Chapter 27

GEOGRAPHICAL OPHTHALMOLOGY

RICHARD D. STUTZMAN, MD*

Major, Medical Corps, US Army; Staff Ophthalmologist, Department of Ophthalmology, Walter Reed Army Medical Center, Washington, DC 20307-5001

INTRODUCTION

Geographical ophthalmology is an area within our specialty that is undergoing rapid changes. In addition to understanding the ophthalmological manifestations of disease, military ophthalmologists in developing nations need to consider disease processes from a public health standpoint. How does this disease process affect the country? The disease process and, more likely, its complications may result in large numbers of individuals being unable to contribute to the socioeconomic development of their country. Are there any identifiable factors that can prevent the disease or its complications? For example, the incidence of trachoma and its blinding complications have been significantly reduced by educating the populace regarding the importance of good hygiene, particularly facial cleanliness among children.

Although the disease processes that are seen in the West also affect developing countries, ophthalmology in the Third World is hindered by several factors, including poverty, inadequate community health education programs, and insufficient numbers of healthcare personnel and services. Underdeveloped nations also have a number of disease processes with significant ocular and systemic morbidity that have been eradicated to a large extent in developed nations. These diseases may manifest significant ocular morbidity, with the most significant sequela being blindness.

Data on the prevalence of blindness are difficult to ascertain. Worldwide there are variations in the definitions as well as the causes of blindness. The World Health Organization (WHO) has been instrumental not only in attempting to determine the prevalence of blindness but also, more importantly, in developing programs aimed at preventing and reducing the incidence of blindness. Worldwide, estimates are that at least 40 to 45 million people are blind, with an additional 160 to 180 million visually disabled.[1] The leading causes of blindness in Third World countries include cataract, glaucoma, trachoma, xerophthalmia, and onchocerciasis. Less common etiologies include Hansen's disease (leprosy), age-related macular degeneration, and diabetic retinopathy. WHO's goal is ultimately to have a blindness prevalence less than 0.5% globally or less than 1% in any country.[1]

Military ophthalmologists need an understanding of ocular diseases that affect countries in the developing world. We may be deployed to any of the underserved regions that are affected by these diseases. We need to be familiar with the disease, its manifestations, and its management. Management includes the treatment of acute and chronic manifestations of the disease and its complications. It also includes the ability to recognize factors that may be useful in the prevention of disease, ranging from the simple—implementing a community health education program—to the complex—providing instruction about surgical techniques to ancillary health personnel.

MEDICAL CARE IN THE THIRD WORLD

In developing countries, medical care is delivered in a tiered system. The first level provides the most basic healthcare to the greatest number of persons, with an emphasis on prevention. Because most of the population of developing nations usually lives in rural areas, these areas are the focus of the first level of care. The personnel providing medical services at this level have limited ophthalmological experience and few resources. They have been trained to evaluate large populations, make simple diagnoses, and provide basic treatments.

Many believe that early diagnosis of a particular disease process leads to a more favorable prognosis. For example, we know that the blinding complications of trachoma occur as a result of reinfection, and not of the acute infection. Therefore, the earlier the diagnosis can be made, the earlier the healthcare system can intervene (from both treatment and prevention standpoints) and potentially reduce the chance of visually significant sequelae. The personnel working at this level are trained to identify and manage the early and acute manifestations of many of the blinding conditions that will be reviewed in this chapter. As mentioned previously, a large part of geographical ophthalmology involves public health. At this echelon, healthcare providers play an important role in educating the population in the remote areas they serve. They promote proper sanitation, both personal and environmental.

The second level of care is more advanced; it has more numerous trained personnel, and hospitals are available. The resources are greater at this level compared with the first, yet more limited than at the third. The primary provider at this level is an ophthalmic assistant, with the occasional support of an ophthalmologist. Ophthalmic assistants are an invaluable asset. They receive extensive train-

ing and provide a broad range of care. They are responsible for examination, diagnosis, and management of most disease processes. Their management also includes the surgical treatment of various diseases. For example, many ophthalmic assistants are capable of providing eyelid repairs in patients with trachoma. The providers at this level give appropriate referrals to the third level of care, thereby improving the efficiency of an already overburdened system.

