Surgical Treatment of Ocular Inflammatory Disease

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Preface

Surgical Treatment of Ocular Inflammatory Disease began as an outgrowth of our chapter, "Uveitis Surgery," in Duane's five-volume text *Clinical Ophthalmology*. At the outset we realized that it was impossible to condense all the recent medical and surgical information, innovation, and instrumentation pertinent to uveitis diagnosis and treatment into one chapter, so we considered an expanded volume to do just that. The result is now before you. Although inflammatory disease is an important part of so many current ophthalmology textbooks, there is no other text in which the surgical considerations and options are central to the perspective of uveitis alone.

Uveitis has always been a diagnostic mystery and therapeutic challenge. Ophthalmologists have often tried to simplify it in order to lessen its confusion. We now live in a technological era that permits us the luxury to do the opposite. By studying its complexity and separating out its many specific disease syndromes and peculiar manifestations, we can offer patients treatment and options, and, hence, cures that have never existed before. The strategies for cataract removal, for example, differ in juvenile rheumatoid arthritis, Fuchs' heterochromic cyclitis, and "burned out" pars planitis. The whole spectrum of intra-ocular lens implantation and inflammatory conditions is continually changing, as is the spectrum of inflammation in normal eyes caused by intra-ocular lenses themselves. The strategy for retinal detachment repair, for example, is different for traction detachment in pars planitis than it is for a combined traction and rhegmatogenous detachment in acute toxoplasmosis, which ushers in principles of medical management as well as immediate surgical intervention. Inflammatory membranes, fibrous scars, and synechiae can now be treated not only with surgical vitrectomy but also with the application of YAG laser surgery.

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To G. Richard O'Connor, whose inspiring scholarship and dedicated teaching have influenced an entire generation of ophthalmologists

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Introduction

Until recently little has been written about the surgical management of the patient with uveitis because of the many failures with complicated surgical uveitis. The lack of success has been complicated by the belief that uveitis is a single disease cluster and that its diagnosis could be determined only with the greatest difficulty. Moreover, there were no special surgical procedures or even major modifications of standard techniques to counteract glaucoma, retinal detachment, or vitreal opacifications in the patient with uveitis.

Recently, remarkable progress has been made. Using a systematic approach, the general ophthalmologist should be able to diagnose properly at least 80% of patients with uveitis. Unquestionably, accurate diagnosis is essential in determining what is the most appropriate treatment. All of the options allowed by the natural history and progression of the disease entity must be taken into account before surgical intervention is considered. It should be kept in mind that not all uveitic entities will respond identically to a specific form of intervention; the chance for success of a procedure therefore is directly related to the correct assignment of a patient to a specific diagnostic category.

Let us examine some of the considerations that have direct bearing on the decision of whether to operate, what procedure to use, and what medical measures to take preoperatively, during surgery, and postoperatively.

Surgery should not be undertaken until the eye has been free of uveitic activity for a prolonged period. The best time to operate is after the active

inflammatory phase of the uveitis has burned out. This may be particularly true in cases of pars planitis or intermediate uveitis, for example, where the natural history of the disease suggests an endpoint to the inflammatory phase. If this is not practical, the next best time to operate is when the uveitis has been inactive for several months without treatment with corticosteroids. This is true in those cases of acute intermittent inflammation such as ankylosing spondylitis or Reiter's disease. If even this is not possible, then corticosteroids with an immunosuppressant should be used to quiet the eye as much as possible for at least a month before surgery. In some situations, the ongoing inflammation is chronic and unrelenting, and the surgical procedure may be necessary to relieve or reduce part of the uveitic problem, as in endophthalmitis or toxoplasmic retinal detachment.

In order to reduce the manipulation of diseased or inflamed tissue, the approach should be through a normal entry wherever possible. For example, if the primary inflammatory site is in the anterior uvea, surgery through a posterior approach may be preferable. Conversely, if the primary inflammatory site is posterior, then the anterior approach is optimum.

Uveitic entities in which there is little or no tendency to develop anterior or posterior synechiae (e.g., pars planitis, Fuchs' heterochromic iridocyclitis) respond to surgical intervention much better than "sticky" uveitic entities (e.g., sarcoid, chronic iridocyclitis of juvenile rheumatoid arthritis). Acute recurrent uveitic eyes tolerate surgery better than chronically uveitic eyes.

