Chapter 15

METALLOSIS BULBI

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INTRODUCTION

Modern weaponry, favoring blast fragmentation munitions, has resulted in an increase in ocular injuries in the battlefield. These often small, high-velocity fragments can easily penetrate the surface of the eye, remaining as a retained intraocular foreign body (IOFB). Damage that occurs to the eye as a direct result of retained metallic IOFBs is called *metallosis bulbi*, and changes that result from this damage are distinct from the changes caused by injuries concomitant with the ocular trauma. Over a period of months to years, toxic effects of metal ions that are taken up by various structures in the eye result in characteristic clinical findings with variable effects on visual function. Although most metallic foreign bodies (FBs) are alloys, or mixtures of metals, the two most common components are iron and copper.

Diagnosis of a retained metallic IOFB can be established in some cases by direct ophthalmoscopic examination. Alternatively, ancillary tests, such as plain film radiography, computed tomography (CT) scanning, ultrasonography, and electroretinograms, can be useful. Decisions regarding management of these cases are usually made in conjunction with other indications for vitreoretinal surgery. In most cases, surgical extraction of the FB is appropriate, although timing is rarely a critical issue.

METALLOSIS BULBI

Metallosis bulbi is defined as tissue damage to ocular structures as a direct result of retained metal particles following penetrating globe injury by an IOFB. In contrast to other sequelae of ocular trauma, most of the damage that ensues in metallosis is not inflammatory or immune-mediated. Instead, the mechanism of damage is thought to be electrolytic dissociation of the metal followed by oxidation and other chemical reactions with surrounding tissues and fluids.[1,2] These effects cause enzyme liberation from lysosomes and increased cellular permeability, resulting in the characteristic damage associated with metallosis.

Metallosis can occur as a consequence of numerous types of metals, but iron and copper alloys are the two most common. When an IOFB contains iron, the form of metallosis that develops is referred to as *siderosis*. Copper-containing IOFBs with less than 85% copper content cause *chalcosis*. Table 15-1 summarizes the most significant differences between siderosis and chalcosis. When copper content exceeds 85%, a sterile endophthalmitis ensues, which is not considered to be part of the spectrum of chalcosis.

Metallosis is a process that develops slowly over a period of months to years after injury—except when an IOFB contains very pure concentrations of copper (> 85%). Therefore, prevention of metallosis is generally not a significant issue that influences decision making in the primary surgical management of ocular trauma. Ferromagnetic objects are the most common cause of posterior segment IOFBs (Figure 15-1), accounting for approximately 80% of such injuries.[3] Copper and aluminum, respectively, are next on the list of common causes of posterior segment IOFBs.[4]

Factors Influencing Damage From IOFBs

The extent of ocular damage is determined by (*a*) mechanical factors and (*b*) the metal composition of the IOFB. Mechanical factors, including the IOFB's size, shape, velocity, final resting location, and concomitant injuries, are discussed extensively in other chapters. Larger objects and those with irregular shapes are associated with more-extensive initial damage. Velocity influences the depth of penetration after impact. To reach the posterior segment, an FB must have sufficient momentum and energy. Therefore, most posterior segment IOFBs are metallic.[1,5,6] In addition to velocity, the site of entry contributes to both the initial extent of injury and the final resting location of the IOFB. IOFBs that penetrate the sclera retain the highest momentum upon reaching the posterior segment, whereas IOFBs that traverse the cornea and anterior segment structures lose some of their momentum before reaching the posterior segment.[7]

Although the initial concomitant injuries to the anterior and posterior segment affect ultimate vision potential, the IOFB's final resting location also has a significant effect on the time course and severity of metallosis bulbi because the tolerance of different ocular tissues for IOFB fragments is variable. In general, the more vascular the tissue and the higher its metabolic activity, the lower its tolerance.[2] This observation is supported by animal studies[8] that demonstrated that iron-containing IOFBs con-

TABLE 15-1

FINDINGS IN SIDEROSIS AND CHALCOSIS

Findings	Siderosis	Chalcosis
Ocular Anatomical Features		
Cornea	Usually normal, but the stroma may develop a diffuse brown haze late in the clinical course	Kayser-Fleischer ring
Iris	Heterochromia with the affected side having a brown discoloration	Heterochromia with the affected side having a greenish color
Lens	Diffuse, brownish discoloration of the anterior capsule and generalized yellowing of cortex	Classic sunflower cataract of the anterior capsule
Retina	RPE degeneration affecting peripheral fundus first and posterior segment later	Refractile deposits in the macular region, with sparing of the periphery
Vitreous	Brownish opacification	Copperlike opacification
Magnetic Properties of IOFB	Yes	No
ERG	Supernormal b-wave, followed by eventual 100% loss of amplitudes	No supernormal b-wave; extent of ERG amplitude reduction usually less than 50%
Pathophysiology	Iron ions deposited intracellularly	Copper ions deposited in basement membranes
Clinical course if IOFB is not removed	Slow, relentless progression with loss of all vision	Variable, but may preserve reasonably good visual function

IOFB: intraocular foreign body
ERG: electroretinogram
RPE: retinal pigment epithelium

Fig. 15-1. An iron-containing foreign body is embedded in the retina adjacent to the nasal margin of the optic disc. Unless surgically removed, this foreign body will slowly undergo ionization and damage the ocular structures, as is typical of siderosis bulbi. Reproduced with permission from Ahmadieh H, Sajjadi H, Azarmina M, Soheleilian M, Baharivand N. Surgical management of intraretinal foreign bodies. *Retina*. 1994;14:398.

fined to the lens (which is avascular and has little metabolic activity) cause far less toxicity than comparable IOFBs situated in the posterior segment.

Mechanical factors notwithstanding, the single most important factor influencing the type and severity of metallosis is the metallic composition of the IOFB (Table 15-2). Metals with lower oxidation–reduction (redox) potentials are considered reactive and tend to undergo ion dissociation. They are more likely to cause tissue damage than metals with higher redox potentials.[2] Pure metals are more reactive than their alloys because the components that make up alloys, such as nickel and zinc, coat the dissociated ions and reduce their propensity for oxidation and, thus, tissue damage. Iron and copper have low redox potentials and therefore are reactive metals. In contrast, relatively inert IOFBs have high redox potentials (Exhibit 15-1).

Diagnosis and Location

As with any form of ocular trauma, when the patient has a penetrating injury to the eye the military ophthalmologist must adhere to a systematic approach, beginning with the history, followed by a thorough examination, and concluding with ancillary testing as indicated.

History

A comprehensive history is crucial with any injury. The history should be obtained from the patient and from anyone else who may have knowledge about the nature of the injury. Particular attention must be given to the circumstances of the trauma that might increase the risk of a metallic IOFB. A history of metal-on-metal contact, explosions, or firearm mechanisms necessitate a high index of suspicion. Whenever possible, it is helpful to obtain samples of the metals involved in the injuries to better evaluate the potential for short- and long-term ocular damage.

