Anophthalmia

The Expert's Guide to Medical and Surgical Management

Thomas E. Johnson
Editor

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Portrait of a Flautist with One Eye, 1566, Anonymous Artist, Louvre Museum, Paris

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Dedicated to my daughter Olivia whose intellectual curiosity, passion for life, and empathy for others inspires me every day. Also dedicated to the rest of my wonderful family including my mom Anna, sister Janan, brother Lant, Maria, Dayra, and to the memory of my dad Arthur.

Foreword

End-stage ophthalmology: That is the title slide for the lecture I have presented for many years on the topics of evisceration, enucleation, and exenteration – operations of last resort when ocular disease has overwhelmed our abilities to salvage an eye. Unfortunately, unlike end-stage renal disease or end-stage cardiac disease, ophthalmologists do not have a biological alternative, such as a kidney or heart transplant, to restore useful function when vision has been lost or a sick eye has become a liability or even a threat to life.

In *Anophthalmia: The Expert's Guide to Medical and Surgical Management*, Dr. Thomas Johnson and his collaborators present a comprehensive approach to managing these always discouraging scenarios. The scope of the book goes considerably beyond the wherefores and standard techniques for removing a diseased eye, including detailed coverage of tertiary care such as congenital anophthalmia, socket expansion, osseointegration, implant exchange, and corneal tattooing. The authors also emphasize the critical partnership between the surgeon and the ocularist, whose skill and artistry are fundamental to a satisfactory functional and aesthetic outcome. Readers should be interested to learn how the expertise of ocularists can be traced to doll-making and dentistry.

As with any area of medicine, ambiguities and controversies remain, such as whether to perform an evisceration or an enucleation in certain circumstances to minimize the risk of sympathetic ophthalmia. After a detailed, balanced review in Chapters 1 and 3 of publications dating back more than two centuries, the authors of Chapter 3 "generally favor enucleation." Personally, I *generally* favor evisceration, which has served my patients well for the past 35 years, but perhaps I have simply been lucky. Another minor quibble is the preference in Chapter 8 for lining an exenterated socket with split-thickness skin grafts over allowing the cavity to heal by second intention. In the Upper Midwest, granulated sockets tend to be less sensitive to winter temperatures than skin grafts on bone. My hardy heartland patients seem not to be troubled by postoperative orbital wound care, and long-term tumor surveillance is rarely problematic with the availability of sophisticated imaging. However, in the absence of unimpeachable level 1 evidence for much of what we do, *vive la différence*!

I particularly appreciate the book's historical perspectives, which emphasize the physical and emotional insults of losing an eye along with the creative approaches that our predecessors have devised and attempted, over many centuries and often unsuccessfully, to improve on wearing a black patch. The wisdom of Carl Becker, quoted in Chapter 1, warrants highlighting: "History prepares us to live more humanely in the present and to meet rather than foretell the future." One hopes, however, that the future will include new technologies and treatments that will render anophthalmia a much less assaultive and distressing condition for both patients and physicians than it is today.

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Preface

The loss of an eye is tragic. Not only do patients suffer a significant functional disability, but also live the rest of their lives with a cosmetic deformity with the real probability of discomfort and inflammation. In the not-so-distant past, ophthalmologists might admit defeat, remove the eye, and then forget about the patient, directing their efforts toward treating eyes that still have vision. Eye removal surgery was often delegated to beginning ophthalmology residents as a way for them to learn surgery with minimal risk. Bad functional and cosmetic outcomes were common, with inflamed sockets, volume loss, implant shifting, eyelid abnormalities, and resultant difficulties in wearing an ocular prosthesis.

But times have changed. We now realize that the loss of an eye is not the final stage of the patients' ophthalmology care. It is a new beginning, a new phase. Improved orbital implants, more refined surgical techniques, recognition of problems causing anophthalmic socket problems, and superior ocular prosthesis fabrication have tremendously improved the quality of life for anophthalmic patients. True, the gift of sight has been lost. But the gifts of comfort, freedom from infection and inflammation, and good cosmesis are now possible, boosting patients' comfort and self-esteem and allowing them to live more fulfilling lives.

The authors of this book have attempted to create a resource that comprehensively covers the field of anophthalmia: Historical perspectives, indications for eye removal along with surgical techniques, prosthesis making, anophthalmic socket care and maintenance, and surgical procedures to correct anophthalmic socket defects are described. Congenital anophthalmia is reviewed. Newer techniques such as osseointegration are illustrated. It provides a quick reference for medical students, ophthalmology residents and fellows, ophthalmologists, psychologists, and everyone else taking care of these patients. In this changing field, we hope newer advancements will allow us to update this book every few years!

I am greatly indebted to my authors for their hard work in contributing to this book. Also thank you to the editors and staff at Springer, including Tracy Marton,

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Part I
Clinical Foundations

Chapter 1
Introduction and Historical Perspectives

Ji Kwan Park and Thomas E. Johnson

Introduction

The art of successfully removing a diseased eye has long been underappreciated. In years past, enucleation was a type of surgery given to first-year ophthalmology residents. What could ever go wrong? The eye was removed, a spherical implant was inserted deep into the muscle cone, and the tissues were closed. The risk was minimal, and the rest of the patients' functional and cosmetic rehabilitation was left in the hands of the ocularist.

Over time, however, almost all of these patients developed significant functional and cosmetic problems. Invariably, the implant would migrate, the inferior fornix would shorten, the lower lid would sag, and the superior fornix would deepen. There would be no way to hide the fact that the patient had an "artificial eye." However, that was the standard of care, and we just accepted that those problems were just part of losing an eye.

The psychological effects of eye loss can be quite serious. Loss of self-esteem is common. The cosmetic deformities of the anophthalmic socket syndrome affect patients' employability, their ability to find a romantic partner successfully, and their ability to make new friends. Feelings of inferiority based on the cosmetic appearance of their eyes may prevent them from achieving their full potential and meeting their goals.

Ophthalmologists recognized these problems and began working on ways to improve the outcomes of eye removal surgery. Implants were improved in an attempt

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to increase prosthesis motility and to replace volume lost due to fat atrophy in the anophthalmic socket. Wrapping materials were employed so that extraocular muscles could be attached, improving socket motility and helping to prevent implant migration. Integrated implants were invented to impart more movement to the overlying prosthesis. Porous integrated implants were developed to allow tissue and vascular ingrowth into the implants, making them a living part of the body and more resistant to extrusion and migration.

Ocularists also improved the fabrication of their prostheses. Better curing of the acrylic material decreased inflammatory responses, resulting in healthier and less inflamed sockets. Impressions were made to allow the custom-fitting of the artificial eye. Patient education improved, and regular prosthesis polishing and cleaning also resulted in healthier sockets.

Early Historical Perspectives

The earliest manuscripts on ocular surgery come from a collection of laws in old Babylonian and Sumerian codes between 3000 BCE and 2250 BCE. One law stated that "if a man destroys the eye of another man, they shall destroy his eye." The law also punished the surgeon, who also served as a temple priest, by cutting off his fingers if he "fails to open an abscess with a bronze lancet and destroys the eye." As early as 2600 BCE, the Chinese devoted a god in the interest of oculists [1, 2]. The oldest known prosthetic eye is dated between 2900 and 2800 BCE (Fig. 1.1) [3, 4]. In 1650 BCE, Egyptians removed the eye from the dead and filled the orbit with wax and precious stones (to simulate the iris) during the process of mummification. Around 500 BCE, Egyptian and Roman priests employed ocular decorations made of clay and held in place by adhesives or thongs to cover phthisical globes [5–7]. Eye removal surgery and cosmetic prostheses were not described until the late sixteenth century in Europe [6, 7].

The *ekblepharon* was the first external prosthesis described by Frenchman Ambroise Paré (1510–1590). The painted leather patch was worn over the disfigured eye and held in place by a metal wire that wrapped around the head (Fig. 1.2a) [8]. In 1749, Burchard Mauchart of Tübingen, Germany, described a prosthesis that would fit in the eye socket. The *hypoblepharae* was a gold shell with the iris painted in colored enamel (Fig. 1.2b). In the seventeenth century, skilled Venetian and German glassblowers made more realistic prosthetic eyes [7]. Lorenz Heister of Nuremberg in 1752 recorded that he preferred the glass eyes over metal prostheses that repelled tear fluids and lost their brightness over time. In 1880, Herman Snellen invented the "Reform" eye, a hollow glass eye with round edges, to improve comfort and facilitate restoration of the socket volume (Fig. 1.2c). Duponcet of Paris also published one of the earliest books on the fabrication of glass prosthetic eyes in 1818. Ludwig Müller-Ur (1811–1888) developed the cryolite glass eye, which was made of arsenic oxide and sodium aluminum fluoride. These glass eyes were exported across the world from the late nineteenth century until the beginning of

