants, and new dry eye symptoms in 28%. These symptoms were generally mild and improving. Visual symptom reporting was much higher (41%) in the online survey than during clinic visits (7%).

Introduction

Laser-assisted in situ keratomileusis (LASIK) has been a U.S. Food and Drug Administration (FDA) approved procedure since 1999. While initially controversial, this procedure to correct refractive errors with excimer laser ablation beneath a corneal flap has been steadily improving and has gained wide acceptance (Schallhorn et al., 2008). Although there have been limited reports on post-LASIK quality-of-life measures, the vast majority of the outcomes reported have been details of visual acuity and refraction. Because of occasional patient dissatisfaction and the lack of patient-reported outcome (PRO) data, a study was designed in collaboration with the National Eye Institute, FDA, and Department of Defense to develop a survey questionnaire to assess subjective outcomes, the Patient Reported Outcomes with LASIK (PROWL) studies (Eydelman & Tarver, 2017).

The studies addressed two populations having LASIK surgery. The PROWL-1 study tested the questionnaire on U.S. Navy personnel, and the PROWL-2 study tested the questionnaire on civilians undergoing LASIK in multiple practices. Questionnaires were completed through the internet before and 1 and 3 months after LASIK in both groups and at 6 months in PROWL-1. The questionnaire, which can be accessed at http://www.fda.gov/LASIK, assessed visual symptoms, dry eye symptoms, and subject satisfaction. The preoperative questionnaire used 154 questions, and the postoperative questionnaire used 112 questions. Each took about 20 minutes to complete. The validity of the questionnaires was confirmed (Hays et al., 2017).

Findings

As expected, both studies confirmed high satisfaction (96%) with LASIK at 3 months. The most interesting findings were the development of new symptoms

of glare and dryness. Before LASIK, visual symptoms such as glare, halos, and starburst were present in 74% of eyes. By 6 months postoperatively, these symptoms were present in 41% of respondents and generally considered to be mild. They were severe enough to limit activities in less than 1%. More concerning was that over 40% of those without preoperative visual symptoms had such symptoms at 3 months. Similarly, dry eye symptoms were common preoperatively and decreased postoperatively, but 28% of subjects developed new dry eye symptoms after LASIK. These were also generally mild (Eydelman et al., 2017). Dry eye may have been associated with the glare, halos, and starburst.

Conclusion

While the development of new visual and dry eye symptoms may be concerning, several caveats should be stressed. These symptoms were assessed at 3 months in PROWL-2 and at 6 months in PROWL-1. Many of these symptoms diminished over this short time and would be expected to diminish further over longer follow-up. The high rate of symptoms, present preoperatively, decreased postoperatively. Despite these symptoms, the satisfaction rates were very high. There were no sight-threatening complications.

Another important finding was that the rates of visual symptoms noted in the online questionnaires were much higher than those reported by the subjects when they were directly examined during their post-LASIK clinic visits. In PROWL-1 at 6 months, 41% of subjects reported visual symptoms through the questionnaire, versus only 7% during clinic visits with the investigators (Eydelman et al, 2017).

The outcomes of these studies confirm the validity of this PRO approach and the PROWL questionnaires. They strongly suggest that such surveys be applied more widely in refractive surgery research and clinical care. They also strongly suggest the need for further research on the causes and treatment of post-LASIK visual and dryness symptoms (Sugar, Hood, & Mian, 2017).

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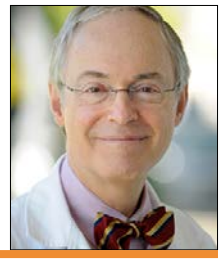

Douglas D. Koch, MD

EYE WONDER WHAT THAT IS?

IOL Options for Addressing Presbyopia

THERE ARE MANY OPTIONS for the treatment of presbyopia in patients undergoing cataract surgery. They include monovision, multifocal intraocular lens (IOLs), extended depth of focus IOLs, and, outside the United States, trifocal IOLs. This article will review those options, addressing their indications, advantages, and limitations.

Monovision

Monovision, where one eye sees far and the other sees near,.is indicated for individuals who have had previous success with monovision contact lenses, desire decreased dependency on spectacles, and will likely tolerate near vision in the second eye.