The most sophisticated level of care occurs at the third level, which usually consists of a central national hospital, typically located within an urban area. Medical subspecialists can be found at this level. Training of healthcare personnel, regardless of level of care, occurs at this level.

CATARACT

Worldwide, cataracts are the leading cause of blindness; the latest estimates reveal that approximately 16 million people are blind secondary to cataract.[2] In the Third World, the prevalence of cataracts is great because of limited material and financial resources, as well as the lack of adequately trained healthcare providers.

The risk factors for cataracts are similar for developed and underdeveloped countries. The most significant risk factor is probably age, and the most common type of cataract is the senile cataract. Other risk factors include gamma radiation, ultraviolet and ionizing radiation, nutritional factors, underlying metabolic disorders (eg, diabetes mellitus), medications (eg, steroids), alcohol, smoking, and geographical location. At present, there is no specific preventive measure to reduce the incidence of cataracts. The management of cataract remains one of surgical intervention. But in the Third World, management can be difficult because of patient fears, lack of access to healthcare, and the severe limitation of resources.

Screening and Assessment

The structure of a healthcare system must be integral to its delivery. In the Third World, the process begins with the promotion of ocular health. There is a strong public health mission imbedded in medical care provided in Third World countries. When a patient presents at the first level of care, he or she needs to be screened for the presence of cataract as well as other ocular diseases. This screening primarily occurs at the first and second levels of care. When a patient is suspected of having a cataract, he or she should be referred to the next level of care so that the ophthalmic assistant can confirm the presence of a cataract and determine whether the cataract warrants surgical intervention.

Cataract assessment is taken for granted in developed regions of the world, and diagnosis of cataract is relatively straightforward. In developing countries, however, examination is more difficult. There, assessment is frequently made with a handheld light and loupes rather than by slitlamp examination. Once a cataract has been determined to require surgical intervention, the patient must decide whether to undergo surgery. In Third World countries, many patients are apprehensive about undergoing surgical correction of cataracts. In India, "cataract camps" have been developed, which provide surgical services to large numbers of individuals. These camps have allowed reluctant patients to feel more comfortable because so many have received treatment and publicly applauded the surgical experience.

Management

In Western nations, the surgical procedure of choice is, without question, small-incision phacoemulsification with insertion of a foldable intraocular lens. In the Third World, the choice of procedure is not so simple. Most developing countries have provided their patients with intracapsular cataract extraction (ICCE), leaving the patients aphakic. Should these countries proceed to extracapsular cataract extraction (ECCE) with posterior chamber intraocular lenses (IOLs)? Most surgeons in developing countries are quite comfortable performing ICCE, and this procedure can be performed with the limited resources that are available. The ICCE technique is relatively straightforward and, once the initial learning period is over, can be performed with low rates of complications.

ECCE is a good procedure but is technically more difficult than ICCE and requires more sophisticated resources. In some of the less-developed countries, mass production of IOLs has reduced the financial burden associated with ECCE, but problems with IOLs need to be recognized. For example, the ability to determine the correct power IOL for a given patient is less precise in the Third World than it is in developed countries. There is greater variability among the IOL *A*-constants. Additionally, the powers and formulas used in Western

nations depend on knowing corneal curvatures and the axial length of the eye. Sophisticated equipment is, therefore, required to determine the "correct" IOL power.

In addition, ECCE frequently is done with a microscope, which adds to the resource burden. ECCE also requires additional training. To reduce the number of patients with visual loss secondary to cataract, we must have an effective means of delivering eye care to large numbers of persons with limited access to care. Various camps have been established in an attempt to decrease the visual impairment associated with cataract. Such facilities include static eye facilities, mass cataract camps, and mobile eye units.[2] Once the surgery has been completed, however, the patient begins a rehabilitation period. It is important to keep the eye protected and free of contamination; therefore, it is important (1) to maintain a good level of personal hygiene and (2) to try to maintain environmental cleanliness, as well. Postoperative medications are frequently used in the West, but such drugs are limited in Third World countries (eg, they frequently have only a single steroid and one or two antibiotics).