Ocular Examination

A thorough examination is performed in all cases of penetrating ocular injuries, with particular attention given to identifying direct signs of retained IOFBs. It is critical to carry out a fundus examination as soon as possible because the first look may be the best look. The view can rapidly deteriorate with the onset of cataract formation, inflammation, or diffusion of blood. The best evidence of an IOFB is direct visualization. But when the view is limited, indirect evidence of an IOFB may include a

TABLE 15-2

METALURGY OF INTRAOCULAR FOREIGN BODIES

Source	Metallic Composition
Shell (naval 5-in. and 155-mm artillery)	High-grade steel (98% iron, 1.7% copper, 0.2% manganese) with 99.5% copper rotation band
Bomb (2,000 lb, 1,000 lb, and 500 lb)	Grade 302/303 stainless steel (69% iron, 18% chromium, 9% nickel, manganese, and molybdenum) and lead-based paint
Cluster bomb unit	Grade 301 steel (69% iron, 19% nickel, 0.15% chromium), pyrotechnic zirconium, and plastic fins
Landmine	Aluminum alloy
Grenade	Zinc alloy case, grade 302 steel lever, barium chromate parts, and zirconium-nickel alloy parts
Bullet (rifle)	Brass or copper jacket, lead-tin alloy and steel core; brass jackets usually have pure copper rotating bands
Bullet (small-caliber)	Lead and lead–tin alloy (contains more lead than tin)
BB	Various manufacturers (brass, copper alloy, steel)
Pellet-gun pellet	Tin–lead alloy (contains more tin than lead)

For a complete detailed list of all military weapon components, access to the MIDAS database may be requested at http://www.dac.army.mil/TD/Midas/Index.htm.

EXHIBIT 15-1

REACTIVE AND NONREACTIVE COMPONENTS OF INTRAOCULAR FOREIGN BODIES

Nonreactive and Inert IOFBs	Reactive IOFBs
Gold	Copper
Platinum	Ferrous iron (Fe^{2+})*
Silver	Ferric iron (Fe^{3+})*
Tantalum	Lead†
Aluminum	Zinc†
Glass	Crystalline lens material
Plastic	Wood
Porcelain	Vegetable matter
Rubber	Cilia or hair
Talc	Bone
Gunpowder residue	
Stone	

*Ferrous iron is more toxic than ferric
†Usually well tolerated but can cause chronic nongranulomatous inflammatory reactions
IOFB: intraocular foreign body

corneal laceration, bubbles of air in the anterior or posterior segment, transillumination defects in the iris, discrete lenticular opacities, or wicks of vitreous hemorrhage not associated with diffuse bleeding.

Ancillary Studies

A variety of diagnostic modalities are available to assist in the evaluation of ocular trauma. Ancillary tests do not necessarily have to be obtained before primary wound closure. In situations where obtaining a diagnostic test will inordinately delay surgery, the test should be deferred until after surgery. Addressing potential IOFBs can be done as part of secondary surgical intervention in the days or weeks following initial repair. In military environments, the probability of a pure copper IOFB is so unlikely that urgent extraction of an IOFB is very rarely a consideration.

Plain film radiography and high-resolution CT scanning are considered the gold standards for evaluating an eye suspected of harboring an IOFB.[9,10] Although CT scans are generally preferable to plain film radiography for detecting and localizing IOFBs, plain films may be the only tool readily available in many military field environments, and plain film radiography is a very sensitive method for detecting metallic FBs larger than 2 mm.

Diagnostic ultrasonography can also be useful, although care should be taken prior to initial wound closure to minimize manipulation of the globe. There are documented cases in which diagnostic ultrasonography detected and localized an IOFB when even high-resolution CT scans missed the object.[10] Magnetic resonance imaging (MRI) is contraindicated when a ferromagnetic IOFB is suspected because of the potential for inducing additional damage from movement of the IOFB during the imaging procedure.

SIDEROSIS

Metallic IOFBs are most commonly made of iron alloys.[5] The group of characteristic clinical findings is called siderosis. All ferromagnetic IOFBs eventually cause some form of ocular damage if they are not removed. Toxic changes may be reversible in the early stages but will become irreversible after enough damage has occurred. Therefore, proper diagnosis and management are essential to preserve vision potential.

Ocular Findings

The ocular structures that are most commonly affected by siderosis are the iris and the lens; as a result, these structures also exhibit the most distinctive clinical changes. In time, however, virtually all structures of the eye can be affected in siderosis. The structures that are initially affected are usually those nearest the retained IOFB (see Figure 15-1). Later, ion dissociation and fluid movement damage more-remote structures.

Anterior Segment

Cornea. In rare cases, the stroma can develop a generalized rust-colored appearance, as can the endothelium. Corneal changes develop late in the clinical course, long after most other clinical findings have appeared.

Iris. Deposition of iron particles in the iris stroma causes a heterochromatic brownish discoloration in the affected eye (Figure 15-2). It is more readily apparent in blue and other lightly colored irides but an asymmetry can sometimes be detected in brown irides, with the affected eye appearing darker. In addition to their effects on iris color, iron particles can result in abnormal pupillary responses. The most common pupil abnormality is a middilated pupil that is minimally reactive to light.[5] Much less common is Adie's pupil, typified by light-near dissociation, segmental iris constriction, and supersensitivity to weak miotic drugs.[11] Pupil abnormalities can result from injury to muscle fibers, cholinergic neurons, or both. Both the heterochromia and pupil defects may be reversible following removal of the IOFB.

Lens. Early in the clinical course, brownish precipitates become apparent due to iron particles in