Distance vision is the key. The uncorrected vision must be good, usually 20/25 or better. I typically operate on the distance eye first and then decide on whether to aim for near in the second eye. How do I determine whether the patient will tolerate near vision in the fellow eye? If they previously wore monovision contacts and liked that vision, then monovision has a high likelihood of success. Also, if they are happy with the distance vision after the first eye surgery and don't feel that the blur from the unoperated eye interferes with their distance vision, then monovision is likely to work well.

Advantages of monovision include preservation of quality of vision, the potential for full correction with glasses, and ability to reverse it with corneal laser surgery. One disadvantage of monovision is the inability to test the patient's ability to tolerate it with a contact lens trial prior to cataract surgery: the blurry vision in one or both eyes precludes true assessment of the visual experience. (However, a contact lens trial can often be helpful if the cataracts are mild.)

Additional disadvantages include poorer vision driving at night, due to the fellow's near vision, and, difficulty with prolonged reading, due to the distance vision in the other eye. As a result, patients might need to have two pairs of glasses: one for distance for the near eye and one for reading for the distance eye. A critical limitation is loss of stereopsis. It has been shown that stereopsis drops precipitously with anisometropia of over 1.5–1.75 D. This means that accurate IOL calculations are critical: the near eye must not be too myopic, or stereopsis will be lost; conversely, too little myopia will result in poor near vision. Finally, some patients just cannot tolerate monovision, describing overall blurry or hazy vision, haloes or glare from the eye being "out-of-focus," or other symptoms suggesting visual

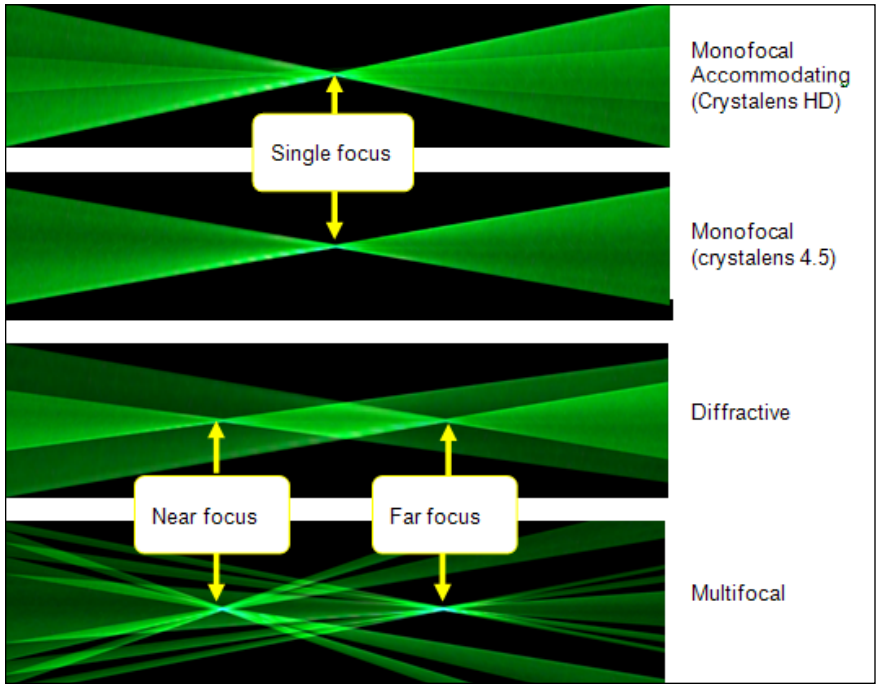

Figure 1. Schematic image showing the single focal point of a monofocal IOL and the splitting of light with a multifocal IOL.

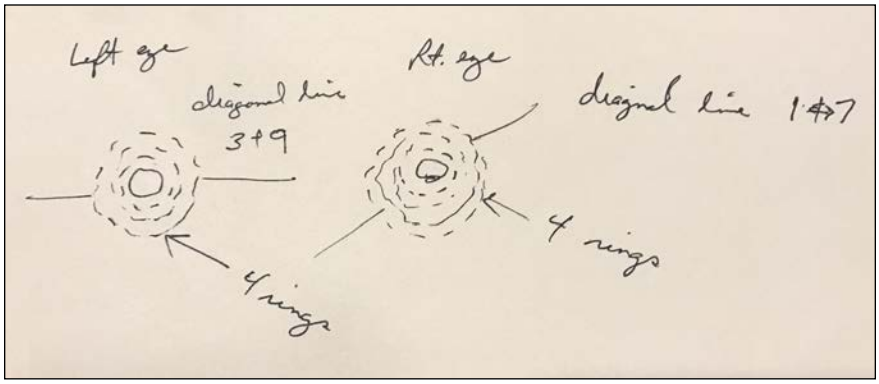

Figure 2. Patient's drawing of halos after implantation of a multifocal IOL.

discomfort. This is easily assessed by holding a correcting minus lens in front of the near eye: the patient will immediately notice greatly improved quality of vision and the necessary correction will be apparent.