The issue of visual rehabilitation must be addressed, as well. An aphakic individual may be provided with an array of aphakic spectacles and advised to try on multiple pairs and determine which pair provides the best subjective visual acuity. If an IOL is inserted, how do you refract the patient? And once a refraction has been determined, how do you provide the individual with a spectacle if neither a facility for making spectacles nor money to pay for them is available?

TRACHOMA

Following cataract and glaucoma, trachoma is the third leading cause of blindness, worldwide. It has been estimated that 150 million people are affected by trachoma and that 6 million are blind as a result of trachoma.[3] Trachoma is a chronic, infectious keratoconjunctivitis that is now limited to developing countries. It is primarily seen in Africa, although it occurs in many other areas, including the Middle East, the Indian subcontinent, Burma, Vietnam, Central Asia, some areas of China, Latin America, Australia, and the Pacific Islands.[4] The disease has been linked to *Chlamydia trachomatis* serotypes A, B, Ba, and C. These serotypes are associated with classic blinding trachoma, which is the endemic form of the disease. It is typically associated with poverty, poor personal hygiene, and inadequate environmental sanitation, and it may be transmitted directly or indirectly from person to person.

Serotypes D through K may produce ocular inflammation and are associated with inclusion conjunctivitis, which is usually associated with sexually transmitted diseases and is rarely visually significant. This form will not be discussed further in this textbook

Classification of Endemic Trachoma

Several classification systems have been developed to aid in the management of patients with trachoma. From a Third World standpoint, the best classification system is simple to understand, so that, potentially, nonophthalmic personnel could stage the disease process and provide the appropriate level of treatment. WHO has developed such a simplified grading scheme for trachoma (Table 27-1)[5]:

TF: trachomatous inflammation, follicular (Figure 27-1a);
TI: trachomatous inflammation, intense;
TS: trachomatous conjunctival scarring (Figure 27-1b);
TT: trachomatous trichiasis; and
CO: corneal opacity (Figure 27-1c).

Clinical Course

As previously mentioned, trachoma is a chronic keratoconjunctivitis. Previously it had been thought that the visual sequelae were secondary to the acute infection. However, over the years it has been found that the process of multiple reinfections is responsible for the blinding complication of trachoma.[6]

The earliest manifestation of trachoma is follicular conjunctivitis (see Figure 27-1a). The follicles are usually associated with an infiltration of lymphocytes and polymorphonuclear cells. The upper tarsus is the more common site of involvement. As the disease progresses beyond the inflammatory phase, the conjunctival tarsus becomes thickened and scarred. The classic scarring pattern produces the line of von Arlt (see Figure 27-1b), which is a distinct horizontal scar in the upper tarsus where the ascending and descending subconjunctival vessels meet. Other patterns of scarring include fine, linear scars; stellate patterns; and broad, confluent, and deeper patterns. The scarring process may extend and involve the lacrimal drainage system and produce obstruction, fistula formation, or dacryocystitis.

TABLE 27-1

WORLD HEALTH ORGANIZATION'S SIMPLIFIED TRACHOMA GRADING SYSTEM

Abbreviation	Classification	Description
TF	Follicular trachoma	The presence of five or more follicles (≥ 0.5 mm) in the upper tarsal conjunctiva (see Figure 27-1a)
TI	Trachomatous inflammation, intense	Pronounced inflammatory thickening of the upper tarsal conjunctiva that obscures more than half of the normal deep tarsal vessels
TS	Trachomatous conjunctival scarring	The presence of easily visible scarring in the tarsal conjunctiva (see Figure 27-1b)
TT	Trachomatous trichiasis	Evidence of at least one eyelash touching the globe; evidence of recent removal of inturned eyelashes is also graded as TT
CO	Corneal opacity	The presence of easily visible corneal opacity that obscures at least part of the pupillary margin (see Figure 27-1c)

Source: Munoz B, West S. Trachoma: The forgotten cause of blindness. *Epidemiol Rev.* 1997;19:205–217.