Uveitis in association with a markedly low intra-ocular pressure (prephthisical), especially in the absence of a cyclitic membrane, may indicate that the eye is a poor surgical risk. The removal of a cyclitic membrane, however, may restore a prephthisical eye to a higher pressure and confer a more positive prognosis.

The pre-operative, operative, and postoperative use of local, systemic, or periocular corticosteroids allows the uveitic eye to tolerate intra-ocular surgery better.

This text presents an overview of the surgical treatment of ocular inflammatory disease, including the general measures and specific indications for surgical intervention in this complicated situation. One must consider the time and approach for surgical intervention and, more specifically, those disease states which require precise knowledge of their inflammatory behavior. Later chapters discuss pre-operative, intra-operative, and postoperative medications for all of the ocular inflammatory diseases, including those which fall in the spectrum of herpetic bacterial and fungal keratouveitis and retinitis as well as endophthalmitis. Difficult diagnostic and surgical considerations for septic emboli to the eye are discussed, as are the ever-increasing and frequent problem of drug-abuse type endophthalmitis. A detailed chapter on the immunology of ocular inflammation is also included.

The chapter on paracentesis of the eye includes a detailed listing of the antigen, antibody, direct and indirect immunofluorescent antibody techniques, such as enzyme immunoassay, enzyme-linked immunosorbent assay, complement

fractions, immunodiffusion, and indirect hemoglutination tests. For many infectious organisms found in the aqueous and vitreous, this is probably the most up-to-date compilation of serology testing for intra-ocular inflammations measured in microtiter quantities. In addition, the discussion of diagnostic paracentesis outlines the findings of tumor cells, eosinophils, microphages, bacteria, and fungi seen in intra-ocular inflammatory disease. Specific instructions on how to retrieve samples and prepare slides is included. This chapter presents material at the cutting edge of intra-ocular diagnosis for both medical and surgical ocular inflammatory disease.

A complete discussion of the corneal manifestations of ocular inflammatory disease, with its necessary surgery for active corneal decompensation, is included. This encompasses a discussion of the herpetic infections of the eye: when, where, and how, more specifically, to proceed with corneal transplantation. When these very common and yet devastating infectious diseases affect the eye, uveitic glaucoma presents a unique challenge for the clinician. The underlying etiology for all of the glaucomas with uveitic conditions is inflammatory. The handling of posterior synechiae may be very different from the simple medical management of posterior synechiae with a pupillary block. The treatment of iris bombé may be very different from that of peripheral synechiae, which may or may not complicate an inflammatory "trabeculitis."

The range of uveitic glaucoma is discussed with pointed references to the clinical features and pathology of inflammatory intra-ocular pressure elevations. Specific note is taken of Posner-Schlossman syndrome, herpes simplex and herpes zoster uveitis, severe or acute iridocyclitis, Fuchs' heterochromic cyclitis, mechanisms of blockage of the trabeculum with debris, peripheral anterior synechiae, trabeculitis, rubeosis iridis, hypersecretion syndromes, and sclerosis of the cortical meshwork. Special mention is made of traumatic glaucoma, as well, which ushers in a whole different set of considerations along with hemorrhagic glaucoma, foreign body inflammation, and infection in the eye with siderosis. This is treated in the glaucoma section as well as in the retinal detachment and trauma sections. While lens-induced glaucoma and lens-induced uveitis are uncommon, their clinical picture can be so specific and their clinical outcome so devastating that they deserve special mention.

A very important topic to be considered in the treatment of ocular inflammatory disease is cataract extraction in specific uveitic syndromes. Cataract extractions pose significant risks for patients with uveitis. The outcome of cataract surgery depends heavily upon the particular uveitic syndrome. In many uveitis syndromes, a cataract may be caused by the inflammation itself, which produces significant lens opacity, or by the chronic use of corticosteroids which, of course, may cause cataracts. It is generally agreed that an eye that has been quiet without medications and has been free of active inflammation for a long time usually poses the least risk for cataract surgery. However, there are situations in which cataract surgery is necessary and the inflammation in the eye is present or minimal but must be dealt with accordingly.