Multifocal IOLs

Multifocal IOLs, still a popular option in the United States, are indicated in patients with healthy eyes who are highly motivated to be spectacle independent. With multifocal IOLs, diffractive optics (which appear as rings on the IOL) divide the light into distance and near focal points; approximately 18% of the light is focused elsewhere (see Figure 1). Poor candidates include patients who demand perfect vision or are averse to halos, patients who have any sight-threatening ocular pathology, and myopic individuals who are used to superb uncorrected near vision. Multifocal IOLs have been largely abandoned in Europe in favor of extended depth of focus IOLs and trifocal IOLs.

Multifocal IOLs offer the potential for spectacle-free vision, but the limitations are a slight reduction in visual quality, halos at night (see Figure 2), and inability to eliminate these problems with spectacle correction.

Extended Depth of Focus and Low-Add Multifocal IOLs

The question remains: Is there an IOL that finally meets both patient and physician expectations of clear, high-quality vision and increased depth of focus? No, but we are getting closer. There is a new generation of IOLs that provide better quality of vision, less glare, good intermediate vision, and occasionally good near vision.

Extended depth of focus (EDOF) IOLs use achromatic diffractive technology to elongate the focus of the eye and reduce chromatic aberration. The result is superb quality of distance vision, good intermediate vision, and better tolerance to astigmatism than standard multifocal IOLs. Although some EDOF patients obtain good near vision, most require low-add readers for detailed near tasks. Like all IOLs, EDOF IOLs split light, and this creates visual disturbances, especially at night. EDOF patients report that when they look at car headlights at night, they see spokes or a spiderweb appearance, whereas multifocal IOL patients see halos.

The only FDA-approved EDOF IOL in the United States is the Tecnis Symfony (Johnson & Johnson Vision; see Figure 3). In Europe, the AT LARA from Carl Zeiss Meditec is also commercially available. Other IOLs with other optical designs are in clinical trials.

This case study demonstrates successful use of EDOF technology. FF is a 58-year-old female attorney/CEO of her family business. Preoperatively, her vision was –6.50 + 1.00 x 60 = 20/30 in OD and –6.25 + 0.75 x 95 = 20/30+1 OS. Symfony lenses were implanted, targeting distance in the dominant eye and –0.50 in the nondominant eye. The patient wanted surgery in her nondominant left eye first to see if night vision disturbances would be acceptable.

Surgery consisted of insertion of the 13.5 D ZXR00 (nontoric Symfony) combined with femtosecond intrastromal relaxing incisions using the Catalys laser. Postoperatively, UCVA was 20/30, J1 with a refraction of –0.50 sphere. She loved the vision.

Similar surgery was performed for the right eye with a target of plano. Postoperatively, UCVA was 20/20, J1 with a refraction of –0.25 sphere. Now she only occasionally needs to use reading glasses and is thrilled with her vision.

Another IOL option available to us in the United States is the Restor 2.5 D (see Figure 4), which is a low-add multifocal that provides great distance and good intermediate vision in most patients. A key advantage is that halos tend to be minimal. As with other IOLs in this category, low-add reading glasses are usually required for near vision, and one approach to improve near vision is so-called micromonovision: aiming for –0.50 to –0.75 in the nondominant eye. The following case study again demonstrates successful implementation of this strategy:

SS is a 74-year-old orthopedic surgeon who was OS dominant and received bilateral Restor 2.5 D IOLs. The target for the left eye, which was operated first, was distance; the target for the right eye was –0.75. His outcome was as follows:

- OS: 20/20, J3 with plano refraction and
- OD: 20/30, J1 with –0.75 refraction.