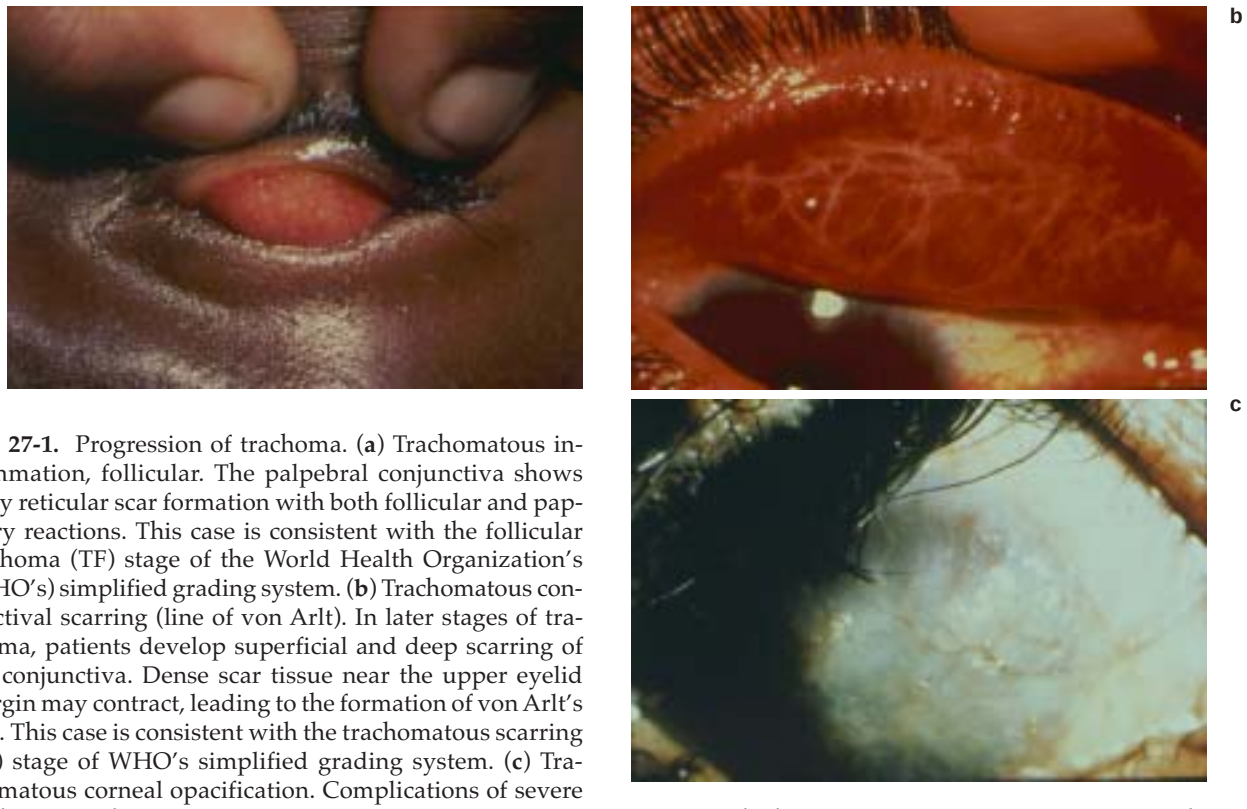

Fig. 27-1. Progression of trachoma. (**a**) Trachomatous inflammation, follicular. The palpebral conjunctiva shows early reticular scar formation with both follicular and papillary reactions. This case is consistent with the follicular trachoma (TF) stage of the World Health Organization's (WHO's) simplified grading system. (**b**) Trachomatous conjunctival scarring (line of von Arlt). In later stages of trachoma, patients develop superficial and deep scarring of the conjunctiva. Dense scar tissue near the upper eyelid margin may contract, leading to the formation of von Arlt's line. This case is consistent with the trachomatous scarring (TS) stage of WHO's simplified grading system. (**c**) Trachomatous corneal opacification. Complications of severe trachoma are the result of conjunctival contraction and deep scar tissue, which can result in cicatricial entropion, trichiasis, and lid shortening. The marked corneal scarring is associated with drying, a result of conjunctival disease. This case is consistent with the corneal opacity (CO) stage of WHO's simplified grading system. Photographs a and b: Courtesy of Sheila West, PhD, Wilmer Ophthalmological Institute, Johns Hopkins Hospital, Baltimore, Md. Photograph c: Reproduced with permission from Spalton DJ, Hitchings RA, Hunter PA. *Atlas of Clinical Ophthalmology*. Philadelphia, Pa: JB Lippincott Co; 1984: Figure 4.37.