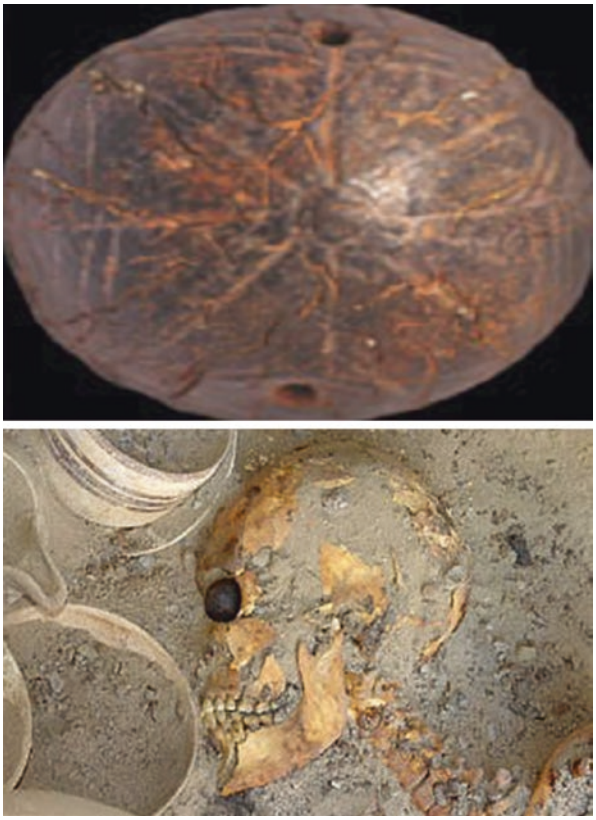

Fig. 1.1 The world's earliest known prosthetic eye was made of a mixture of natural tar and animal fat overlaid with a thin layer of gold. The central corneal circle had radial lines fanning out like the rays of the sun and represented light emanating from the eye. Fine lines were drawn to simulate conjunctival vessels. A small hole on each side of the half sphere allowed golden threads to pass through and hold it in place. The prosthesis also had imprints from chronic skin contact and marks suggestive of an abscess of the eyelids. Archeologists believe it was worn by a young ancient Persian priestess who lived between 2900 and 2800 BCE. (Images reproduced with permission)

World War II, when all trade with Germany ceased (Fig. 1.2d). British dental technicians discovered polymethylmethacrylate (PMMA) as an alternative material to make eye prostheses in the 1930s. PMMA was not only well tolerated by the orbital tissues but also allowed for molding and curing of the prosthesis. For the first time, a custom-fit prosthesis was made from an impression of the patient's socket. Fritz Jardon, who immigrated to the United States from Germany, also developed PMMA prosthetic eyes and improved impression techniques [7, 9]. By the early 1940s, scleral cosmetic lenses were introduced as these plastic shells eliminated the risk of breakage and injury to the eyes [10]. Advances in orbital implants also led to the development of a combined ocular prosthesis by Ruedemann in 1946 (Fig. 1.2e) [12, 13].

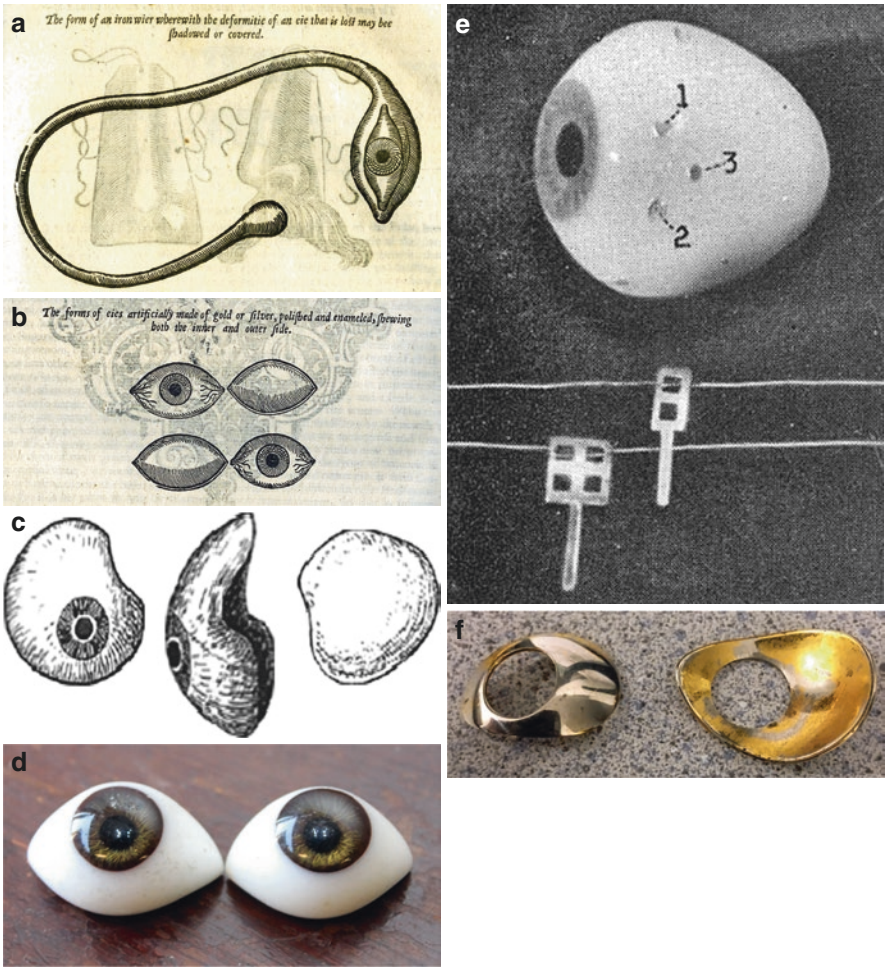

Fig. 1.2 (**a**) The *ekblepharon*. This painted leather patch was worn over the disfigured eye and held in place by a metal wire that wrapped around the head. (**b**) The *hypoblepharae* was a gold shell with the iris painted in colored enamel. It was the first prosthesis that would fit in the eye socket. (**c**) Snellen's *Reform* glass eyes had round edges to improve comfort and facilitate the restoration of the socket volume [11]. (Image courtesy of Arbaz Sajjad, MD). (**d**) A glass eye made in the early twentieth century from Germany. (**e**) A combined motility implant and ocular prosthesis was introduced by Ruedemann in 1946. Numbers 1 and 2 indicate the holes used to pass the needle and secure the metal muscle paddle, which is anchored at the hole labeled as number 3. A high rate of infection, difficulty with alignment, and inability to remove the prosthesis limited its use [12, 13]. Image reproduced with permission. (**f**) A gold-plated ocular conformer was used in 1929. In 1902, Fox believed that the conformer aided in tissue healing following his gold sphere placement [14, 15]. (Image courtesy of Michael O. Hughes, BCO)

Extirpation

Extirpation was a subtotal exenteration traditionally performed without anesthesia. In 1583, Georg Bartisch, of Dresden, Germany, first described the surgical technique in his book, the *Augendienst*. The operation was reiterated by Johannes Lange (1485–1565), of Lowenberg, Silesia (Germany) [1, 16]. The surgery was so excruciatingly painful that the patient had to be tied down and bled to a state of delirium before the operation. A thick suture was passed through the globe to exert forward traction, while a curved knife was passed into the orbit. Hemostasis was achieved with ice water. The operation not only removed the globe but also sacrificed the conjunctiva, orbital fascia, and portions of the extraocular muscles (Fig. 1.3a–c). The socket was then allowed to spontaneously granulate, and the surgery left the conjunctival fornices unsuitable for ocular prosthesis wear [1, 5]. Instead, an external prosthesis complete with eyelids, lashes, and a painted globe was held in position with an external strap [7]. This surgical procedure was rejected by many physicians and declared as "inhuman except under the greatest and most urgent necessity." The last recorded extirpation was performed by John Whitaker Hulke of Moorfields Eye Hospital, London, in 1848 [5, 6], suggesting that extirpation had been a common surgical practice for over two and a half centuries!

Enucleation

Enucleation refers to the removal of the globe and its contents with the preservation of the surrounding periorbital and orbital structures. In the first known description of enucleation recorded in 1826, Cleoburey (Saxon) stated that the conjunctiva should be divided with a thin, sharp-pointed knife followed by the detachment of all the muscles that are inserted into the globe. Further dissection was carried out toward the posterior part of the orbit to divide the optic nerve. He stated, "The nerve will be easily divided by directing the knife back into the orbit on the nasal side of the globe, as the optic nerve is situated nearer on this side [1, 17]." However, his technique was later dismissed owing to the final result being a deep-set, immobile prosthesis [6].

Enucleation surgery in this era resulted in a large amount of blood loss and a high complication rate. Complications included postoperative infection, meningitis, and sometimes mortality. The sockets were often left without an implant, and this caused the ocular prosthesis to sink back and with a resultant deep superior sulcus deformity. Nonetheless, enucleation was deemed necessary to prevent the contralateral eye from developing sympathetic ophthalmia following trauma [15, 18, 19]. In 1841, O'Ferral (Dublin) and Bonnet (Paris) introduced a more anatomic approach that laid the foundation for modern enucleation. O'Ferral reported that by separating a new fascial tissue called "tunica vaginalis oculi" from the sclera, and then severing the muscles at their insertion to the globe, the surgeon could remove the

Fig. 1.3 (**a**) Preparing for extirpation, as described by Georg Bartisch in his book the *Augendienst* in 1583. (**b**) Passing a suture through the globe followed by forwarding traction and severing the optic nerve and surrounding tissues with a curved knife to remove the eye. (**c**) Surgical instruments used to perform the extirpation

globe with minimal blood loss. This "new" fascia was described by Rene Tenon in 1806 and is now known as Tenon's capsule [5]. In 1842, Stoeber also described his technique of "shelling the eyeball" within the Tenon's capsule. In 1855, Critchett reported several successful enucleations for nonmalignant ocular conditions [1].

In 1906, Gallemaerts introduced an interim prosthesis that was placed between the closed bulbar conjunctiva and the palpebral conjunctiva. Holes were drilled through the center of this temporary prosthesis, which allowed the drainage of secretions. This device was initially criticized as a source of infection that caused severe sepsis and the eventual death of a patient [7]. However, most surgeons soon understood that the insertion of a conformer between the lids helps to tamponade postoperative conjunctival edema and it prevents socket contracture (Fig. 1.2f) [1, 14]. In 1847, the introduction of general anesthesia with ether and chloroform changed the field of surgery drastically, including advances in eye removal surgery [6].