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IOL Options for Addressing Presbyopia

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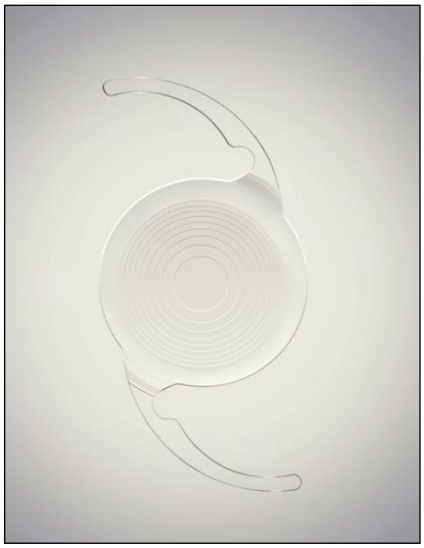

Figure 3. Tecnis Symfony

Figure 4. 2.5 D Restor (SV25T0)

The patient is very happy with the results, although he sometimes needs +1.00 readers.

Since EDOF and low-add multifocals provide excellent quality of vision, they allow us to modestly expand the pool of potential patients who might benefit from their insertion. I have had good success with post-LASIK patients who have fairly regular topography, and I am also comfortable using these IOLs in patients with conditions such as the very early stages of AMD or well-controlled, mild glaucoma. Here is one example:

ML is a 70-year-old male with prior hyperopic LASIK OU. His preoperative readings were as follows: OD, +1.50 + 0.75 x 135; and OS, +1.50 + 0.25 x 65. Symfony IOLs were implanted, aiming for a distance target. In both eyes postoperative UCVA was 20/20, J1+ with minimal starburst at night.

Mixing and Matching

The EDOF and low-add IOLs can be combined with a standard multifocal in the nondominant eye to enhance uncorrected reading vision. For example, the Symfony can be combined with the ZLB00 (3.25 D Tecnis multifocal), and the Restor 2.5 D can be combined with the Restor SN6AD1 (+3.00 add multifocal). Good candidates are patients who are happy with distance and intermediate vision with the EDOF or low-add IOL in the dominant eye and are willing to accept more halos to get better reading vision in the nondominant eye.

What's on the Horizon?

Two categories of IOLs are not yet available in the United States. The first is the trifocal IOL, which uses technology to redirect some of the light lost with bifocal designs to give distance, intermediate, and near vision with ostensibly no more or even less glare than occurs with multifocal IOLs. In Europe, trifocal and EDOF IOLs dominate the market, but we in the United States will have to wait at least two to three years before the first trifocal IOL gets FDA approval.

Accommodating IOLs are still in early phases of development or preliminary clinical trials. These IOLs would theoretically respond, as does our (young) natural crystalline lens, by changing power with an accommodative stimulus. The challenges are daunting due to concerns about long-term capsular flexibility if inserted in the capsule and long-term safety if inserted in the ciliary sulcus. I am not holding my breath on this one.

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Keller Johnson-Thompson and Laura C. Beckwith

The Strength, Courage, and Mission of Helen Keller: Part II

Part I of this series, featured in the previous issue of Insight, focused on Helen Keller's early days, including her friendship with her teacher, Anne Sullivan; her schooling, travel, and speaking engagements; the movie about her life; her vaudeville act; and her fundraising and advocacy efforts. Part II continues to highlight her strength, courage, and mission.

After Anne's death, the world continued to beckon Helen, inviting her to visit and provide advice, support, and publicity for work regarding the blind and deaf-blind. For the next 11 years, she visited 35 countries on five continents, eager to change the world for the better.

Helen loved the people of Japan and visited them three times during her world tours. In 1948, huge crowds turned out to see her. In Tokyo, Helen spoke outside the Imperial Palace. She attracted a crowd numbering in the tens of thousands. Her primary goal was to aid the blind and to promote Japanese-American goodwill. Shortly before her departure to Japan, President Franklin D. Roosevelt sent her this message: "I feel confident that your presence will prove a lasting inspiration to those Japanese laboring under physical handicap, and that your association with Japanese individuals and groups interested in humanitarian endeavors will contribute to promoting that spirit of friendship and goodwill between our people and the people of Japan upon which good international relations must rest. You are so well qualified to convey to the Japanese people the cordial greets of the American people. I take this opportunity to express my hope for the success of your mission."

Helen and Polly Thomson toured Egypt, Lebanon, Syria, Jordan, and Israel. Helen was entranced and wrote about her visit to her friend and colleague Georges Raverat, director of the American Foundation for Overseas Blind (now Helen Keller International), in Paris. During her visit, she met leading cultural and political figures of the region, including the Egyptian writer and intellectual Taha Hussein, Queen Noor of Jordan, and Golda Meir, Israel's foreign minister. She wrote, "I could not help wondering how it would fare with us in our work in Egypt. To my surprise the people we met showed us warm friendliness and were most hospitable. We visited the few schools that exist for children without sight. I was grieved to find what meager openings the adult blind of Egypt have for re-education or employment. As one of the charming, progressive Egyptian women said to whom I was introduced, 'Our people have a strong willpower, but you must make them believe in a movement before they support it.' How true that is of the work for the blind and the deaf!"