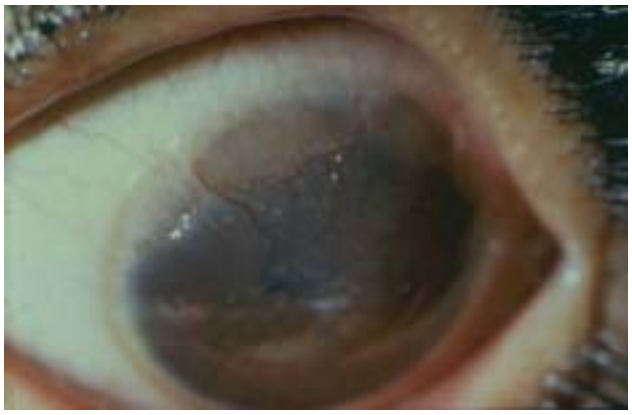

Fig. 27-2. Active trachoma with limbal follicles and an active corneal pannus (ie, dilated limbal blood vessels and diffuse infiltrate affecting the upper cornea). Reproduced with permission from Spalton DJ, Hitchings RA, Hunter PA. *Atlas of Clinical Ophthalmology*. Philadelphia, Pa: JB Lippincott; 1984: Figure 4.33.

As the conjunctival findings progress, they reach a cicatricial stage in which goblet cells are lost, which results in a loss of mucous secretion, which then produces an inadequate tear film and sets the framework for corneal complications. Corneal changes may arise at the same time as the conjunctival findings, but they are more commonly are seen after repeated bouts of the disease. The cornea may show focal inflammatory infiltrates, with histopathology similar to that seen in the conjunctival follicles. As the inflammation progresses, a superior vascular pannus usually develops (Figure 27-2). Pannus ulcers may develop anterior to the advancing border of the vascular pannus. They typically appear as horizontal-oval epithelial defects. Clinically, they may appear similar to the shield ulcer of vernal keratoconjunctivitis. The vascular pannus is most commonly located superiorly but may involve the entire limbus. Herbert's pits are also a manifestation of trachoma (Figure 27-3). The pits are most commonly found at the limbus and represent residual of inflammation.

The blinding sequelae of trachoma are usually secondary to cicatricial changes. These changes alter the normal lid position, resulting in entropion and trichiasis. The trichiasis can further compromise corneal integrity and create breakdown. Because of trachoma's association with poor hygiene, individuals afflicted with the disease are at increased risk for developing bacterial or viral superinfection, complications that can also cause blindness.

The clinical diagnosis of trachoma requires that two or more of the following findings be present:

- follicles on the upper tarsal conjunctiva,
- limbal follicles or Herbert's pits,
- typical conjunctival scarring, and
- vascular pannus, most notably involving the superior limbus.

Management

A variety of therapies have been used to treat the active infectious process. Traditional therapies have included such agents as topical tetracycline, erythromycin, and sulfa-based medications. Each of these medications, however, has problems associated with its use. The most significant limitations are the needs for multiday dosing and for prolonged treatment periods; these requirements decrease patient adherence to treatment, thereby decreasing the likelihood of eradicating the disease. Tetracycline cannot be used in the pediatric population, and trachoma predominantly affects this population. Sulfa-based medications are associated with high rates of allergic responses, the most serious being the potentially life-threatening Stevens–Johnson syndrome.

More recently, azithromycin has been used in the treatment of trachoma; it requires only a single dose but may not completely eradicate the organism. Studies are underway to determine when the medication dose needs to be repeated. Another limitation of azithromycin is its significant expense.