Evisceration

Evisceration involves the removal of the intraocular content while leaving the sclera, the attached extraocular muscles, and the optic nerve intact. The cornea may or may not be removed. The first evisceration was accredited to James Beer in 1817. While performing an iridectomy for acute angle glaucoma, his case was complicated by an expulsive hemorrhage that necessitated the removal of the contents of the globe [1, 8]. In 1874, Noyes routinely performed evisceration on patients with severe ocular infections. He reported excellent cosmetic outcomes, with no cases of sympathetic ophthalmia [1, 20]. In 1884, Philip Henry Mules placed a hollow glass sphere into the scleral cavity after the removal of the cornea and the intraocular contents [21]. His technique not only replaced the lost orbital volume, it also reduced the incidence of socket contraction [7]. Various orbital implants were developed after his revolutionary discovery and are discussed in Chap. 10. Further advances in the surgical techniques led to the modern approach in evisceration without keratectomy as described by Burch in 1939 [22]. In 1956, Berens published a large case series of successful eviscerations with keratectomy and reported no cases of sympathetic ophthalmia and a low rate of implant extrusion [23].

The perpetual controversy over evisceration versus enucleation has been ongoing for more than a century. In 1887, Frost reported a series of patients who developed sympathetic ophthalmia after evisceration. Although he considered evisceration to be inferior to the enucleation, he complimented on the excellent outcomes of using Mules' glass sphere following evisceration. He proposed that a good cosmetic prognosis may convince patients to choose surgery after eye trauma rather than to keep the injured eye and take the risk of losing the fellow eye from sympathetic ophthalmia [24]. However, surgeons in this era objected to the use of evisceration due to concerns for the development of sympathetic ophthalmia, the spread of a previously undetected intraocular tumor, and the loss of ocular tissues for patho-

logic studies. In 1898, the Ophthalmological Society of the United Kingdom assigned a committee to compare a simple excision of the eyeball, evisceration with or without the insertion of an implant, enucleation with the insertion of an implant in Tenon's capsule, and other procedures. The committee decided that the simple enucleation of the globe within Tenon's capsule with or without implant placement was the most appropriate procedure. George Edmund de Schweinitz presented similar conclusions at the International Congress in 1900. However, some members felt that evisceration was not sufficiently recognized. They filed a minority report stating that the excision should be limited to cases of intraocular and orbital malignancies, extensive lacerated or contused wounds of the sclera, markedly shrunken globes, and sympathetic ophthalmia [1]. Nonetheless, most surgeons in Great Britain, Europe, and the United States were in favor of enucleation due to the fear of sympathetic ophthalmia that was prevalent in the literature between 1887 and 1908 [25, 26]. This resulted in a near abandonment of evisceration for more than half a century, and it was considered a substandard procedure by World War I. Only a few ophthalmologists stood firm and advocated for evisceration [22, 26]. Some authors continued to report isolated cases of sympathetic ophthalmia following evisceration until the 1970s [26].

In 1963, Ruedemann questioned the validity of previous case reports in an attempt to reignite interest in evisceration. He found that 17 out of 47 reported cases since 1887 did not meet his diagnostic criteria for sympathetic ophthalmia. These cases not only lacked sufficient clinical details to support the diagnosis but rarely reported exam findings of the uninjured eye. The histopathological results were routinely missed in the case reports. For example, one contributor sent a biopsy of the anterior chamber for analysis but discarded the posterior segment contents. While most patients had eviscerations following severe eye trauma, Ruedemann speculated that some of the patients instead received incomplete enucleations [26]. Other authors believe that early ophthalmologists often confused sympathetic ophthalmia with a variety of other types of uveitis [27]. In Ruedemann's report of 506 cases of evisceration, not a single case of sympathetic ophthalmia was found. In 1972, Green also admitted that his reported cases of sympathetic ophthalmia might have been initiated by the original trauma rather than the evisceration itself [26].

Between the late 1970s and early 2000s, more surgeons were performing eviscerations, although the total number of eye removal surgeries decreased [28–30]. Hansen et al. attributed such a shift in practice to the general acceptance by surgeons who favored enhanced cosmetic and motility outcomes following eviscerations [28]. In 1985, a questionnaire sent out by the American Society of Ophthalmic Plastic and Reconstructive Surgery (ASOPRS) found that none of the 140 respondents had seen a case of sympathetic ophthalmia after evisceration [31]. A similar but larger survey in the late 1990s revealed 5 recalled cases of sympathetic ophthalmia out of 841 eviscerations, 3 of which were post-trauma-related. Despite the increasing number of eviscerations performed across the United States, no cases of sympathetic ophthalmia were reported between 1972 and 1997. In 1999, Levine et al. did not find any cases of sympathetic ophthalmia in his review of 90 evisceration surgeries over a 35-year period. He concluded that evisceration is a safe proce-

dure with a low risk for sympathetic ophthalmia [32]. Although retinal surgery is now suggested as the leading cause of sympathetic ophthalmia [33–35], reports of sympathetic ophthalmia after evisceration are not unheard of in the twenty-first century [36–41]. A number of unsuspected malignant melanomas following eviscerations have been reported since the early 1900s [42–48]. Historically, the incidence of this finding was about 0.5% [49]. Some authors believe that this condition is underreported, and the risk of accidentally eviscerating an eye with an intraocular tumor may be higher than the risk of sympathetic ophthalmia [45].

Exenteration

Orbital exenteration refers to complete removal of the globe, eyelids, muscles, fat, and nerves of the orbit. The first reported exenteration was described by Gooch in 1767 [50]. Langenbeck in 1821 and Dupuytren in 1833 further advanced this surgical technique [51]. Collis in 1864 and von Arlt in 1874 described detailed surgical steps of exenteration, most of which are still used today. In 1888, Jacobson reported an exenteration of an orbital "rodent ulcer" using the Arlt method. After cutting the outer commissure to the margin of the orbit, the lids were folded back upon the cheek and the forehead. The orbital tissues were dissected beyond the conjunctival fornices and away from the globe. The tumor or the orbital contents were seized and drawn forward using a pair of forceps with hooks at the tip of each blade, also known as a vulsellum. A blunt elevator was used to separate the mass from each outer wall. The optic nerve and the muscles were then severed with a sharp pair of curved scissors. When the tumor was adherent to the periosteum, it was incised at its margin with a scalpel [52]. His technique had been influenced by the "lid-sparing technique" introduced by Streatfeild in 1872, where the upper and the lower eyelids were sutured together to cover the exenterated socket. At about the same time, Noyes included the eyelids during exenterations. He made the initial incisions vertically through the middle of the upper and lower eyelids. A knife was used to deeply dissect the orbit along the roof and the floor. Horizontal cuts were made through the inner and outer angles. The orbital contents were then separated from the medial and lateral walls without any tissue collapse. The cuts were made diagonally to reach the apex of the orbit [53]. In 1909, Golovine reported an extended orbital exenteration, which included the removal of the adjacent maxillary sinuses [54].

Most surgeons in the early 1800s reserved orbital exenteration for malignant tumors involving the orbit and the periorbital tissue. The empty socket was allowed to epithelialize spontaneously by the granulation tissues [55]. By the early 1900s, many surgeons found that the cicatricial healing of the surrounding soft tissues caused postoperative discomfort and resulted in poor cosmesis. Some patients and family members were appalled at the hollow appearance of the desquamating orbital cavity and found the routine care of the exenterated socket distasteful [56, 57]. The Ollier-Thiersch split-thickness graft, which was first introduced in 1872, was used to line the orbital cavity, but the technique was not well-accepted [56, 58]. The

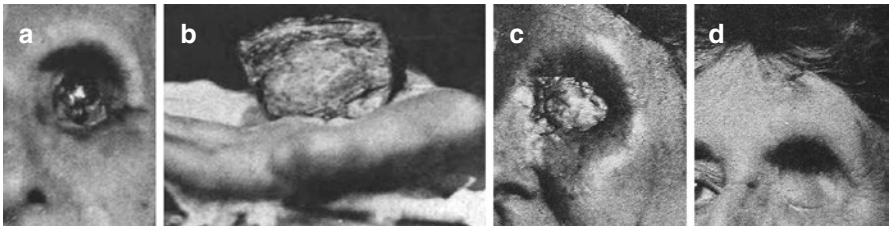

Fig. 1.4 (**a**) Cicatrization of the surrounding tissues drew the facial skin and soft parts into the orbit and caused pain. (**b**) In 1919, Davis harvested a pedunculated flap of thick fat and skin from the abdominal wall and implanted it to an incision on the palm. (**c**) Once the circulation was established, the flap was transferred and shaped to fit the defect in the orbital cavity. The sutures were then removed after 10–14 days. (**d**) Twelve months later, the skin remained soft and covered the cavity without puckering the surrounding tissues [56]

Schirmer method filled the cavity with a free fat graft and then covered the orbital opening with a pedunculated flap from the forehead or cheek. This technique, however, left extensive facial scars [56, 59]. In 1919, Davis introduced a double transfer method using a pedunculated flap from the abdominal wall to cover the orbital cavity (Fig. 1.4) [56]. Numerous primary reconstructive methods, including primary skin grafts, temporalis muscle flaps, pectoralis major muscle flaps, and single flap repairs, were introduced throughout the twentieth century [57, 59–61]. Exenteration and reconstruction techniques are further discussed in Chap. 9.