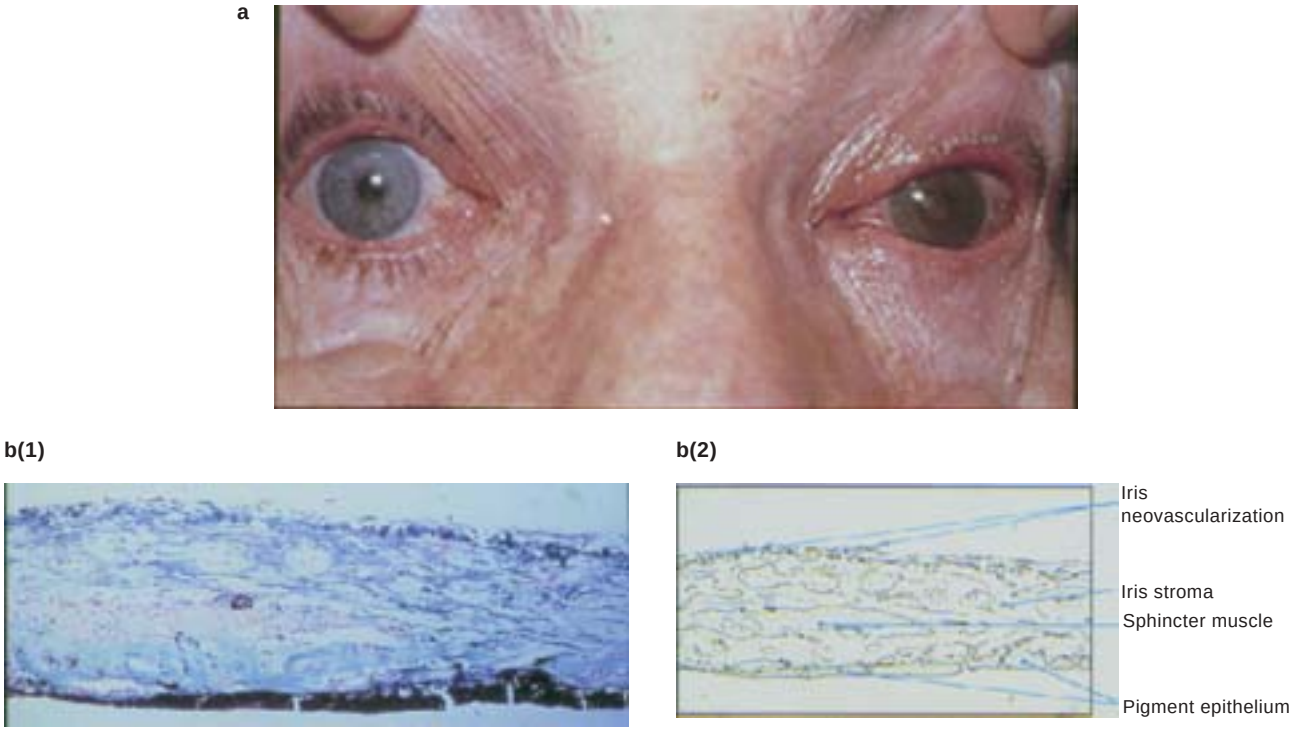

Fig. 15-2. (**a**) Iris heterochromia is seen in a patient with a retained ferromagnetic intraocular foreign body in the left eye. Iron particles deposited in the iris have caused the left eye to appear darker than the right eye. (**b**) Perls's stain imparts a blue color to iron and reveals the presence of diffuse iron deposition in the stroma and in the anterior layer of the iris pigment epithelium. Note the presence of iris neovascularization, a poor prognostic sign (there may be an increased risk of secondary glaucoma). Note that drawing b(2) is a schematic representation of photograph b(1), which is the actual photograph of the iris histopathological specimen. The labels in b(2) refer to the same structures in b(1). Reproduced with permission from Yanoff M, Fine BS. Surgical and nonsurgical trauma. In: *Ocular Pathology: A Color Atlas.* Philadelphia, Pa: JB Lippincott; 1988: Figures 5.36A and 5.36B.

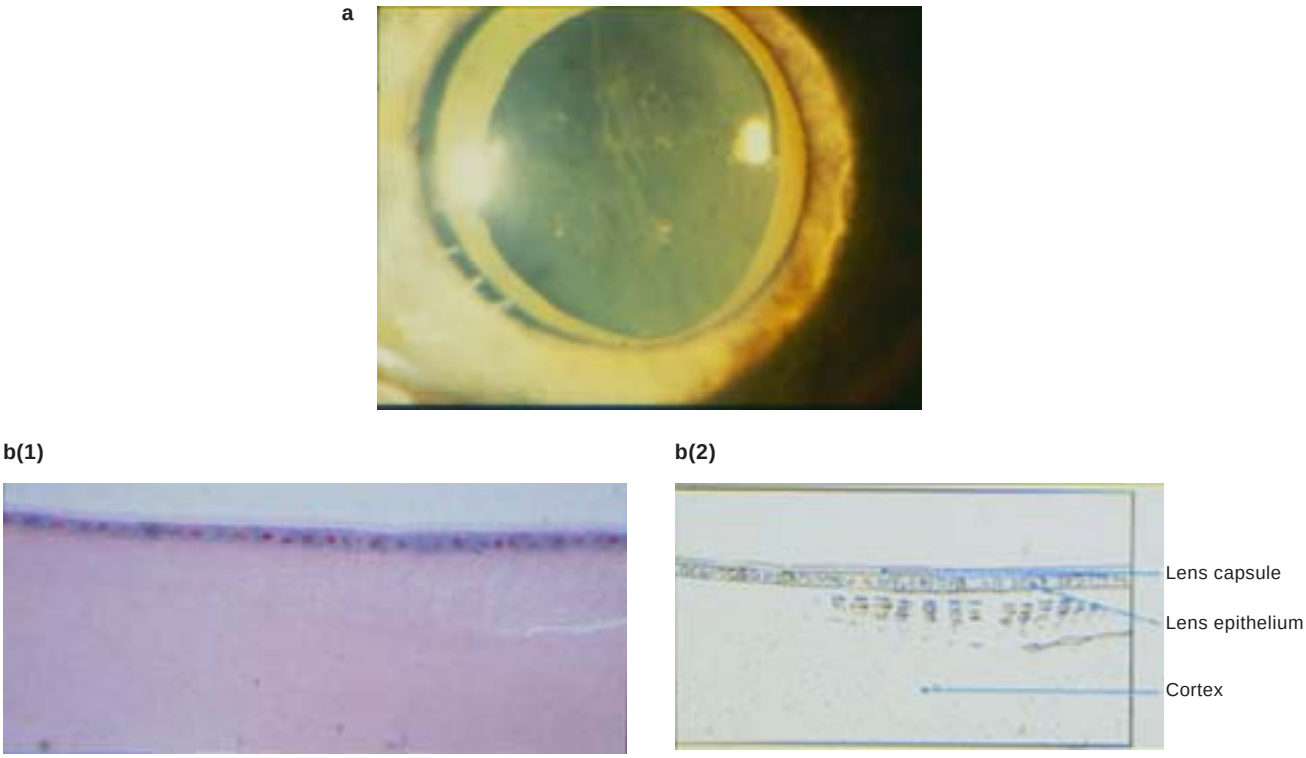

Fig. 15-3. (**a**) Anterior segment of a patient who underwent cataract extraction and posterior chamber lens implantation 5 years after penetrating ocular trauma with a retained ferromagnetic intraocular foreign body. Note the prominent rust-brown discoloration of the anterior lens capsule, which is due to iron deposition in the epithelial cells. The anterior vitreous demonstrates early fibrillar degeneration and mild opacification. (**b**) Perl's stain of the anterior lens demonstrates iron, as signified by the blue color, deposited in the epithelial cells. The lens capsule and cortex are normal. Note that drawing b(2) is a schematic representation of photograph b(1), which is the actual photograph of the histopathological specimen. The labels in b(2) refer to the same structures in b(1). Photograph a: Department of Ophthalmology, Naval Medical Center San Diego, San Diego, Calif. Views b(1) and b(2): Reproduced with permission from Yanoff M, Fine BS. Surgical and nonsurgical trauma. In: *Ocular Pathology: A Color Atlas.* Philadelphia, Pa: JB Lippincott; 1988: Figure 5.36D.

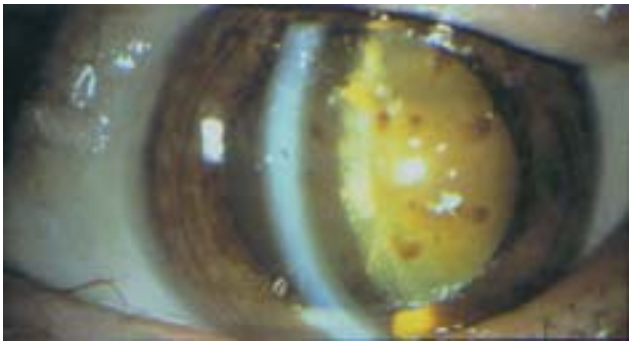

Fig. 15-4. A patient with long-standing hemorrhage in the eye. Iron deposition in the lens has caused a generalized cataract with patches of rust-brown discoloration. Hemosiderosis and siderosis are indistinguishable histologically. Reproduced with permission from Yanoff M, Fine BS. Surgical and nonsurgical trauma. In: *Ocular Pathology: A Color Atlas.* Philadelphia, Pa: JB Lippincott; 1988: Figure 5.36D.

the epithelial cells of the anterior lens capsule (Figure 15-3). Later, a nonspecific cataract develops with widespread yellowing of the lens cortex, mixed with large, rust-brown patches containing iron (Figure 15-4).