The lid complications of trachoma typically require surgical correction. In many Third World

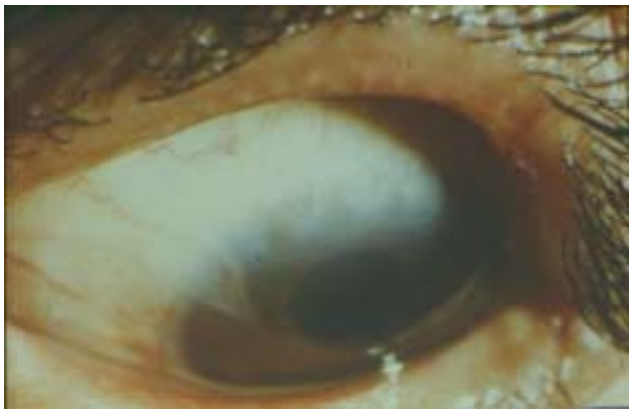

Fig. 27-3. In later stages of trachoma, patients may develop an inactive pannus (downgrowth of vessels and scarring without active inflammation) in which shallow depressions, known as Herbert's pits, can be observed. Reproduced with permission from Spalton DJ, Hitchings RA, Hunter PA. *Atlas of Clinical Ophthalmology.* Philadelphia, Pa: JB Lippincott; 1984: Figure 4.36.

countries, ophthalmic assistants are taught to perform these corrective procedures, thereby reducing the burden for the ophthalmologist.

Management of trachoma requires a multidisciplinary approach. The disease is associated with poverty, poor sanitary conditions, and poor environmental conditions with an abundance of flies and overall poor personal hygiene.[7] The populations in which trachoma is endemic must be educated about the ways they might be able to alter these factors and reduce the incidence of disease. An initiative known as "VISION 2020: Global Elimination of Avoidable Blindness 2020," is a consortium of nongovernmental developmental organizations, donor organizations, field experts, and WHO. One of the goals of this initiative is to eliminate new cases of trachomatous blindness by 2020 through public health, medical, and surgical management efforts. To this end, WHO has developed the SAFE strategy (*s*urgery, *a*ntibiotics, *f*acial cleanliness, *e*nvironmental improvement) to help fight blinding trachoma.[8] The VISION 2020 group believes that the use of the SAFE strategy in affected areas should lead to the elimination of trachoma as a blinding disease by the year 2020.[9] In addition, VISION 2020 has been working with the pharmaceutical industry to provide free azithromycin to populations in whom trachoma is endemic.

ONCHOCERCIASIS

Onchocerciasis is a parasitic disease that has ocular as well as systemic manifestations and is caused by the microfilariae of *Onchocerca volvulus*. Various estimates report approximately 18 million persons infected, 270,000 persons blinded, and 500,000 severely visually disabled.[10] The disease is commonly known as river blindness because of the disease's association with close proximity to rivers and fast-flowing streams where black flies breed.[11] Humans are the only natural host; the disease is transmitted via the bite of the black fly, *Simulium* species, which transmits infectious larvae to the human.

The disease itself is most commonly seen in the African continent with a few small foci in Central and South America. Within Africa there are varying patterns of severity of ocular disease. The most significant ocular disease may be found within the savanna woodland belt. Less-significant ocular disease is associated with the African rain forests and the highlands.

Clinical Course

The ocular and dermatological manifestations of onchocerciasis occur as a result of microfilariae deaths. The well-known Mazzotti reaction is an intense inflammatory response secondary to the deaths of millions of microfilariae in association with diethylcarbamazine (DEC) treatment.

Proposals for the route of ocular entry have included the microfilariae entering the eye through several routes[10]: along the sheaths of the posterior ciliary arteries and nerves, through the blood or cerebrospinal fluid, or via the orbital septum. Ocular onchocerciasis may involve any ocular tissue, and the manifestation of ocular disease depends on which tissue or tissues are affected.[12,13]

A relatively benign corneal manifestation takes the form of *punctate keratitis*. The dead microfilariae are surrounded by an inflammatory infiltrate and appear as ill-defined punctate opacities. Histopathologically, these are focal collections of lymphocytes and eosinophils with associated edema. Typically, the lesions clear and leave no significant visual sequelae.