Conclusion

As historian Carl L. Becker would say, "the value of history is not scientific but moral … it prepares us to live more humanely in the present and to meet rather than to foretell the future." Surgeons from every era strived to meet a moral standard to find the best approach to remove a patient's eye while maintaining the pristine condition of the anophthalmic socket to preserve the patient's comfort, aesthetic appearance, vision in the contralateral eye, and overall health. As technology advanced, new techniques were developed, and existing methods were modified, resulting in a variety of surgical options to achieve better outcomes. Ocularists also searched for new methods and materials to create natural-appearing, comfortable eye prostheses. Some surgical techniques and certain prostheses surpassed the test of time and remained unchanged over a century. By understanding the history of anophthalmia, we are ready to utilize present techniques and also face the future.

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Chapter 2
Clinical Decision-Making

Nathan W. Blessing

Introduction

The decision to remove a patient's eye or orbit can be challenging clinically for the physician and emotionally for the patient. For these reasons, careful consideration must be given to the specific indications for eye removal, the surgical methods employed, and the expected rehabilitative process for the patient. Goals of eye removal surgery may include the elimination of chronic pain and suffering, complete removal of a malignancy to prevent disease progression, reduction of the risk of sympathetic ophthalmia, or prevention of the spread of a potentially life-threatening infection. A careful discussion of the risks, benefits, and alternatives to eye removal should be extensively reviewed with every patient with particular attention paid to the postsurgical rehabilitative course. Wherever possible, patients should be included in the clinical decision-making process with appropriate preoperative illustration of orbital implants and prostheses. This is especially important in cases where the eye or orbit being removed is still functioning at a reasonable level. This chapter addresses the indications for eye removal with consideration given to an appropriate surgical approach to achieve clinical goals while mitigating unnecessary patient rehabilitation.

Indications for Eye Removal

The clinical scenarios which might dictate the removal of a patient's eye may be broadly grouped into four categories: infectious, neoplastic, traumatic, and palliative. Although the utilized surgical approach always results in the removal of a

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patient's eye, the clinical goals dictating the approach may differ considerably between patients. Blindness in the absence of persistent pain or ongoing infection unresponsive to local antibiotic therapy is not an indication for eye removal, and phthisical patients with cosmetic concerns can often be addressed using a cosmetic scleral shell as long as corneal sensation is absent or significantly diminished.

Infectious

A number of infectious organisms may affect the eye and surrounding orbit and can arise from invasive surgical procedures (e.g., cataract surgery, glaucoma surgery, intravitreal injections), chronic contact lens wear with poor hygiene, traumatic imbrication with organism-laden foreign material, endogenous spread from a remote infection (endocarditis, fungemia), or local spread from an adjacent sinus (*Mucor*, *Aspergillus*). Atypical infections that may result in eye removal also include parasites (*Toxocara canis*, *Baylisascaris procyonis*) and protozoa (*Acanthamoeba*).

Surgical removal of the eye is indicated in three scenarios. First, if an infection causes the eye to perforate and the visual potential of the eye is poor due to either chronic long-standing disease or irreparable intraocular damage, then removal of the eye is indicated to reduce the risk of sympathetic ophthalmia with subsequent loss of vision in the contralateral eye. Second, if an infected eye or orbit with low visual potential has failed to respond to more conservative medical or surgical therapy and there is risk for intracranial progression, then the eye may be removed to prevent further infectious morbidity or mortality. In cases of intraocular infection, the visual potential is often poor, and the patient may have significant pain. Additionally, the presence of a glaucoma shunt or other foreign bodies may predispose the development of orbital cellulitis and possible extensive orbital scarring which may impede the patient's anophthalmic rehabilitation. In these cases, early intervention is considered to prevent additional orbital morbidity. In cases of rhino-orbital fungal disease, a patient's orbit may be involved to the extent that medical therapy is ineffective, but the orbit and eye are functioning normally. In these cases, eye removal is indicated to prevent intracranial spread and is often difficult for the patient from an emotional standpoint. Similarly, patients with periorbital necrotizing fasciitis may develop orbital involvement (Fig. 2.1). The third scenario whereby eye removal may be considered is chronic indolent infection causing significant pain. In these cases, although there may be some visual potential, a patient may elect for eye removal for palliative reasons (covered later in this chapter).

Neoplastic

Neoplasms may arise in the eye or orbit either primarily, via adjacent spread, or via hematogenous metastasis. When a primary intraocular neoplasm such as uveal melanoma or retinoblastoma cannot be treated with more conservative therapy, eye removal is indicated to prevent regional or distant metastasis. In other instances, an

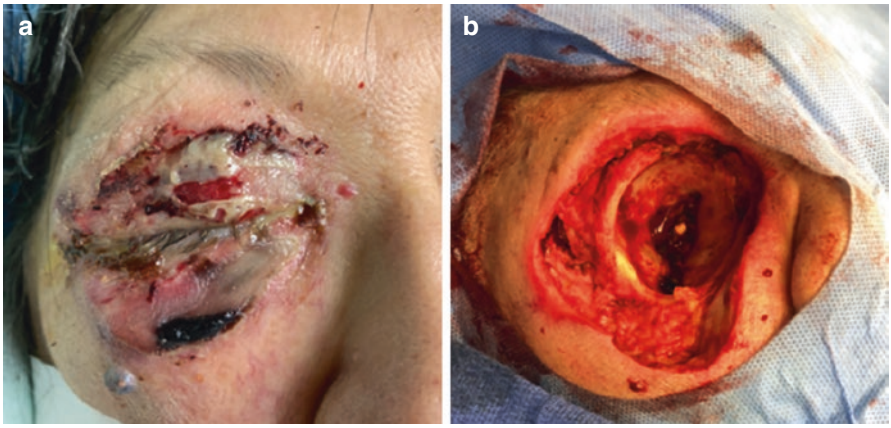

Fig. 2.1 Right periorbital necrotizing fasciitis with both orbital and ocular involvement (**a**) and the same patient immediately following extensive periorbital debridement with concurrent orbital exenteration (**b**)

extraocular malignancy arising from the ocular surface may progress to the point of failure of local medical control such as topical chemotherapy. Additionally, disease from the adjacent facial structures such as the paranasal sinuses and facial skin may have invaded the orbit to such an extent that both the eye and the orbit may be removed to achieve local disease control.

Occasionally, appropriate treatment of an intraocular or orbital malignancy may result in the removal of a comfortable eye that sees perfectly well. In these instances, it is important to counsel the patient appropriately regarding the benefits of early elimination of a potentially fatal malignancy versus the risk of inaction with subsequent morbidity and mortality.

Traumatic

Globe trauma with secondary rupture is a significant cause of ocular morbidity resulting in eye removal. Although the degree of trauma may vary, the typical underlying concern is the development of sympathetic ophthalmia in the contralateral eye. This may result from irreparable posterior ruptures or globe trauma so severe that the sclera is shredded resulting in diffuse uveal exposure. In either instance, the surgical goal is to remove the eye and especially the uvea while identifying and utilizing the extraocular muscles for future implant motility wherever possible. Additionally, blunt anterior trauma can result in dehiscence of a previously placed full-thickness corneal transplant with expulsive suprachoroidal hemorrhage. These cases are often amenable to primary evisceration and should be performed expediently to prevent secondary infection (Fig. 2.2).

Primary enucleation should be avoided except in cases where delaying surgery will result in an increased risk of sympathetic ophthalmia or infection (e.g., diffuse ante-

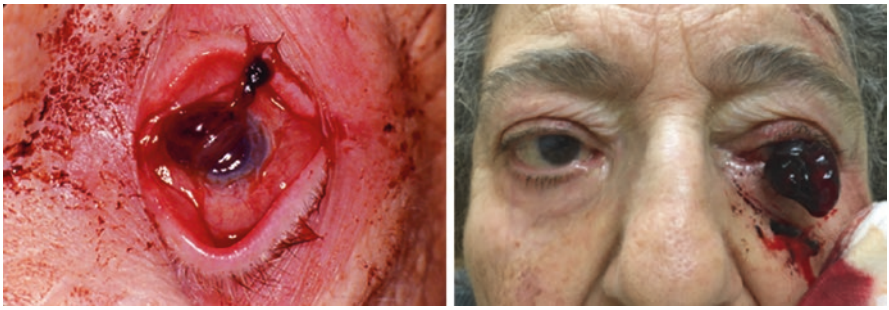

Fig. 2.2 Two patients with a history of prior penetrating keratoplasty who sustained blunt trauma to the globe with subsequent graft dehiscence and expulsion of intraocular contents; both were successfully treated via evisceration

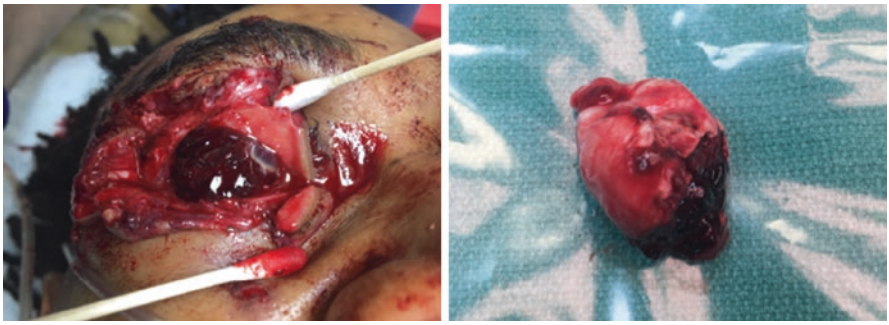

Fig. 2.3 External photo showing a gunshot injury to the right side of the face and orbit (left). The eyelids are extensively damaged as is the anterior aspect of the globe. Gross photo showing the same globe immediately following enucleation surgery (right). The anterior portion of the globe was irreparably damaged, and there were few identifiable structures remaining

rior rupture in a persistently intubated patient with other medical comorbidities). Patient decision-making is critical in proposing primary enucleation in an unsalvageable eye. In situations where patients cannot personally consent due to capacity, such as following a severe trauma with traumatic brain injury, the decision to primarily remove a patient's eye should be undertaken only after several independent physicians have deemed and documented that the eye is unsalvageable and poses a significant risk to the patient (Fig. 2.3). Large irreparable posterior ruptures can often be observed for 1 week while a patient deliberates the prospect of eye removal surgery.