Trabecular Meshwork and Glaucoma. Gonioscopy rarely reveals distinct clinical findings of iron deposition, but histological studies have confirmed the presence of iron particles in the trabecular meshwork (Figure 15-5). Deposition of iron particles or secondary scarring of the trabecular meshwork can impede aqueous outflow, causing a secondary glaucoma. In some cases, the only clinical manifestation of siderosis may be glaucoma, which has been termed *subclinical siderosis secondary glaucoma.*[12] End-stage cases of secondary glaucoma may be associated with rubeosis irides, although the cause of angiogenesis has not been clearly established.[13]

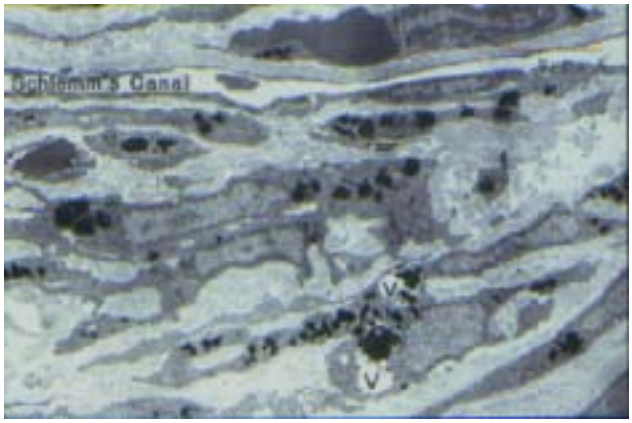

Fig. 15-5. The anterior chamber angle structures in a patient with siderosis demonstrate an open Schlemm's canal, but endothelial cells in the trabecular meshwork contain many siderosomes in their cytoplasm (dark, round granules). Some endothelial cells contain large cytoplasmic vacuoles (V). Reproduced with permission from Tawara A. Transformation and cytotoxicity of iron in siderosis bulbi. *Invest Ophthalmol Vis Sci.* 1986;27:235.

Posterior Segment

Retina. Iron deposition is first found in the cells of the retinal pigment epithelium (RPE) and the cells of Müller (Figure 15-6). This phenomenon results in a characteristic pigmentary degeneration of the RPE, which begins in the peripheral fundus and later extends to the posterior pole (Figure 15-7). The rate of progressive degeneration ranges from months to years. Later in the disease course, the RPE may disappear in widespread areas, the retina can take on an atrophic appearance, and gliosis may ensue in localized areas.[13]

Vitreous. The vitreous can take on a nonspecific, brownish discoloration and opacification. This effect is thought to be the result of iron interacting with hyaluronic acid, causing it to depolymerize. Additional factors influencing vitreous degeneration are unknown.

Electrophysiology Findings

The electroretinogram (ERG) is perhaps the most sensitive indicator of the early effects of siderosis and can demonstrate abnormalities even before clinical signs become apparent.[4,14] The time from initial injury until the onset of changes is apparent on ERG is variable, but it is usually at least several months. Because the peripheral retina is the first to develop clinical signs of degeneration, the ERG can detect abnormalities long before visual function becomes impaired. ERG may also be a valuable tool to measure progression of retinal damage over time in cases where surgical extraction of the IOFB is either deferred or not possible for whatever reason. In general, siderosis follows a continuously progressive detrimental course unless the IOFB is removed, and the ERG reflects the deterioration.

Sometimes, in the early stages of the disease, the ERG may reveal a so-called supernormal b-wave, which is defined as having an amplitude greater than 25% from baseline. The most common finding is a reduction in b-wave amplitudes. Later, progressive losses of amplitudes in both a- and b-waves

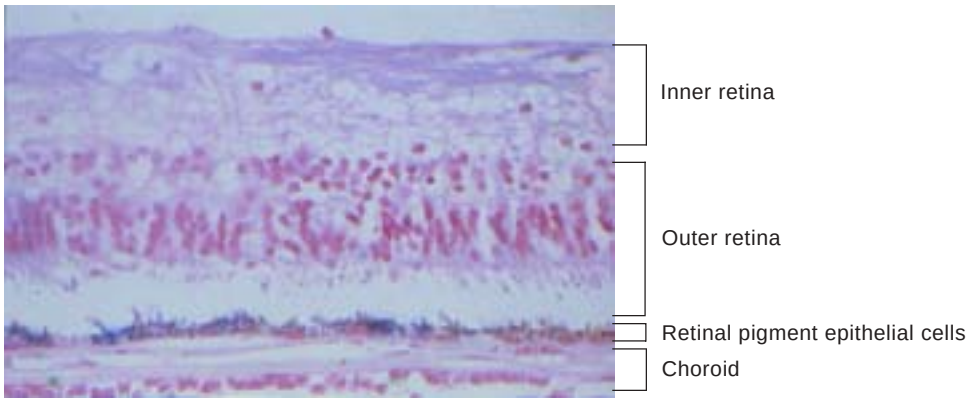

Fig. 15-6. Perls' stain demonstrates iron deposition in the retinal pigment epithelial cells and, to a lesser extent, in the retina. Note the prominent degeneration of the inner retina. Reproduced with permission from Yanoff M, Fine BS. Surgical and nonsurgical trauma. In: *Ocular Pathology: A Color Atlas.* Philadelphia, Pa: JB Lippincott; 1988: Figure 5.37C.

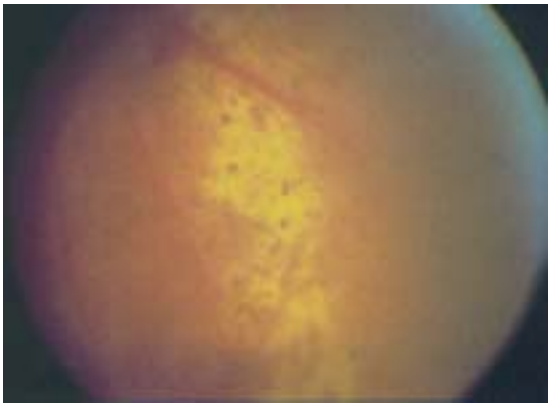

Fig. 15-7. Distinctive mottling of the pigment epithelium in the peripheral fundus is caused by a retained intraocular, iron-containing foreign body. Reproduced with permission from Yanoff M, Fine BS. Surgical and nonsurgical trauma. In: *Ocular Pathology: A Color Atlas.* Philadelphia, Pa: JB Lippincott; 1988: Figure 5.37B.

may occur (Figure 15-8), leading ultimately to flattening of the wave forms. ERG changes may be fully reversible if the IOFB is removed before a 50% reduction in amplitude occurs. When the amplitude is reduced by more than 50% from baseline, the changes are usually irreversible.[11]

Metal purity significantly influences the time course of ERG changes. Experimental studies with animals[4] demonstrated that pure iron particles decrease the ERG amplitude to a nonrecordable level in 100 days; in contrast, iron alloys containing 5% nickel had only a 50% ERG amplitude reduction at 100 days and required 240 days to cause an 80% reduction. These findings substantiate the observation that alloys cause less tissue damage than pure metals do.