A more severe corneal finding—and an important cause of blindness—is *sclerosing keratitis*.[14] This process begins peripherally, at the limbus within the interpalpebral fissure, and progresses toward the central cornea. Initially, sclerosing keratitis presents as increasing limbal haze with progressive fibrovascular pannus and an inflammatory infiltrate (Figure 27-4). The inflammation usually extends to the level of Bowman's membrane. Progressive changes

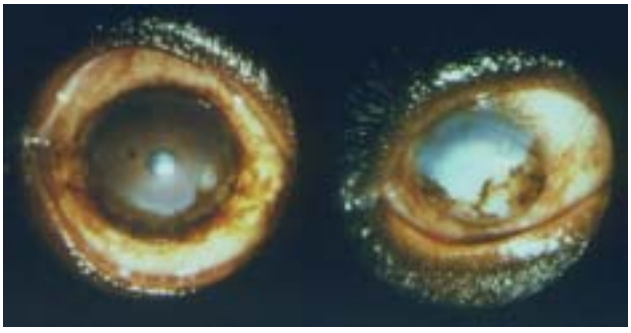

Fig. 27-4. Onchocerciasis can cause a mild (left) or severe (right) sclerosing keratitis with corneal scarring, vascularization, and pigmentary migration. Photograph: Reproduced with permission from Spalton DJ, Hitchings RA, Hunter PA. *Atlas of Clinical Ophthalmology.* Philadelphia, Pa: JB Lippincott; 1984: Figure 4.53.

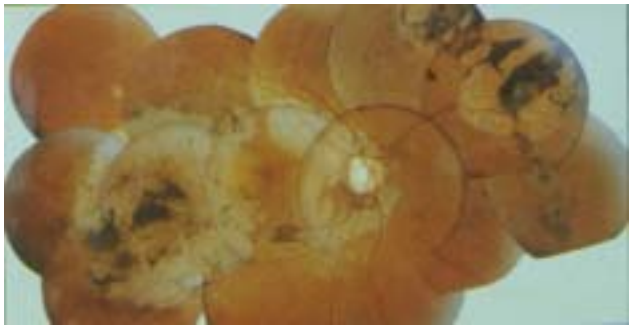

Fig. 27-5. Onchocerciasis chorioretinitis. Focal or diffuse chorioretinitis can occur, leading to a significant loss of vision. Additional findings in the posterior segment can include hemorrhage, choroidal granuloma, retinal edema, and optic atrophy.

continue in the form of advancing corneal opacification. Sclerosing keratitis is more commonly associated with regions receiving high amounts of sunlight. Microfilariae may be seen within the anterior chamber with or without an associated inflammatory component. When inflammation is present, it usually manifests as a granulomatous uveitis, which can be further complicated by secondary glaucoma and cataract.

Another leading cause of onchocercal blindness is *chorioretinitis* (Figure 27-5). The pathogenesis of the chorioretinitis is uncertain, although various mechanisms have been proposed. Such postulations include local inflammatory reaction occurring secondary to microfilariae, autoimmune response, and destruction of the retinal pigment epithelium. Clinically, retinal pigment epithelial atrophy, chorioretinal atrophy, and subretinal fibrosis can be seen. Histopathological examination has demonstrated a chronic nongranulomatous chorioretinitis with infiltration by lymphocytes, plasma cells, and eosinophils. There is a secondary degenerative change in the overlying choriocapillaris, retinal pigment epithelium, and neuroretina. Additional posterior segment findings include retinal edema, intraretinal deposits, hemorrhages, cotton wool spots, and choroidal granulomas. Patients may also present with an optic neuritis or optic atrophy; however, these findings are more common in patients who have been treated with DEC or suramin sodium.

Dermatological manifestations of onchocerciasis may also be noted by the ophthalmologist. One of the most common complaints is itching, which can be so severe that patients scratch themselves to the point of skin breakdown and develop a secondary bacterial infection. Pigmentary changes are frequently seen and produce what is known as the "leopard skin" appearance. There may be dermal scarring with loss of elasticity, and atrophy of the overlying epidermis gives the appearance of being prematurely aged. *Sowdah*, a reactive onchodermatitis, is an enhanced cell-mediated and humoral immune response. Histopathological examination shows dermal invasion with plasma cells, edema, and fibrosis. A final manifestation is an asymptomatic skin nodule (Figure 27-6). These nodules are usually located near the pelvis or joints and are firm, round masses at the dermis or deep fascial planes.

Onchocerciasis can be diagnosed in several ways. The most common is the skin-snip test. On average, six sites are biopsied (epidermis and dermis), incubated within tissue culture medium, and then examined for microfilariae. Microfilariae may also be observed within the anterior chamber of the eye and in various body fluids including urine, sputum, vaginal secretions, cerebrospinal fluid, and blood. Another diagnostic modality involves excising nodules and looking for adult worms.