Palliative

In some patients, an eye with either very poor vision or no vision may develop intractable pain or become cosmetically disfiguring. The patient's particular circumstances will dictate whether surgery is advisable and which technique should be

employed. However, in cosmetically disfiguring cases, surgery is not always necessary. In cases where a globe is phthisical but painless, an assessment of corneal sensation should be performed, as diminished or absent corneal sensation may allow the patient to tolerate a cosmetic scleral shell without the need for invasive surgery (Fig. 2.4).

In other cases a long-standing painless but blind eye may develop intractable pain for which topical and medical therapy fail. Examples include patients with a history of neovascular glaucoma in which the intraocular pressure is significantly elevated, congenital glaucoma patients who develop profound buphthalmos with mechanical lagophthalmos (Fig. 2.5), or patients with blind phthisical eyes who develop suprachoroidal hemorrhage. B-scan ultrasound can help to elucidate anatomical changes consistent with the development of pain when the ocular media is

Fig. 2.4 External photo of the right eye demonstrating a phthisical globe with a shrunken and opacified cornea (left). The same patient after scleral shell fitting (right)

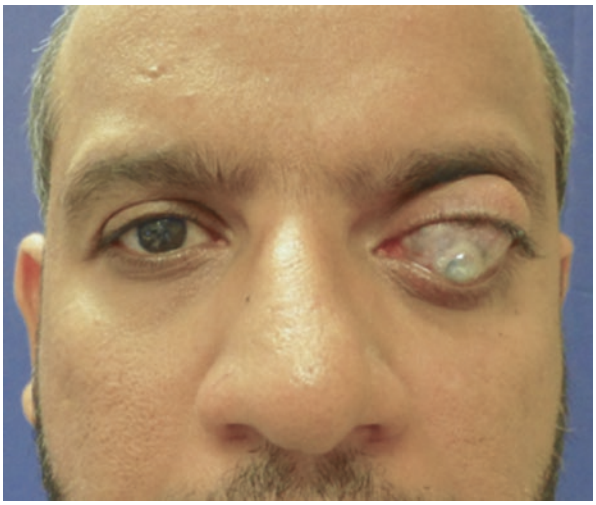

Fig. 2.5 External photo of a patient with a long-standing history of congenital glaucoma in the left eye which responded poorly to treatment. He subsequently developed buphthalmos with extensive scleral thinning and chronic irritation. He was successfully treated via enucleation

otherwise opacified and can be employed to detect new hemorrhage inside an eye. These patients may initially respond to medical therapy but ultimately develop chronic pain for which globe removal would be advantageous. Some patients may develop discomfort due to chronic corneal disease such as band keratopathy or bullous keratopathy and may be amenable to local treatment with EDTA chelation, superficial keratectomy, stromal keratotomy, or Gundersen flap placement. Such patients often experience significant pain relief with topical anesthetic placement. However, some patients may complain of chronic intractable pain but no anatomical explanation for the patient's pain is evident (Fig. 2.6). These patients often have vague complaints such as a headache which may originate in the region near the suspect eye. Caution should be taken in recommending eye removal surgery in such cases unless the patient and provider are reasonably convinced that the patient's chronic pain is a result of the eye in question. All efforts should be made to medically control suspected non-ocular pain prior to pursuing eye removal, as the surgery itself may result in significant postoperative discomfort. In patients with truly painful eyes, the postoperative discomfort is typically less than the pain they were experiencing pre-procedure, and eye removal results in the elimination of their chronic pain. Patients whose symptomatology is non-ocular in origin may continue to complain of persistent chronic pain despite having an anophthalmic socket.

Finally, some patients may have such significant ocular morbidity with poor visual potential that the ongoing pain necessary to achieve ocular stability outweighs the potential visual benefits of retaining the eye. An example might include an elderly patient with a history of penetrating keratoplasty who develops a corneal ulcer, endophthalmitis, and panophthalmitis with worsening pain despite maximal medical therapy (Fig. 2.7a). These patients may elect for expedient eye removal to ameliorate their pain, whereas a younger and healthier patient may elect to continue

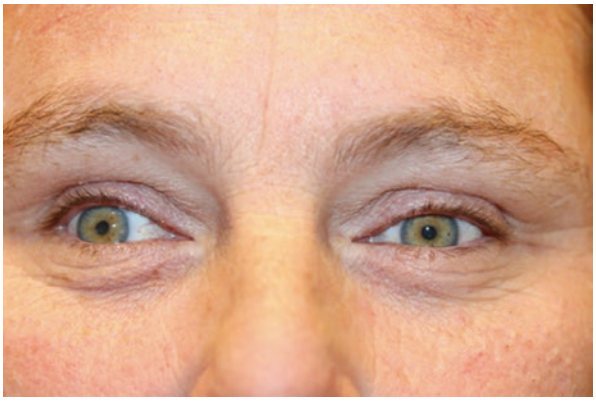

Fig. 2.6 External photo of a patient referred for headaches thought secondary to her blind and exotropic right eye which on examination was anatomically normal other than extensive retinal scarring from a prior traumatic injury. Subsequent investigation revealed symptomatology classic for cluster-type headaches which were successfully treated by a neurologist with expertise in headache treatment

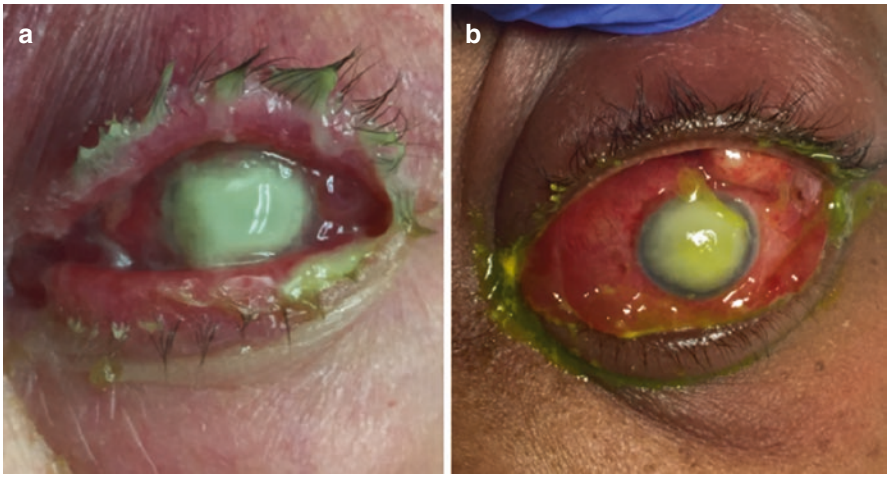

Fig. 2.7 Two patients with extensive panophthalmitis refractory to medical therapy referred for palliative eye removal

all efforts to save their vision (Fig. 2.7b). In these cases, it is most appropriate that the patient understands their visual potential and the necessary surgical steps and timeline required to potentially save the eye. It is the patient that must decide that the pain they are experiencing outweighs any residual visual potential.

Choice of Surgical Technique

Choosing a surgical technique to remove a particular patient's eye is dependent upon the condition of the patient's sclera and the degree of orbital involvement. The particulars of each individual surgical technique are addressed in their own respective chapters, but in general patients with diffuse orbital malignancies are best treated via exenteration in order to obtain adequate surgical margins. When choosing between evisceration and enucleation, consideration should be given to the condition of the patient's sclera, particularly the degree of phthisis, buphthalmos, or traumatic damage. Phthisical eyes with significant scleral contraction cannot retain a large enough implant via evisceration to permit adequate anophthalmic rehabilitation without using a very large prosthesis. Some drawbacks of a large prosthesis include poor motility and chronic elongation and relaxation of the supporting lower eyelid. As such, phthisical eyes are best addressed via enucleation. Additionally, buphthalmic eyes from long-standing congenital glaucoma often have significant scleral enlargement and thinning and are best treated via enucleation. Eyes with intraocular neoplasms are always treated via enucleation in order to obtain adequate surgical margins and prevent unnecessary exposure of the open orbit to a potentially invasive malignancy. Traumatic anterior globe ruptures can be treated via evisceration so long as there is adequate

sclera to permit placement of a reasonably sized orbital implant (at least 14–16 mm in diameter). Evisceration is often considered in elderly patients with significant medical comorbidities and those on blood thinners who would benefit from a shorter, less invasive surgery and is the technique of choice in patients with dehisced penetrating keratoplasty grafts and expulsive choroidal hemorrhages.