Pathophysiology

Ferromagnetic IOFBs undergo electrolytic dissociation, resulting in gradual degradation of the FB and distribution of trivalent ferric ions throughout the eye. Following ion dissociation, the iron particles convert to ferric hydroxyphosphate and com-

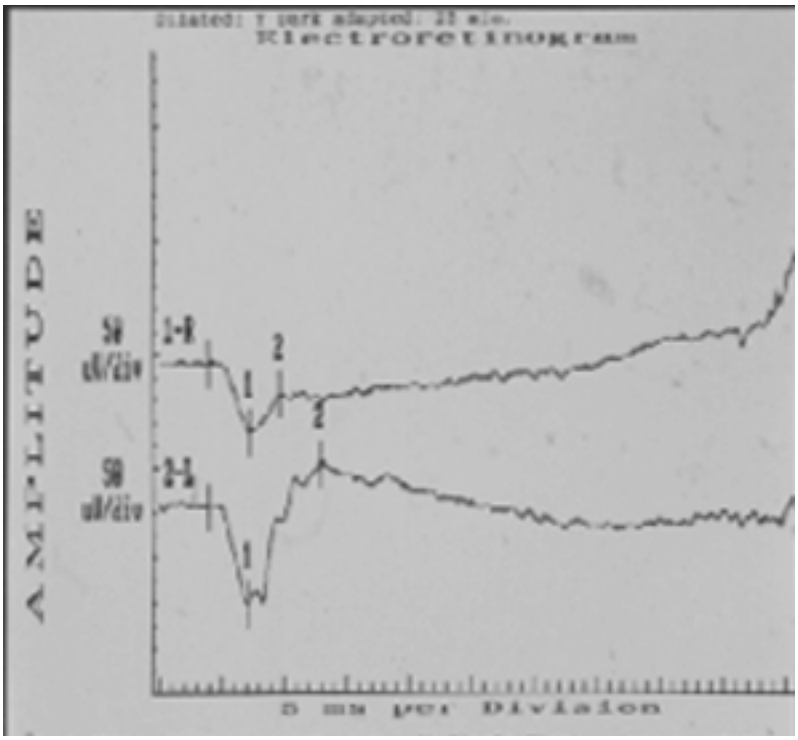

Fig. 15-8. A dark-adapted, bright-flash stimulus electroretinogram (ERG) from a patient with siderosis of the right eye (upper curve; lower curve represents the normal left eye) demonstrates reduction of nearly 75% in b-wave ("2" on ERG) amplitude and a reduction of approximately 25% in a-wave ("1" on ERG) amplitude. Electroretinogram: Department of Ophthalmology, Naval Medical Center San Diego, San Diego, Calif.

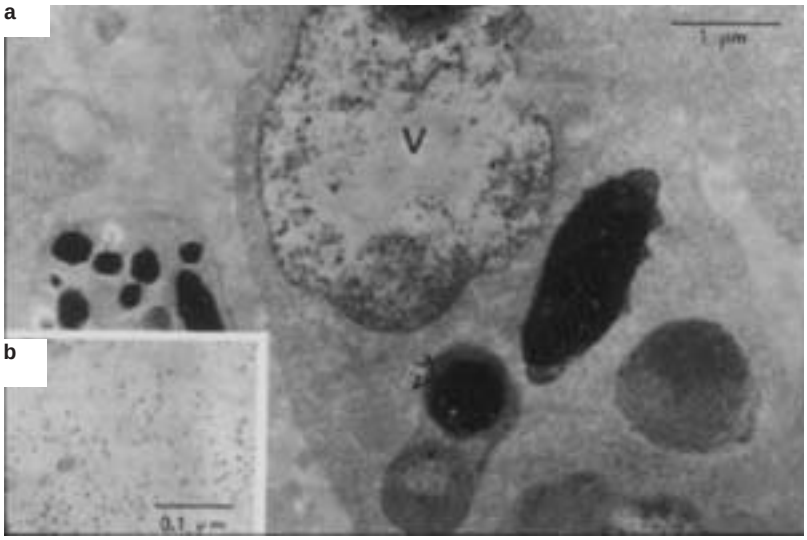

Fig. 15-9. (**a**) Fibroblasts and a melanocyte of the iris. There are numerous scattered ferritin particles and some siderosomes within the cytoplasm. A large vacuole (V) that contains ferritin particles and a siderosome (arrow) that includes both a pigment granule and ferritin particles are shown. Few ferritin particles are observed in the extracellular tissues (no stain, original magnification x 21,000). (**b**) A higher magnification of electron-dense particles within the vacuole. Typical square figures of the cores of ferritin are diffuse (no stain, original magnification x 150,000). Reproduced with permission from Tawara A. Transformation and cytotoxicity of iron in siderosis bulbi. *Invest Ophthalmol Vis Sci.* 1986;27:234.

bine with protein molecules known as apoferritin to form ferritin particles. Ferritin particles can be deposited intracellularly, where they can be found within the cytoplasm or occasionally within the cell nucleus. Ferritin particles can also be deposited extracellularly.[13]

Most of the intracellular ferritin particles are located in the cytoplasm, either as independent structures or in aggregate collections inside phagosome structures known as siderosomes (Figure 15-9).[15–17] Studies of the retina in siderosis using electron microscopy have demonstrated electron-opaque cores of ferritin, primarily in RPE cells and the cells of Müller (Figure 15-10).[15,16,18–21] Histologically, the findings of siderosis are indistinguishable from those of hemosiderosis, although the amount of iron is said to differ among cells in siderosis bulbi.[22,23] The reasons for this difference remain unknown.

Intracellular ferritin and siderosomes cause an interruption of normal cellular function and subsequent cell damage. The mechanism of damage relates to breakdown of lysosomes with the release of proteolytic enzymes, alterations in cell membrane permeability, and subsequent cellular degeneration and death.[13]

The distribution of ferritin particles among susceptible ocular structures varies, depending to a large extent on the resting location of the IOFB. Ferromagnetic IOFBs located in the posterior segment result in greater ferritin deposition in posterior structures such as the retina. In these circumstances, iron particles diffuse to adjacent structures. In con-

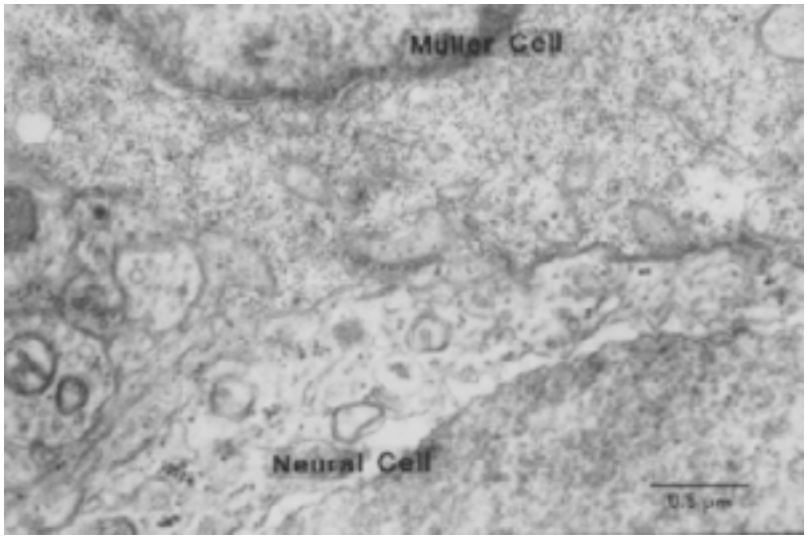

Fig. 15-10. A Müller cell (top) and a neural cell (bottom) are shown (no stain, original magnification x 38,000). There are numerous scattered ferritin particles in the Müller cell's cytoplasm but relatively few particles in the nucleus. There are also relatively few ferritin particles in the adjacent neural cell. Reproduced with permission from Tawara A. Transformation and cytotoxicity of iron in siderosis bulbi. *Invest Ophthalmol Vis Sci.* 1986;27:231.