The earliest results of extracapsular cataract extraction in patients with juvenile rheumatoid arthritis were discouraging, owing to the frequent loss of vitreous, incarcerations into the wound, and the consequent development of cyclitic membrane with the subsequent development of ciliary body detachment and eventual phthisis. With the advent of the lensectomy-vitrectomy surgery using modern vitrectomy instruments, this is no longer the case and the cyclitic membrane can be entirely extirpated, leaving the ciliary body without detachment or traction, thus greatly lessening the potential for eventual hypotension and phthisis in these eyes. Other specific uveitic syndromes, such as pars planitis or intermediate uveitis and Fuchs' heterochromic iridocyclitis, do well with cataract extraction (cataract development is an integral part of the late stages of Fuchs' heterochromic iridocyclitis along with glaucoma). There are a few specific situations in which intra-ocular lens placement is not contraindicated in uveitis, Fuchs' heterochromic iridocyclitis being one of the generally accepted ones. In general, the implantation of intra-ocular lenses is contraindicated in active uveitis and should only be considered in cases that are "burned out," as when pars planitis eventually becomes quiescent of its own natural history.

Uveitis may be a consequence of cataract surgery itself, since inflammation in the early postoperative period following either cataract surgery or intra-ocular lens implantation may, in part, be related to surgical manipulation. What occurs is a response to change in breakdown of the blood aqueous barrier or to retained lens material, following extracapsular cataract extraction, or to tissue damage itself. Some surgeons have even postulated an "immunologic" inflammation due to the implant material. Some of this persistent type of intra-ocular inflammation may be minimized or reduced by prostaglandin inhibitors such as indomethacin, nonsteroidal agents, or aspirin. The retained lens material usually causes an inflammatory response that is transient and mild, and only in rare cases will it be prolonged, significant, or necessitate surgical removal. The incidence of this type of transient iridocyclitis following extracapsular surgery has decreased markedly from the early days of intra-ocular lens implantation. Interestingly, most studies have shown that infectious endophthalmitis does not occur with a higher frequency after intraocular lens implantation than one might anticipate following simple cataract removal.

We have witnessed, with the advent of the most modern extracapsular extractions with intra-ocular lens implantations, a lessening of many of the fears of postoperative infection that were present earlier with the more bulky and clumsy surgeries available at that time. It is well known that the infectious endophthalmitis that occurs after cataract surgery is usually fungal or bacterial and is often associated with intra-ocular lenses. The success of treatment varies in these cases and, while removal of the implant may be required in some situations, the implant can be retained in others with successful treatment. The general approach in surgical management of cataract extraction, with and without intra-ocular lens implantation, in uveitis patients is documented. Special problems and considerations that occur are synechiae, cyclitic membrane; inflammatory mem-

brane over the surface of the lens, which may or may not be connected to the iris, management of the iris, vitreous cells and opacities, as well as intra-ocular lens manipulation.

At present, the indications for pars plana vitrectomy in cases of intra-ocular inflammation is twofold. It is used as a controlled biopsy of the vitreous to establish histologic diagnosis of endophthalmitis, large cell lymphoma, and other unusual infiltrations of the vitreous. But it also serves as a therapeutic intervention in many cases. A combined lensectomy-vitrectomy has recently been advocated as an intervention to ameliorate the crippling cystoid macular edema that often occurs in inflammatory diseases of the back of the eye.

Certain forms of ocular inflammation do lend themselves to diagnostic vitrectomy. This is a standard consideration for patients with large cell lymphoma (reticulum cell sarcoma), and diagnostic as well as therapeutic vitrectomy is now advocated for almost all types of endophthalmitis with the possible exclusion of *Staphylococcus aureus* and *Staphylococcus epidermidis*, which may be controlled medically. Vitrectomy has also been advocated in cases of *Toxocara canis* endophthalmitis, and all patients who are drug-abusing suspects (thought to be manifesting a profound uveitis, endophthalmitis, or both) certainly should undergo therapeutic vitreous removal, if not a diagnostic vitreous biopsy. Although the approach to suspected infectious endophthalmitis is controversial, it is generally accepted that immediate aqueous and vitreous taps for culture and smears are important first steps, and that topical, subconjunctival, and parenteral antibiotics are necessary, while the role of intravitreal antibiotics is less well defined. We feel that intravitreal antibiotics are indicated in most cases of suspected bacterial endophthalmitis and that these can be injected during aqueous and vitreous paracentesis.

There is, likewise, some general agreement that if marked vitreous exudation obscures the retinal vasculature (i.e., by indirect ophthalmoscopy), therapeutic vitrectomy is indicated by that measure as well. If the retina can be easily visualized with minimal vitreous reactions, it is probably safer to treat the patient with subconjunctival, parenteral, and intravitreal antibiotics and to follow the patient closely. If the disease progresses and there is further clouding of the vitreous, we recommend immediate vitrectomy. The vitrectomy may also allow the medications that are given parenterally and topically to penetrate more deeply, because surgical intervention is known to further disrupt the blood-retinal barrier.