With regard to infected eyes, a technique is chosen which will eliminate the offending infectious agent with the least risk for persistent infection and the best anophthalmic outcome. It is critical to identify the offending organism and their antibiotic sensitivities wherever possible. A pan-sensitive bacteria may be easily eliminated with placement of a donor sclera and a porous implant for optimal anophthalmic socket topography and motility. However, a resistant bacteria may easily colonize a porous implant resulting in subsequent anophthalmic socket infection and implant exposure. In these cases, it is best to either place a smooth implant that will extrude easily if infection persists or to stage the socket reconstruction with secondary implant placement. In patients who do not desire rehabilitation, implant placement can be deferred indefinitely.

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Chapter 3
Sympathetic Ophthalmia

Chrisfouad R. Alabiad, Lily Zhang, and Janet L. Davis

Introduction

Definition Sympathetic ophthalmia [SO] is a bilateral, diffuse, granulomatous uveitis following trauma or surgery in one eye. The eye with a history of injury is referred to as the "exciting" or "inciting" eye, and the contralateral eye is known as the "sympathizing" eye. Descriptions of sympathetic ophthalmia have been linked back far in history to Hippocrates where reports of injury to one eye were said to put "the other eye in great danger" [1]. In 1840, William Mackenzie coined the term "sympathetic ophthalmitis," and by 1905, Fuchs described the classic histopathology of SO with inflammatory infiltration of the uvea and formation of nodular depigmented aggregations beneath the retinal pigment epithelium, now known as Dalen-Fuchs nodules.

Immunopathogenesis The etiology is not fully understood but is believed to be due to an acquired T-cell-mediated immune reaction to previously unexposed ocular antigens after penetrating trauma or injury. The precise antigen causing this reaction is unknown, but self-antigens found in the lens [2, 3], retina [4, 5], RPE [6], and uveal tract [7] have been implicated.

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Background: Epidemiology and Risk Factors

Immune Privilege The eye is one of the few structures in the body heralded as an immune-privileged site. Sir Peter Medawar demonstrated this in 1948 after a homologous graft of skin transplanted to the anterior chamber of the eye failed to elicit signs of tissue rejection [8]. This results from (1) blood tissue barriers from tight junctions at the levels of the retinal vascular endothelium [9] and the retinal pigment epithelium (RPE); (2) the lack of intraocular lymphatic drainage [10]; and (3) an immunosuppressive ocular microenvironment [11–15]. When these antigens escape the intraocular environment via violation of globe integrity, the antigens are subject to exposure to the host's immune system as they drain through conjunctival lymphatic channels, abrogating the immune privilege. This is hypothesized to stimulate an autoimmune reaction against intraocular tissue, specifically, the uvea.

Etiology In the past, the leading cause of sympathetic ophthalmia was penetrating trauma. Recent studies have shown conflicting data on whether surgical or accidental trauma is now the most common risk factor. Kilmartin et al. reported vitreoretinal surgery as the main risk factor in the UK [16]. The change in the principal etiology has been attributed to increased prevalence of ocular surgery and better management and prevention of ocular injuries. Other studies have found trauma still to be the most prevalent cause [17]. Sympathetic ophthalmia has also been described in relation to non-penetrating injuries including intravitreal injections [18], non-penetrating procedures including irradiation for melanoma [19], plaque brachytherapy [20], and laser cyclodestructive procedures [21], as well as infectious and noninfectious keratitis [22, 23]. The mechanism for immune exposure in these cases is hypothesized to be due to ocular antigens entering the systemic circulation through the vortex veins after leaving the intraocular compartment through the trabecular meshwork.

Incidence and Prevalence Sympathetic ophthalmia is rare and its incidence is therefore difficult to confirm. Recent estimates are that the 1-year incidence is a minimum of 0.03 per 100,000 people [16]. Because SO may be a lifelong illness, the prevalence is higher, approximately 0.3% of uveitis in the general population [16]. Among patients with eye injuries, the incidence ranges from 0% to 3.1% [24]. It has no racial, gender, or age predilection other than differences in demographics related to the frequency of ocular trauma and surgeries.

HLA Association Certain patients may be more at risk for SO because of HLA Class II antigens. Moderately strong HLA associations with SO have been described for HLA-DRB1∗04 and HLA-DQB1∗03 [25, 26]. Similar HLA haplotypes in patients are associated with Vogt-Koyanagi-Harada disease (VKH), a panuveitis with many features resembling SO [25, 26]. Other than HLA restriction limiting the number of people at risk and the need for an inciting event, another factor assumed to contribute to the current low incidence of sympathetic ophthalmia is improvement in surgical techniques, including management of open globe injuries.

Reduction of Risk of SO

Risk-Benefit Considerations In the setting of ocular trauma, the Ocular Trauma Score [OTS] is often used to predict visual prognosis [27]. When OTS suggests poor long-term visual prognosis and the eye is severely damaged, surgical removal of the injured eye is often performed to reduce the risk of sympathetic ophthalmia. There is at least some evidence to suggest that HLA typing of patients could help clinicians assess individual risk of SO more precisely [see above]. Once a decision has been made to remove an injured eye to reduce the risk of sympathetic ophthalmia, the main surgical options are enucleation and evisceration.

Controversies in Surgical Technique and Timing It is controversial whether enucleation is preferable to evisceration in reducing the risk of SO. Optimal timing for the procedure after the initial insult is also a concern. Given the low incidence of disease, a prospective study to compare surgical techniques and timing is not feasible. Traditional teaching is that removal of the inciting eye by evisceration or enucleation within 2 weeks of injury is necessary to reduce the risk of SO. Advantages of each technique have been well described and are addressed in detail in another chapter. Evisceration is felt by many practitioners to be faster, simpler, and less invasive and to provide better cosmesis and prosthetic motility. Regarding risk of SO, there are two major concerns about evisceration: (1) scleral emissary channels may retain antigens that will continue to promote SO, and (2) previously sequestered intraocular antigens may be released during evisceration and actually cause SO or permit dissemination of an unsuspected intraocular tumor. Case reports of SO after evisceration have been reported as far back as the 1800s [28] with a handful of reports thereafter [29–32]. Because of the concerns about SO after evisceration, the authors of this manuscript generally favor enucleation. In a retrospective analysis, most patients at risk for SO did undergo enucleation; however, Zheng and Wu recommended evisceration over enucleation when patients were reliable for follow-up due to the low incidence of SO [33].

Modification of Evisceration Technique to Reduce Risk If evisceration is elected, modifications in technique may reduce the risk of antigenic exposure. Scraping the scleral bed free of pigment and applying absolute alcohol to the scleral bed after evisceration may denature residual retinal and uveal proteins adherent to sclera and decrease their antigenicity. The authors also suggest that surgeons treat previous surgical or traumatic sclerotomies either with application of absolute alcohol or with focal excision of sclera. In addition, preoperative preparation should include a dilated fundus examination to rule out intraocular tumor, or B-scan ultrasonography should be performed.

Limitations in Risk Reduction It must be emphasized that removal of the injured eye is only recommended when the eye has poor prognosis for visual function and reconstruction is impossible. If sympathetic ophthalmia occurs, the inciting eye

may have better visual function than the sympathizing eye [34]; therefore, many patients and doctors will reasonably choose not to enucleate an injured eye. Additionally, enucleation may not always protect against SO [33] as a case of SO has been reported as early as 5 days after injury [35]. Prophylactic corticosteroids do not prevent the development of sympathetic ophthalmia [36].

Lifelong Risk of SO The risk for developing sympathetic ophthalmia after an ocular trauma is lifelong as demonstrated by a case of SO reported 66 years after traumatic injury. It remains to be determined if there will be an increase in the incidence of SO in years to come. Though techniques of intraocular surgery are improving as well as trauma prevention and surgical management, current ophthalmic practice includes an increasing number of intraocular surgeries that manipulate retinal/uveal tissues, such as pars plana vitrectomy, intravitreal injections, laser procedures, and plaque radiation therapy.

Elective Intraocular Surgery in Severely Damaged Eyes Providers managing monocular patients, regardless of etiology, should carefully consider the potential risk of SO when offering intraocular therapies such as repeated pars plana vitrectomy in eyes with very low visual potential, which might incite SO in a normal fellow eye. Minimizing the number of surgical entries into a severely damaged eye may be prudent. As above, HLA typing may help individualize risk.

Presentation and Diagnosis

Time to Onset Most patients (90%) who develop sympathetic ophthalmia will present within 1 year of the inciting injury. The majority of cases (65%) present between 2 and 8 weeks [37]. Documented cases have ranged in presentation from 5 days to 66 years [38]. Cases resulting from trauma have been found to present earlier than surgically induced cases, with a median of 6.5 months after the inciting trauma compared to a median of 14.3 months after surgery [17].

Clinical Diagnosis Diagnosis of sympathetic ophthalmia is usually made by history and clinical examination. History of trauma is significant in differentiating from other similar presentations including Vogt-Koyanagi-Harada syndrome and sarcoidosis. While extraocular manifestations are quite rare, there may be findings similar to VKH, including sensorineural hearing loss, alopecia, poliosis, and vitiligo.

Ocular Features Onset may be acute or insidious onset. Although this is a bilateral process, symptoms and signs of disease may be asymmetric. Severely damaged inciting eyes may be difficult to assess for inflammation. Symptoms vary in intensity between patients and include photophobia, blurry vision, and pain. In addition to a decrease in visual acuity, there may be changes in intraocular pressure, which may be elevated due to trabeculitis or decreased due to ciliary body dysfunction.

Examination of the anterior segment may disclose mutton fat keratic precipitates, anterior chamber cell and flare, posterior synechiae, and iris thickening. Examination of the posterior segment may demonstrate vitritis, cream-/yellow-colored subretinal infiltrates colloquially known as Dalen-Fuchs nodules but is a histopathologic term (Fig. 3.1), exudative/serous retinal detachments (Fig. 3.2), and optic nerve edema.