trast, when an IOFB is located more anteriorly, iron particles disseminate via diffusion and the flow of aqueous humor.[13]

Clinical Course

Clinical observations and electrophysiological studies have conclusively demonstrated[14] that eyes with retained ferromagnetic IOFBs will undergo a slow, progressive, and unrelenting deterioration in visual function, resulting in the loss of all vision unless the IOFB is removed. When surgical intervention takes place before a 50% reduction in ERG amplitudes, much of the damage can be reversed.

Other forms of metallosis bulbi, such as chalcosis, do not have the same dismal prognosis as siderosis. The reason for this relates to differences in pathophysiology: siderosis results in intracellular ferritin and siderosome deposition with subsequent cellular death, whereas chalcosis is limited to deposition of iron particles in basement membranes. The pathophysiological mechanisms of cellular damage in chalcosis is not well understood, but the ensuing toxic effects associated with basement membrane deposition are far less significant than those due to intracellular iron deposition. The time course for cellular and visual dysfunction in siderosis varies, depending in part on the size and location of the IOFB and the purity of the iron. At the very least, the process requires several months before signs of the disease become manifest.

CHALCOSIS

IOFBs consisting of pure copper are extremely rare. Most copper-containing FBs are made of alloys such as brass or bronze. In the rare circumstance when an IOFB contains more than 85% copper, an acute and suppurative reaction develops that is clinically indistinguishable from fulminant infectious endophthalmitis. If not appropriately managed, this sterile endophthalmitis results in phthisis.[2,24] In contrast, chalcosis is a much milder condition that develops very slowly when IOFBs contain less than 85% copper. Brass is an alloy consisting of 68% copper, 30% zinc, and 2% iron. Zinc oxides coat the dissociated copper ions, rendering them less toxic to the tissues that absorb them. This composition is of particular relevance in military environments, because bullet casings or shells from firearms are typically made of brass (see Table 15-2).

Unlike those of iron, copper alloys are generally nonmagnetic. This distinction is significant when deciding on diagnostic imaging modalities and surgical extraction techniques.

Ocular Findings

The structures most commonly affected by chalcosis are the cornea, iris, lens, and macula. With the exception of macular involvement, the clinical characteristics of chalcosis are indistinguishable from those of hepatolenticular degeneration (Wilson's disease).

Anterior Segment

Cornea. The typical green-blue ring in the peripheral cornea, known as the Kayser-Fleischer ring, is a consequence of copper deposition in Descemet's membrane and the posterior stroma. The discoloration may often be segmental, most commonly affecting the superior and inferior cornea.[25] The nasal and temporal perilimbal regions may never develop discoloration, which could result in an observer's missing the Kayser-Fleischer ring unless the entire cornea is thoroughly examined.

Anterior Chamber and Iris. Bright, refractile particles may be seen circulating in the aqueous. As these particles settle and are taken up by the iris, heterochromia develops, with the affected iris exhibiting a greenish discoloration, in contrast to the brownish hue of the iris that develops in siderosis. The pupil may also be sluggish and minimally reactive; there have been no reports, however, of Adie's pupil in chalcosis.

Lens. The so-called sunflower cataract is pathognomonic of chalcosis (Figure 15-11). Copper ions are deposited in the anterior lens capsule basement membrane. When significant vitreous reaction is present, a nonspecific, posterior subcapsular cataract can also be seen.[25] The radial appearance of the anterior subcapsular cataract is related to the folds in the posterior surface of the iris. Movement of the iris with changes in pupillary aperture have a direct influence on the distribution of copper particles in the lens.[2]

Posterior Segment

Retina. In contradistinction to siderosis, most of the retinal changes in chalcosis are confined to the posterior pole. The peripheral retina generally appears normal, except for changes directly related

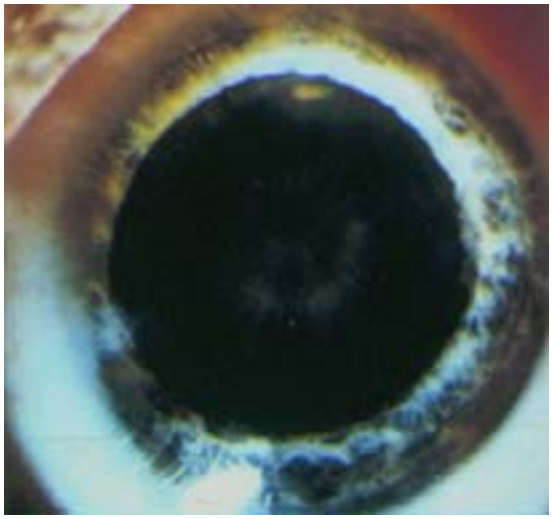

Fig. 15-11. Copper deposition in the anterior subcapsular regions of the lens in an eye with a retained intraocular foreign body has caused a sunflower cataract. Faint white circular area in the center of the photograph: sunflower cataract; yellow discoloration at the corneal limbus: Kayser-Fleischer ring of copper deposition; blue circular structure: iris. Reproduced with permission from Rosenthal AR, Marmor MF, Leuenberger P. Chalcosis: A study of natural history. *Ophthalmology.* 1979;86:1961.

to the initial injury itself. The most characteristic finding is the presence of glistening, refractile particles deposited in the macula and around vessels in the posterior pole, which may increase over time (Figure 15-12). These particles are located in the internal limiting membrane. In some cases, the entire internal limiting membrane of the macula appears to have a copper-colored sheen.[25]

Vitreous. The vitreous can undergo fibrillar degeneration, which is usually observed to some extent in all patients with chalcosis. Typically, these changes are most apparent in the anterior vitreous and consist of condensations of fibrils and cellular infiltrates that are sharply delineated from the rest of the vitreous[25] (Figure 15-13). Other changes may include a copper-colored opacification of the vitreous, as well as organization and strands adjacent to the IOFB. All of the vitreous changes may progressively worsen with time.