The possibility of the retina having a toxic reaction to medications (i.e., amphotericin) is greater during and after vitrectomy, because the medication contacts the retina more directly. Therefore, more dilute solutions of the drugs should be used during and after the vitrectomy procedure than before.

Technically, a total vitrectomy may not be necessary and a "core" vitrectomy will suffice. The inflammatory membranes that result from endophthalmitis often adhere tightly to the retina, and a total vitrectomy can pose the threat of severely damaging the retina, although it may be necessary to peel these membranes during vitrectomy. We currently consider the indications for lensectomy-

vitrectomy in patients with intra-ocular inflammation to be: (1) a need for better vision, (2) progressive disease (hypotony, premonitory signs of phthisis, especially in the presence of cyclitic membrane), (3) complications requiring surgery (e.g., retinal detachment, tractional or rhegmatogenous) and, (4) iris bombé (closed angle with synechiae) with hypotony (indicating the presence of a cyclitic membrane). A whole discussion of the technicalities of the assessment of visual functions in patients before surgery is included so that patients do not undergo surgery unnecessarily when the common end goal of vision is what is ultimately to be considered. The complications of vitrectomy (especially too aggressive a vitrectomy in certain inflammatory situations) are discussed. These complications often include retinal tears which, combined with the underlying inflammatory disorder, may eventuate in proliferative vitreoretinopathy (PVR or MPP) with subretinal membrane growth. Further, a separate chapter on endophthalmitis is included that details the recognition, the diagnosis, and the surgical techniques involved. It encompasses very specific indications for surgery, alluded to in the chapters preceding it on vitrectomy and inflammatory diseases.

A problem that goes hand in hand with the foregoing topics and presents an ever-increasing national health hazard is drug abuse. An entire chapter is dedicated to a discussion of drug abuse, the various substances that are abused, the ophthalmalogic clinical pictures that present with drug abuse, as well as the treatment of drug abuse endophthalmitis, which involves bacterial and fungal endophthalmitis. All of us as ophthalmologists must be able to recognize these complicated patients when they present. They frequently present with a myriad of strange and perplexing signs and symptoms for which the earliest intervention may prevent the most disastrous outcome. There is often needless delay because patients who are drug-abuse victims do not come forth with proper history; therefore, untoward complications (such as disastrous endophthalmitis and inflammatory retinal detachment) occur which might have been prevented with early medical or surgical intervention. Furthermore, it behooves us to try to direct these difficult patients to the appropriate physical and psychosocial health workers who will help them with the overall scope of their problem. Drug abuse ushers in a host of new considerations in the medical management of these young patients with mysterious complaints and illnesses and often a disastrous disease spectrum. A young person who has not undergone ocular surgery and who presents with what appears to be a metastatic endophthalmitis should be suspected of intravenous drug abuse until proven otherwise. These patients may also be at risk for acquired immune deficiency syndrome (AIDS) and all of the opportunistic infections that are currently killing young people. The virulence of the HIV agent causing AIDS in parenteral drug abusers is possibly related to the synergistic effect of antigenic overload from chronic exposure to chemical contamination with illicit drugs. It must also be remembered that many female drug abusers are also involved in prostitution and, increasingly, are contributing to the contagion of AIDS.

Inflammatory retinal detachment presents a great clinical challenge to the ophthalmologist. Uveitis and retinal detachment can be related in three ways: exudative retinal detachment can be a component of the underlying uveitis; uveitis can be a late complication of chronic rhegmatogenous retinal detachment; and rhegmatogenous or traction retinal detachment can be a complication of uveitis. Patients with uveitis and retinal detachment have all the clinical signs and symptoms of both disorders. Previously, retinal detachment surgery was notoriously unsuccessful in patients with underlying or secondary uveitis. The treatment of retinal detachment has progressed remarkably with the advent of vitrectomy as a coexisting procedure to help in its management. The use of air, gas, and viscous bubbles (i.e., silicon) has also helped in the surgical manipulation of the retina, and now far fewer patients with inflammatory retinal detachment experience the disastrous and untoward eventuality of progressive vitreoretinopathy (PVR, MPP).