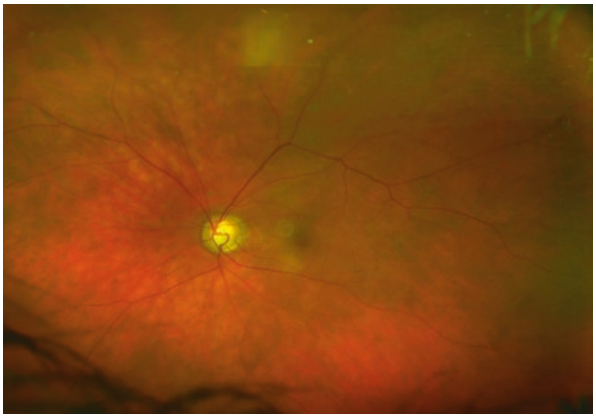

Fig. 3.1 Fundus photo, left eye. Sympathetic ophthalmia. Although there is only trace vitreous haze, the choroid appears thickened and infiltrated by focal yellow lesions despite the use of high doses of oral corticosteroids for 3 weeks. There is glaucomatous cupping of the optic nerve. Sympathetic ophthalmia developed in the aftermath of glaucoma surgery, endophthalmitis, and pars plana vitrectomy of the right eye

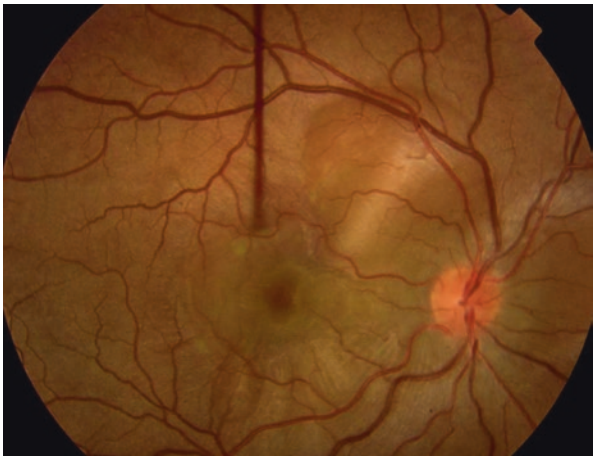

Fig. 3.2 Fundus photo, right eye. Sympathetic ophthalmia. There are collections of subretinal fluid surrounding the optic nerve. Vessels and nerves are healthy and the media is clear. This presentation resembles the acute phases of VKH. The diseases are differentiated by the history of ocular injury or surgery and by the greater frequency of neurologic and dermatologic manifestations in VKH

Because the principal site of inflammation is in the uvea and retina rather than in the vitreous cavity, the amount of cellular inflammation may be less than expected despite severe posterior disease, and the view into the fundus may be quite clear, confounding diagnosis.

Ancillary Testing Ophthalmic imaging provides supportive findings for SO. Fluorescein angiography (FA) shows hyperfluorescent leakage in the venous phase that continues to the late phase (Fig. 3.3a). Indocyanine green angiography (ICG) shows hypofluorescent areas that represent choroidal inflammatory cellular infiltration and edema [39] (Fig. 3.3b). Ocular coherence tomography (OCT) can demonstrate serous retinal detachments and choroidal infiltration that can be used to monitor progression and response to treatment [40]. Although the exudative changes usually resolve quickly and could be monitored clinically, it is important to monitor SO with simultaneous FA/ICG to confirm that uveal inflammation has subsided (Figs. 3.4 and 3.5).

Prognosis When poorly controlled or left untreated, this lifelong uveitic process carries significant ocular morbidity with poor visual prognosis. Sight-threatening consequences include cataract, secondary glaucoma, cystoid macular edema, optic nerve pallor, choroidal neovascular membrane and subretinal fibrosis in the macula or in the peripapillary region (Fig. 3.6), choroidal atrophy, and depigmentation of the RPE and choroid akin to the "sunset glow" fundus seen in VKH. Changes in pigmentation may be slow to develop and difficult to recognize but are a sign of inadequate control. Fundus photography can be used to document progressive choroidal depigmentation associated with suboptimally controlled disease (Fig. 3.7). Phthisis may occur solely from the uveitis [41].

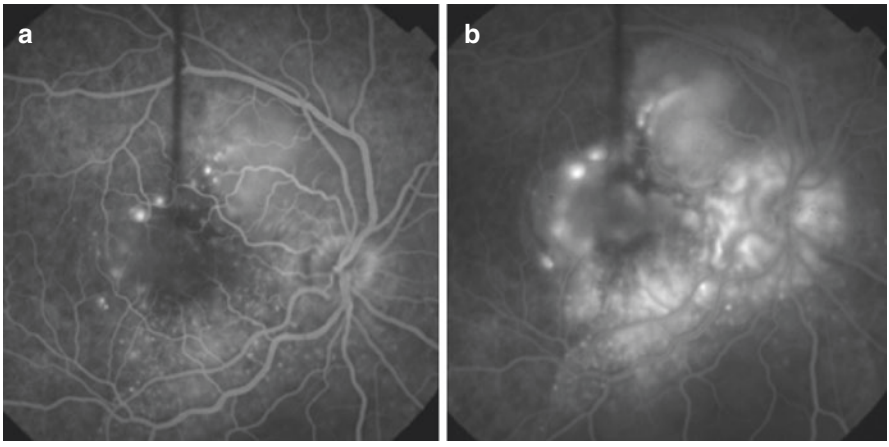

Fig. 3.3 Fluorescein angiogram of the eye in Fig. 3.2. (**a**) Early phase FA. Pinpoint choroidal leaks are present posteriorly and more diffuse leakage is starting. (**b**) Late phase FA. Pooling under the retina increases with retinal elevation. There is a vertical artifact from the fixation device

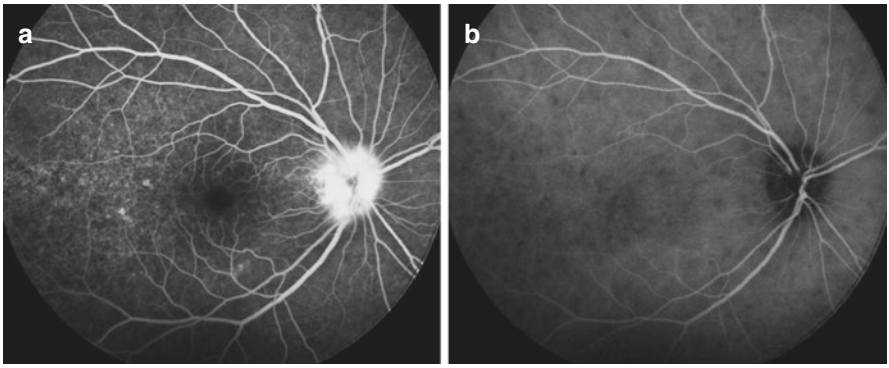

Fig. 3.4 FA and simultaneous indocyanine angiogram of right eye. Sympathetic ophthalmia in the initial stages of treatment with non-corticosteroid systemic immunomodulatory therapy. (**a**) There is speckled hyperfluorescence temporally related to choroidal leakage and RPE changes, but no pooling. The optic nerve leaks. (**b**) ICG reveals that the choroidal inflammation remains active with many small choroidal infiltrates

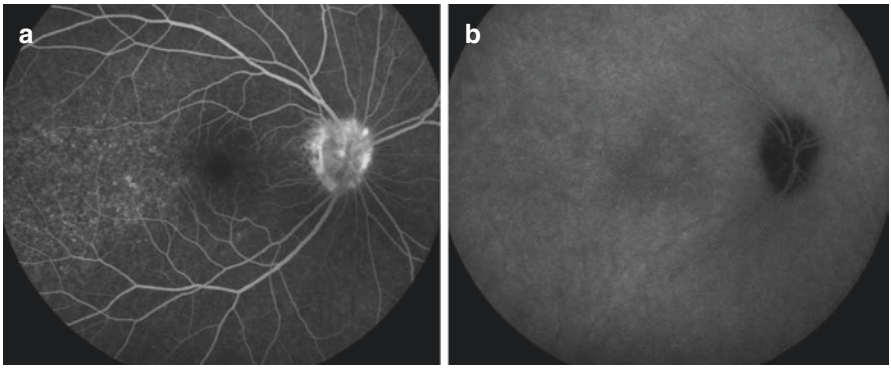

Fig. 3.5 FA and ICG. Same eye as Fig. 3.4 after additional treatment. These images are from later in the angiogram when pathologic leakage would normally be more visible. (**a**) The RPE is altered in the temporal macula, but there is less choroidal leakage, and the optic nerve no longer leaks. (**b**) ICG shows resolution of the choroidal infiltrates. There is satisfactory control of the acute inflammation

Management

Importance of Initial Therapy Sympathetic ophthalmia responds best to early, intense treatment with systemic corticosteroid and non-corticosteroid immunosuppression as demonstrated by controlled inflammation and retention of visual function in patients who receive early treatment. Most patients maintain functional visual acuity, with many patients achieving a final visual acuity of 20/60 or better [17, 36, 42]. Long-term remission off corticosteroids and immunomodulation is possible [43]; however, it must be emphasized that SO is usually a lifelong disease.