Helen was an enormous success, and in Egypt her timing could not have been better; the visit took place just two months before Gamal Abdel Nasser overthrew King Farouk. Kim Nielsen, in her book *The Radical Lives of Helen Keller*, notes that the U.S. State Department, unlike the CIA, was unaware of the monarch's imminent overthrow. Helen's presence was an affirmation of U.S. values at a time when America was becoming increasingly concerned about Egyptian sympathies for the Soviet Union.

Helen's chief concern had become the blind and deaf of the world. Consequently, when the Rev. Arthur Blaxall of the South African National Council

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The Strength, Courage, and Mission of Helen Keller: Part II

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for the Blind, whom she had met at the 1931 World Conference, bade her to come to South Africa to spur support for the blind and the deaf, she immediately began to make arrangements. In February 1951, Helen and Polly boarded a ship for Cape Town. Her itinerary included 28 schools and institutions; she addressed 48 meetings and receptions, and she visited every important urban center in the Union, pleading with the various races of Africa to take an equal share in promoting the welfare and happiness of their handicapped friends and neighbors. The Zulus gave her the name "Homvueselelo," meaning, "You have aroused the consciences of many."

Helen was truly an American ambassador. She was to some a saint, to others a blessing, and to all, a national treasure.

As a result of her work throughout the United States and the world, U.S. presidents were eager to make her acquaintance. She personally met every president from Calvin Coolidge to John F. Kennedy. She told President Kennedy that he had to be the best-looking

president America had ever had, and while she was feeling Dwight Eisenhower's face, he accidently opened his mouth as she went to feel his lips, causing her to comment, "Oh, Mr. President! What a big mouth you have."

Helen was especially close to First Lady Eleanor Roosevelt, whom she met in 1938, Eleanor's husband, Franklin D. Roosevelt, proclaimed his admiration: "Whatever Helen Keller is for – I am for."

World War II created thousands of war veterans who needed Helen's particular brand of optimism and courage. Helen wanted to help, so she asked Polly to make arrangements so that she might visit the wounded men. She clearly knew in her heart how the wounded men felt. "Life [is] not over," she told them. "It [is] different, but not over, and [you can] still find meaning and satisfaction in it." It was a message she lived herself, and she gained enormously from her visits. She wrote, "Often it was not verbal encouragement that was asked of me, but a kiss or the laying of my hand on a wearied head. This always made me feel as if I was partaking of a sacrament. Visiting the war wounded was the crowning achievement of my life."

In 1952, Helen was awarded the Gold Medal of the National Institute of Social Sciences, given annually to a distinguished individual who has been of outstanding service to humanity.

Also in 1952, the World's Ambassadors to the United States honored Helen at the Waldorf Astoria in New York as she was ready to embark on another world tour. While many called her "an ambassador to the world," she called herself "an international beggar." This was to be the last of her world tours.

During her lifetime, Helen Keller witnessed great advances in civilization. Inventions, such as the radio, airplane, and automobile, demonstrated the immeasurable will of the human spirit to progress. However, she also lived during the creation and use of the atomic bomb, the bomber, and the tank. Colonization, two world wars, and increasing labor conflicts continued to draw out her will to change the world for the better. She believed that humanity's destiny is our responsibility, and she was never timid in expressing her opinion of society as a whole or in her attempts to better it. She wrote, "Until the spirit of love for our fellowmen, regardless of race, color or creed, shall fill the world, making real in our lives and our deeds, that actuality of human brotherhood – until the great mass of the people shall be filled with the sense of responsibility for each other's welfare, social justice will never be attained."

At the Harvard commencement exercises in 1955, Helen became the first woman to receive an honorary degree. The entire audience gave her a standing ovation!

Indeed, Helen received awards and honors of distinction throughout the world, from every country that she visited. She won an Academy Award for Best Documentary Feature in 1956 for Helen Keller in Her Story. On September 14, 1964, President Lyndon Baines Johnson presented Helen with the highest civilian award presented in the United States, the Presidential Medal of Freedom, one of only 30 that had been presented up to that time. A year later, she was elected to the Women's Hall of Fame at the New York World's Fair.