Certain infectious etiologies, such as toxoplasmosis and *Toxocara canis*, lead to rhegmatogenous retinal detachment. These will be covered in detail. A discussion of the natural history and progression of pars planitis is included. This disorder warrants special mention as a phenomenon with continuous low-grade inflammation and often a progressive, long-term retinal traction followed by detachment. Although this occurs only in a minority of patients, it should be remembered that if they are left with none of the serious sequelae of the disease at the time of their "burn out" (i.e., cataract, glaucoma, or, most importantly, a sclerotic type of cystoid macular edema, and retinal traction or detachment), they may possess good vision for the future. One must be constantly prepared for the development of any of these complications so that intervention may allow these patients to preserve good vision with few complications.

The inception of intra-ocular inflammation in pars planitis patients is either silent or accompanied by minimal symptoms of blurred vision or floaters. By the time the condition is diagnosed, however, serious visual loss may be present in almost one half of cases. The course of pars planitis, as noted, is quite variable. In severe cases, which are rare, the perivasculitis in the posterior pole may be a prominent feature and all the retinal blood vessels, including the arteries in the retinal periphery, may close. The more usual, very benign form of pars planitis is usually slowly progressive, with many remissions and exacerbations, and becomes quiescent at an early stage. However, one must remember that the original data put forth by Schepens shows that 40% of cases of pars planitis exhibit some degree of rhegmatogenous retinal detachment, and this may occur bilaterally.

A discussion is also included on intra-ocular foreign body with uveitis, retinal detachment, or both because foreign bodies may often be a masquerade syndrome for uveitis with retinal detachment. The presence of a foreign body may be relatively infrequent in fresh cases of retinal detachment, but in cases of patients with smoldering uveitis, eyes may have harbored a foreign body for months, sometimes years, and these cases are often refractory to the usual treat-

ment of both intra-ocular inflammation and retinal detachment. In all cases of intra-ocular foreign body there is always the danger of subsequent retinal detachment, whether it occurs at the initial injury or not.

Two metals are exceptionally toxic to the eye: iron and copper. Since the signs that these metals elicit inside the eye are pathognomonic for their damage to ocular structures, it is imperative that steps be taken for their retrieval when these signs are present, even in the absence of a positive history of ocular trauma with foreign body entrance or the localization or identification of an intra-ocular foreign body. The profound nature of the ocular disturbance depends upon the concentration of the iron or copper content of the foreign body and its location. All haste must be used to retrieve such foreign bodies as part of surgical intervention. Chalcosis, caused by copper or copper alloys, may often produce an equally violent reaction in the eye. Copper may, in fact, be the most injurious metal to the eye. When it is present in the vitreous cavity, dense infiltrates, which usually occur within just a few days of injury, adhere to the retina. Bluish-green rings form in the cornea in or near the periphery of Descemet's membrane and represent a traumatic Kayser-Fleisher ring. A sunflower cataract may be produced early, which is said to be pathognomonic of chalcosis, and the iris itself may become green with fine metallic particles visible on its surface and in the aqueous overlying it. Eyes that are subject to such metallic foreign bodies often have intractable intra-ocular inflammation until the foreign body itself is removed as part of the treatment. A concomitant rhegmatogenous detachment cannot be repaired until the foreign body is removed because of the violent exudative reaction it causes. Methods of extraction of a foreign body are detailed in a later chapter in the book.

Finally, with the advent of light energy in the treatment of various ocular disorders, a chapter on laser surgery for ocular inflammatory disease is included. This details the basic mechanism of laser use and treatment and explains the specific indications for laser treatment of ocular inflammatory disease. Adhesions and synechiae are becoming increasingly amenable to careful and detailed laser treatment of posterior capsular overgrowth in patients who have undergone extracapsular surgery with uveitis necessitating YAG laser capsulotomy. The use of laser for treatment of inflammatory vitreal bands causing traction on the retina is another frontier in the future of uveitis treatment. This application is yet one more manifestation of the laser providing the ophthalmologist with a quiet and noninvasive "knife" that can cut membranes, adhesions, and synechiae thus obviating the opening of the eye for a surgical procedure.

Surgical decisions for uveitis patients must be based upon an accurate anticipation and prediction of the added risks presented by the uveitis patient. Uveitis, as already noted, is not one disease but a collection of many different diseases linked because they all produce intra ocular inflammation. For most of the common uveitic syndromes, the course, complications, treatment, as well as short- and long-term outlook, are all quite well known. Yet, it is common to hear surgeons refer to much of uveitis as "idiopathic." By using recently described,