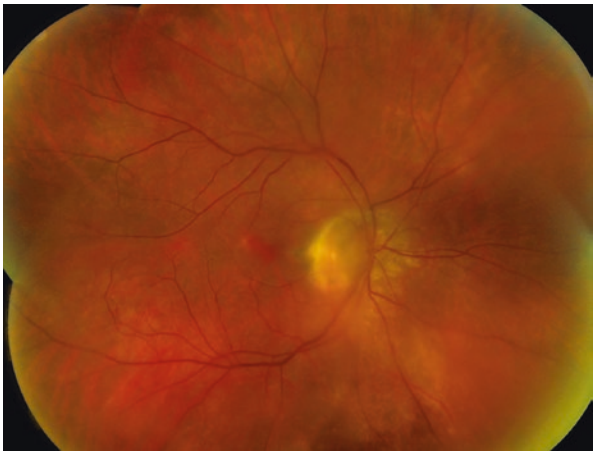

Fig. 3.6 Fundus photo, right eye. Sympathetic ophthalmia, acute stage. Yellow choroidal infiltrates are seen, but in addition, there is peripapillary fibrosis. These fibrotic rings usually have a neovascular component and typically progress to involve the center of the macula. Immunomodulatory therapy and anti-VEGF therapy may both be needed to control the process. Pigmentary changes are beginning inferonasal to the optic nerve

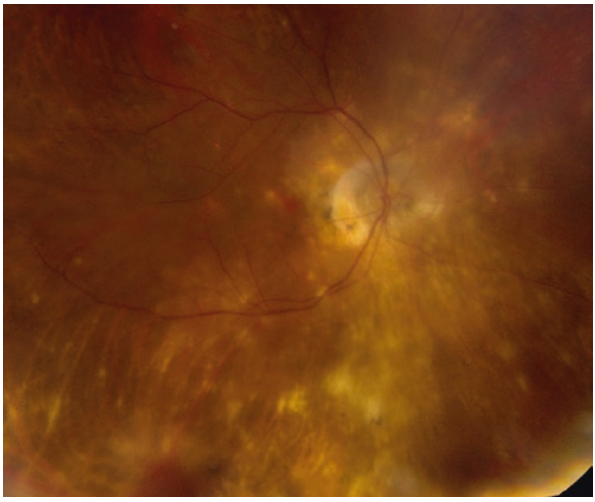

Fig. 3.7 Same eye as in Fig. 3.6. Sympathetic ophthalmia, convalescent phase. The patient had difficult tolerating any immunomodulatory therapy due to bone marrow suppression and was ultimately switched to adalimumab with improved control. The peripapillary neovascularization has been controlled by multiple anti-VEGF injections and is regularly monitored with OCT. There are extensive pigmentary changes related to the prolonged choroidal inflammation. The findings are concerning for progressive loss of retinal function

Serial follow-up is required to monitor for disease control and for side effects from treatment.

Choice of Initial Therapy Sympathetic ophthalmia treatment calls for systemic immunosuppression through the use of corticosteroids and immunomodulatory agents. Treatment for the acute phase of the disease includes high-dose oral prednisone up to 1 mg/kg/day [36]. Exudative detachment or vision loss from choroidal infiltrates may benefit from treatment with intravenous steroids 0.5–1 gram daily for 3 days [44]. Topical corticosteroids and cycloplegics help treat the anterior uveitis and prevent formation of posterior synechia. The speed of action of corticosteroids is unique among available agents, and it is very difficult to replace them with non-corticosteroid systemic immunomodulatory agents in the initial phases of treatment. Once corticosteroid treatment has been initiated, immunomodulatory therapy should be started as soon as possible, anticipating that long-term treatment will be needed and that the alternative drugs will require a longer time to become effective.

Preparatory to Medical Treatment Although corticosteroids must often be started urgently, it is important to obtain laboratory testing in all patients suspected of sympathetic ophthalmia to assess them for conditions that may be affected by treatment. Recommended tests include complete blood count, comprehensive metabolic panel, urinalysis, FTA with reflex RPR, hepatitis B surface antigen, hepatitis C antibody, HIV antibody, and urine pregnancy test. An interferon-gamma release assay test for tuberculosis is more practical than a PPD as the results will not be affected if the blood is drawn before corticosteroids are started, whereas the TB skin test might fail to show a reaction if large doses of corticosteroids are being given. A chest X-ray should be scheduled. There should be consideration of age-appropriate vaccinations with recombinant or killed vaccines before immunosuppression deepens; live vaccines are contraindicated while on therapy.

Non-corticosteroid Systemic Immunomodulatory Therapy Several immunomodulatory agents have been used as steroid-sparing long-term agents for sympathetic ophthalmia including mycophenolate mofetil [45], azathioprine [46], cyclosporine [47], tacrolimus [48], and chlorambucil [49]. These agents are introduced in an effort to fully taper the patient off corticosteroids and thus avoid devastating long-term complications of steroid use. Management of these agents is most appropriately reserved for an experienced uveitis or rheumatology practitioner as they require frequent monitoring to assess for compromise of the hematologic, renal, and hepatic systems. Dosing is adjusted according to the clinical activity of the uveitis, so communication between the ophthalmologist, usually a retina or uveitis specialist, and a managing rheumatologist is particularly important. Vote et al. published an algorithm in 2004 for the medical management of sympathetic ophthalmic using corticosteroids and non-corticosteroid drugs without consideration of biologic agents [50]. The current 2016 consensus guidelines for treatment of noninfectious intermediate, posterior, and panuveitis should be consulted for additional

information regarding current therapies. [51]. There are case reports of the use of tumor necrosis factor-α (TNF-α) inhibitors in refractory SO in pediatric and adult patients [52–54]. Insight into the cytokine and chemokine milieu of SO [55] may help identify efficacious targeted therapies with fewer systemic side effects than conventional corticosteroid and non-corticosteroid drugs.

Intraocular Treatment of SO Corticosteroid drug delivery intravitreal implants have been used in SO to reduce or eliminate systemic corticosteroid treatment [56–58]. Intravitreal injections of triamcinolone acetonide may also decrease the dose of systemic steroid needed to treat SO [40, 59]. These agents are best used as adjuncts rather than primary therapy. In addition to the inadvisability of short-duration therapies for a long-duration disease, the risk of complications or infection with intravitreally delivered drugs in monocular patients may be unacceptable.

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Chapter 4
Psychological and Cognitive Adjustment to Vision Loss

Virginia A. Jacko

As a successful executive at one of our major institutions of higher education, toward the end of my 20-year career I learned I had a degenerative eye disease most likely resulting in total blindness. The first person I phoned was my mother. Looking back, I ask myself "How was I able to cope with this diagnosis?" I wonder sometimes if it was the reaction my mother had when she responded to my initial phone call telling her of the diagnosis. I said, "Mother, I just got my diagnosis, and I am going to go totally blind!" She responded in her very pragmatic style, "Well, I will just have to pray that you then do big things for the blind!" I know that at the time, quite frankly, she annoyed me because I expected some pity, some sadness, or maybe even some motherly love. Looking back, what she was saying was, "I have confidence in you, and you will learn about blindness and then help others." This was the best thing she could have said because it made me proactive, and I did not waste any time figuring out what I needed to do. I learned that the Miami Lighthouse for the Blind and Visually Impaired (Fig. 4.1) was a founder of the University of Miami Bascom Palmer Eye Institute where my ophthalmologist was on the faculty. I also learned that the Miami Lighthouse was the first private agency in the USA to rehabilitate blind adults for competitive mainstream employment, so it seemed reasonable that I enroll as a client.

As soon as I could wrap up crucial university business and identify my interim replacement, I began a four-month rehabilitation program at Miami Lighthouse for the Blind. During this period, I lost all of my vision except for light perception. At Miami Lighthouse, I learned personal management, which gave me the training I needed for my independent living skills such as grooming including putting on my makeup, cooking, writing checks, addressing envelopes, telephone skills, and shopping. I learned how to use all Microsoft Office applications with supplemental screen-reading software called JAWS. My physical adjustment to blindness required

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Fig. 4.1 Miami lighthouse for the blind in Miami, Florida

that I learn how to use the white cane. One-on-one Orientation and Mobility classes involved learning how to safely take the stairs and cross busy intersections, walk down the sidewalk to the park and take public transportation without the assistance of a sighted guide. Going to these classes, I met others who were successful despite having lost their eyesight, and this interaction motivated me to be the very best blind person I could be. At the end of my program, when I was told, "You would be a great guide dog user," I was shocked. That was not on my radar; however, I traveled to New York and went to an accredited guide dog school, Guiding Eyes for the Blind, lived there for nearly a month and returned to Miami with my first guide dog. I had no idea how the orientation and mobility instruction I received at Miami Lighthouse would enable me to travel safely with a guide dog, including traveling to France and throughout the USA.

Now as President and CEO of the Miami Lighthouse for the Blind, I use the executive skills I gained in my sighted career; this is not a change for me. However, access to information is quite different. I read through my computer or use other innovative technology like the OrCam. This is a pair of glasses with a tiny camera mounted on the front and a small CPU with a few buttons that enable me to have it read text on a page or identify faces. I have, in essence, trained the computer for face recognition of my colleagues and acquaintances. I use an iPhone, like everyone else, but the setting of "voice over" enables me to get auditory feedback instead of reading the phone screen. Recent technology innovations like these help the blind to be independent users; however, training on these devices is critical.

A few years ago, I received a phone call from a hospital administrator in ophthalmology. The call went like this "Virginia, we have a patient coming out of surgery, and we need to tell the patient's wife and mother that he is totally blind. Could you come over?" Looking back and thinking about the perspective of this family, I heard on the phone tremendous hope with these words: "Perhaps if they see you, they will have confidence that their loved one will be okay despite being blind."