Helen had a heart attack in late May 1968. A few days later, on June 1, she died quietly, according to the nurse who was with her. Helen never feared death; she was sure that in eternity, she would be able to both see and hear.

In the end, Helen died as she had lived, dignified and courageous, with her sightless eyes focused firmly on the future. Her ashes were interred in the National Cathedral in Washington, D.C. At her memorial service, Senator Lister Hill of Alabama remarked, "She will live on, one of the few, the immortal names not born to die. Her spirit will endure as long as man can read and stories can be told of the woman who showed the world that there are no boundaries to courage and faith."

Throughout her long life, Helen worked tirelessly to change the world, not only for the blind and the deaf-blind but for all people. And she succeeded. Today, work in her name is being carried on in every part of the world.

Twenty years after her death, members of my family helped establish the Helen Keller Foundation to align her legacy with research and education solutions to sight

and hearing loss. Aunt Helen is our guiding light, and the work that we do in her name is changing the world for the better.

As the twentieth century concluded, with Time magazine naming Helen Keller as one of the century's 100 most important figures, the Helen Keller Foundation completed its first decade of work in her name. Helen Keller Foundation researchers were the first to report a revolutionary surgery to repair the diseased macula, the human center of vision.

The Foundation proved that recently injured eyes with no remaining light perception (NLP) need no longer be removed or abandoned to reconstruction – that these eyes could often be surgically restored to useful vision.

Foundation researchers also developed a laser treatment that could prevent retinal detachment with 95% certainty. This ameliorated a scourge that has plagued humankind since ancient times, producing blindness that became partially treatable only in modern times. For those who have already suffered the blinding condition of retinal detachment, the Foundation has also developed a surgical eye treatment that reduces scar tissue complications in retinal detachment repair by 88%!

During the first decade of the new millennium, the Helen Keller Foundation developed a cure that saves central vision in diabetic retinopathy – the leading cause of sight loss in the working-age populations of developed countries worldwide. The same laser-based technique offers better hope for those over age 65 who develop strokes of the retina.

The Foundation is confident that when these research breakthroughs are fully implemented into patient care, millions of years of lost eyesight will be saved, and cost savings to public health and productivity will have been made for pennies on the dollar! That is the power of the modern biomedical research era that dawned in the 1960s, even as Helen was leaving us.

As Helen's great-grandniece, I have taught her famous story to school children and adults throughout the United States and abroad for more than a decade. I now plan to begin webcasting to schools worldwide from Aunt Helen's birthplace in Tuscumbia, Alabama.

The Helen Keller Foundation is ensuring that her life lessons, still beloved by literate people worldwide, will be known to generations yet to come, and that public support for sight research will forever be mobilized in her name.

If you or someone you know has an interest in our work and/or are interested in helping our cause, "to help hasten the day when there shall be no preventable blindness," please contact us at (205) 933-9389, or visit our website, www.helenkellerfoundation.org.

"Alone we can do so little; together we can do so much."
– Helen Keller

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Viewpoint

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setting (IOM, 2010). In this complex health care environment nurses may encounter many uncertainties in their practice, yet the opportunities for leadership, innovation, influence, role enhancement, and demonstrating nursing value have never been more critical. Strong and immediate ambulatory care nurse actions are identified to improve health and display their value. Among these are (AAACN, 2017, p.45):

- Communicate the story of ambulatory care nurses and their ability to positively impact outcomes.
- Ensure robust clinical documentation tools are in place to support practice.
- Expand nursing knowledge by applying or conducting scientific studies.
- Lead organizational efforts to define and implement nursing roles that promote autonomy, collaboration, care coordination, transition management, and improve practice.
- Design cultures and structures that promote and reward innovation.
- Establish health system and academic institution alliances to prepare ambulatory care nurses.
- Develop an agenda that informs others – the nursing community, health care professionals, and other stakeholders – of ambulatory care nurses' value and cost effectiveness.

Professional nurses are the most versatile member of the health care team. They carry the knowledge and expertise to positively impact health by providing greater access to health care services, decreasing costs, and improving quality. Ophthalmic nurses should seize this opportunity to describe and demonstrate their value.

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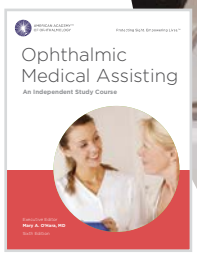

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