Electrophysiology Findings

As in patients with siderosis, patients with chalcosis may exhibit reduced b-wave amplitude on ERG. A supernormal b-wave has not been observed. An abnormal ERG eventually develops in all eyes with retained intravitreal copper FBs and precedes clinical findings in 50% of patients.[14] However, the ERG changes in chalcosis are much less severe than those seen in siderosis: very few patients with chal-

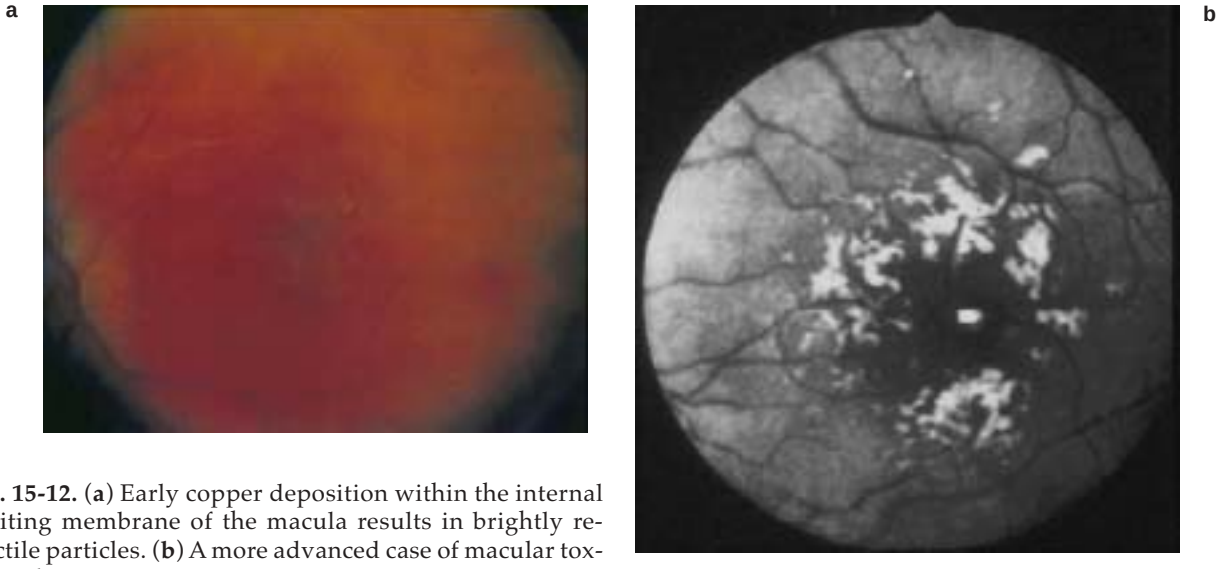

Fig. 15-12. (**a**) Early copper deposition within the internal limiting membrane of the macula results in brightly refractile particles. (**b**) A more advanced case of macular toxicity, characterized by extensive copper accumulation in the internal limiting membrane. Photograph a: Reproduced with permission from Rosenthal AR, Marmor MF, Leuenberger P. Chalcosis: A study of natural history. *Ophthalmology.* 1979;86:1961. Photograph b: Reproduced with permission from Delaney WV. Presumed ocular chalcosis: A reversible maculopathy. *Ann Ophthalmol.* 1975;7:378.

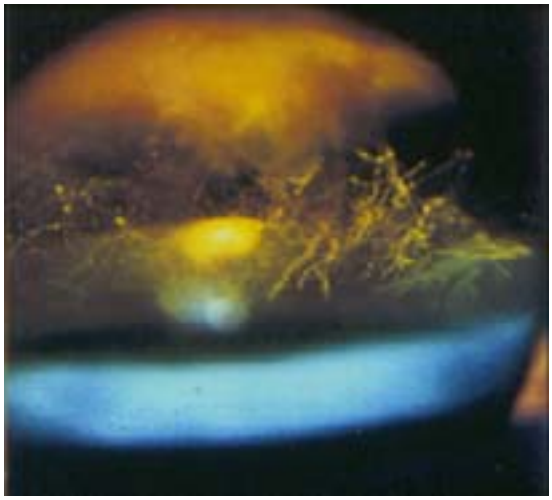

Fig. 15-13. Vitreous changes secondary to the presence of an intravitreal copper foreign body. A marked fibrillar degeneration and brownish tinge of the vitreous is apparent. Reproduced with permission from Rosenthal AR, Marmor MF, Leuenberger P. Chalcosis: A study of natural history. *Ophthalmology.* 1979;86:1962.

cosis experience more than a 50% reduction in b-wave amplitude. Moreover, after the ERG amplitudes fall to a certain level, they may remain stable without further deterioration for many years.[25] In addition to ERG observations in humans, electrophysiology studies[4] in rabbits have demonstrated that chalcosis causes far less damage than siderosis does. It is widely assumed that ERG changes of chalcosis are reversible, based on case reports of complete resolution of all clinical signs following removal of the instigating IOFB.[26] These case reports, the relatively benign nature of ERG changes in chalcosis, and the reversibility of ERG changes in siderosis after removal of ferromagnetic IOFBs all support the presumed ERG reversibility in chalcosis. However, no published case reports have actually documented reversibility.

Pathophysiology

Copper's interaction with intraocular fluids and tissues causes its ionization. Most copper ions become coated with zinc oxides, and this coating minimizes the potential for tissue toxicity. These coated ions have a propensity to be deposited on limiting membranes, in contrast to the tendency of iron particles to be distributed intracellularly. The most common ocular structures affected are Descemet's membrane, the anterior lens capsule, and the internal limiting membrane of the retina.[1,2]

As stated in the discussion of siderosis, the lack of intracellular deposits of toxic particles likely accounts for the more benign clinical course in chalcosis. In the rare case in which an IOFB contains more than 85% copper, the sterile endophthalmitis that develops is attributed to copper's chemotactic properties. The severe inflammatory response is characterized by abscess formation in the vitreous.[2,24,27]

Distribution of ions within the eye may be related to the standing electrical potential.[5] The cornea exhibits a positive charge relative to the optic nerve, which may induce ion distribution based on electrostatic forces. It is unclear why the macular region is selectively predisposed to copper deposition. Some observers[26] have speculated that it may be linked to the macula's higher metabolic rate as well as fluid movements in the eye. It is quite likely, however, that other factors are involved, because this theory fails to explain why siderosis initially affects the peripheral retina.

Vitreous opacification results from the degradation of hyaluronic acid, as is also seen in siderosis. Depolymerization of hyaluronic acid is associated with oxidation of ascorbic acid, and copper is known to accelerate the oxidation of ascorbic acid.

Clinical Course

The clinical course of chalcosis is variable but generally less severe than it is in siderosis, and chalcosis does not have a uniformly poor outcome. The extent of damage and visual impairment depends on several factors, including the size, alloy composition, and intraocular location of the IOFB, and adjacent tissue reaction. A retained copper-containing IOFB can be tolerated for years without serious toxicity to the retina or RPE.

One case series[25] reported on 10 patients with retained IOFBs of copper alloys who were followed from 4 months to 29 years; 9 of the 10 patients retained a final visual acuity of 20/60 or better. All 10 had clinical findings typical of chalcosis. IOFBs located in the vitreous were more likely to cause chalcosis, whereas in the anterior segment or the lens nucleus, small FBs could cause very few changes typical of this disease. Not all patients with chalcosis will maintain such a high degree of visual function. The two clinical findings that have the most deleterious impact on vision are (1) vitreous opacification and (2) macular toxicity.

The time for clinical signs of chalcosis to develop ranges from 4 months to 2 years.[25] Most of the ocular findings may resolve spontaneously if the IOFB

dissolves, is spontaneously extruded, or is surgically removed.[28] In addition to the effects on visual acuity, abnormalities in color vision and visual field have been reported.[25] It is unclear, however, whether these findings are true sequelae of retinal dysfunction. It may be that they are the result of media changes, the effects of the initial trauma to ocular structures, or both.

MANAGEMENT

The goals in surgical management of penetrating IOFB injuries include optimal wound closure, restoration and preservation of ocular anatomy to the extent possible, prevention of secondary infection, and, in most cases, removal of the IOFB. Management of retained IOFBs was revolutionized in 1879 by the development of the Hirschberg hand-held electromagnet; its inventor used it to treat more than 100 patients. A landmark article[29] published in 1894 compared Hirschberg's series with another large series of electromagnetic IOFB extractions in 66 patients. Both series demonstrated excellent visual outcomes in nearly all anterior segment cases and outstanding results in 30% of posterior segment cases.

Some of the lessons learned nearly 100 years ago are still valid today:

- localize the metal as well as possible,
- remove metallic IOFBs early, and
- choose the extraction site and technique that minimize vitreous traction and collateral damage.

Modern advances in the management of these cases include the following:

- diagnostic imaging modalities that have improved IOFB localization,
- advent of vitreous surgery combined with wide-field intraoperative viewing systems,
- surgical instrumentation,
- improved magnets, and
- development and use of antibiotics to prevent and treat infections.

Results of modern vitreous surgery are such that approximately 33% of posterior segment IOFB cases recover visual acuity of 20/40 or better, 67% recover 20/200 or better, and 75% have ambulatory vision of 5/200 or better.[5,30–33] These results compare favorably with those pertaining to cases of penetrating ocular trauma without IOFBs. Discussions of current surgical techniques are found elsewhere in this textbook.

Prevention of metallosis is rarely a significant issue in the early, or primary, surgical management of ocular trauma. The only true indication for early removal of a metallic IOFB as part of the primary surgical procedure is when the object contains more than 85% copper or if there is a high probability of infection. Failure to intervene promptly in such cases is associated with a high risk of endophthalmitis and phthisis.[3,24] In all other forms of metallosis, the onset of clinical findings and toxicity generally requires at least several months and may be fully reversible even after delayed surgical intervention. Therefore, there is seldom an urgent indication to remove the IOFB.

The decision of when and whether to remove a metallic IOFB often becomes a side issue in the larger picture of managing ocular trauma. More times than not, removal of the IOFB is incorporated into the vitreoretinal surgery for treating more pressing indications, including

- the presence of a retinal tear or detachment,
- dense vitreous hemorrhage,
- prominent vitreous wicks following the path of an IOFB,
- significant lens disruption, and
- infection.

In the absence of other indications for surgery, determining when and if an IOFB should be removed assumes greater relevance. Inert IOFBs, particularly if they are small and not associated with other indications for surgery, may be reasonable to observe. Reactive metals, such as iron and copper alloys, however, deserve further consideration.

Siderosis

In general, there is seldom any dispute with the recommendation that all ferromagnetic IOFBs be removed to prevent the slow but relentless deterioration in visual function that occurs with siderosis. However, in certain circumstances, surgery might increase the risk of a poor visual outcome (eg, a deeply embedded IOFB in the posterior wall of the globe, or if the patient is reluctant to undergo a procedure). In one case series[3] of 84 eyes harboring iron-containing IOFBs, surgery was not performed

in 8 eyes. When surgery is deferred for whatever reasons, observation for signs of siderosis onset and progression should be undertaken. The fact that the retinal changes affect the peripheral fundus before evolving to the macula enables the military ophthalmologist to monitor the patient with an added degree of comfort. Serial ERGs can be very useful in these circumstances. When reductions in b-wave amplitudes approach 50% of baseline, the option for surgery can be considered before further toxicity results in irreversible damage.

Chalcosis

In contrast to siderosis, no consensus exists around the timing and indications for surgery to remove copper-containing IOFBs, largely because the clinical course of chalcosis is more benign and self-limiting than it is for siderosis. Those who historically have favored a conservative approach recommend observation to determine if and when significant toxicity develops, usually in the form of vitreous opacification, advanced macular toxicity, or both.

Reports in the literature support the viewpoint that surgical intervention can be delayed in selected cases and may not always be necessary. In the case series[25] of 10 patients referred to previously, 7 patients maintained visual acuity of 20/40 or better for many years—even in the presence of sunflower cataracts and early maculopathy. Furthermore, case reports[28,34] have documented complete resolution of the clinical findings when the IOFB is either removed surgically or extrudes spontaneously as long as 15 years after the initial trauma.

With the advent of modern vitreoretinal surgical techniques, the ability to successfully intervene in IOFB cases and minimize iatrogenic complications has shifted current opinion more in favor of earlier surgical management—even before signs of chalcosis develop. Advocates[35] of surgical extraction of copper IOFBs refer to the same 10 patients[25] who were followed for up to 29 years and point out that only 2 had final visual acuity of 20/20. Furthermore, 6 of the 8 who had ERG testing demonstrated some degree of abnormality, and all 10 had vitreous degeneration to some extent. The authors[35] conclude that chalcosis is not completely benign and that it is not possible to accurately predict which cases will do well without intervention or for how long. Therefore, surgery is an appropriate consideration even when there are no other pressing indications for pars plana vitrectomy.

SUMMARY

Metallosis bulbi is the name of the condition in which retained metallic IOFBs damage ocular structures; the intraocular changes evolve slowly over months to years. Metallic FBs interact with surrounding tissues to undergo ionization, which is followed by distribution and uptake of liberated ions in various parts of the eye. Toxic effects of the ions result in characteristic clinical findings.

The two most common metals involved in ocular trauma are iron and copper. Iron-containing FBs cause a form of metallosis known as siderosis, and copper-containing FBs cause chalcosis. When a penetrating FB contains more than 85% copper, an acute and suppurative sterile endophthalmitis develops. The clinical findings most commonly seen in siderosis are

- iris heterochromia, with the affected eye having a rust-brown discoloration,
- diffuse cataract,
- RPE degeneration affecting the peripheral retina in the early stages before progressing to the posterior pole, and
- vitreous opacification.

Chalcosis, on the other hand, is characterized by

- the Kayser-Fleischer ring,
- iris heterochromia, with the affected eye having a greenish discoloration,
- a pathognomonic sunflower cataract,
- refractile precipitates in the macular region, and
- vitreous opacification.

Diagnostic modalities that are helpful in detecting metallic FBs include plain film radiography, CT scanning, ultrasonography, and electroretinograms. Electroretinograms often demonstrate reduction in b-wave amplitudes even before clinical signs become apparent. In general, the adverse affects on visual function are more severe in siderosis than chalcosis.

Unless the inciting FB is removed in siderosis, there will be progressive visual deterioration with loss of most vision. In chalcosis, in contrast, relatively good visual acuity may be preserved even in the presence of cataract and macular toxicity. The reason for the difference in prognosis relates to

pathophysiology: siderosis is associated with deposition of iron ions intracellularly, whereas chalcosis results in copper ion deposition in basement membranes. Damage to ocular structures is far more extensive when the toxic products accumulate intracellularly.

Management of retained IOFBs must be considered within the context of other issues pertinent to surgical decision making. With the rare exception of copper-containing objects that are more than 85% pure, there is no need to incorporate removal of the FB in conjunction with primary wound closure. Very often, secondary surgical procedures are indicated in trauma cases, and removal of FBs is performed at that time. In the absence of any other indications for vitreoretinal surgery, inert IOFBs can be observed, but metallic iron and copper-containing objects should be removed. The early findings in metallosis may be reversible if the IOFB is removed prior to a 50% reduction in electroretinogram amplitudes, after which the damage may be permanent.

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