Fig. 27-6. Onchocerciasis skin nodule. The adult worm (*Onchocerca volvulus*) lives in subcutaneous nodules usually near the pelvis or joints. Reproduced with permission from Spalton DJ, Hitchings RA, Hunter PA. *Atlas of Clinical Ophthalmology.* Philadelphia, Pa: JB Lippincott; 1984: Figure 4.50.

Management

The treatment of onchocerciasis is aimed at prevention but also includes the medical management of active disease. Disease prevention needs to be geared toward preventing insect bites by avoiding breeding sites near the hours of dusk and dawn, when black fly activity is greatest. Protective clothing and insect repellents also decrease the chance of insect bites. The Onchocerciasis Control Programme[15] is focusing on vector control by spraying breeding grounds with larvicidal agents to kill the offending organism during its larval stage. This large-scale endeavor has numerous complicating factors, including expense; changes in water flow; and poorly accessible breeding grounds, which makes effective spraying difficult.

Medical management now consists of the use of ivermectin,[16–18] an agonist for the neurotransmitter γ-aminobutyric acid (GABA). Ivermectin produces a spastic paralysis of the microfilariae. This drug is associated with less-severe Mazzotti reactions than is DEC. Patients receiving ivermectin require long-term treatment at a dose of 150 μg/kg/y. It is not known, however, how many years of treatment are required. Treatment with ivermectin produces fewer side effects, compared with suramin or DEC. The latter two agents, which had been the mainstay of therapy until ivermectin became available, are now reserved for high-risk individuals facing severe infection or impending blindness. The inflammatory reaction caused by the death of the microfilariae is intense, and use of the drugs may further be complicated by optic nerve disease, which can further compromise vision.

NUTRITIONAL BLINDNESS

An aspect of ophthalmology that we are less familiar with in the developed world is nutritional blindness, most of which is caused by vitamin A deficiency.[19] In the Third World, the deficiency is most commonly associated with an inadequate dietary intake. However, other causes—all of which are associated with impaired vitamin A absorption—include lack of dietary lipids, impaired secretions of digestive enzymes, gastroenteritis, celiac sprue, and protein deficiencies. Vitamin A stores can also be depleted during febrile illnesses such as measles, severe gastroenteritis, and bronchopneumonia. The disease is seen in Asia, the Caribbean, and Central and South America, and frequently affects pregnant women and children younger than 6 years of age. Women are susceptible because of the number and frequency of their pregnancies and their suboptimal diet. Various theories have evolved regarding the high risk in the child subpopulation[2,20–22]:

- Children born to vitamin A–deficient mothers receive very little vitamin A in breast milk.
- Rapid growth during childhood creates a high demand on vitamin A stores.
- Children are fed sweetened condensed milk, which is deficient in both vitamin A and protein.
- Cultural beliefs teach the withholding of food from seriously ill children, which further exacerbates the problem.

Clinical Course

Vitamin A deficiency may manifest with numerous systemic findings, leading to a high incidence of systemic morbidity and mortality.[21] Such systemic findings include respiratory disease, diarrhea, anemia, and growth retardation.

Ocular manifestations involve mainly the conjunctiva and cornea, but posterior segment manifestations have also been documented (Table 27-2).[20,23] The earliest manifestation may be night blindness. The vitamin A–deficient state causes an alteration of dark-adapted (ie, scotopic) vision. If vitamin A therapy is instituted, then vision, specifically night vision, improves within 24 to 48 hours.

Patients with conjunctival xerosis present with patchy, granular areas of dryness that are unable to

TABLE 27-2

WORLD HEALTH ORGANIZATION CLASSIFICATION OF XEROPHTHALMIA

Abbreviation	Classification of Xerophthalmia
XN	Night blindness
X1A	Conjunctival xerosis
X1B	Bitot's spots
X2	Corneal xerosis
X3A	Corneal ulceration xerosis involving <1/3 corneal surface
X3B	Corneal ulceration xerosis involving >1/3 corneal surface
X5	Corneal scar
XF	Xerophthalmic fundus

Source: Steinkuller PG. Nutritional blindness in Africa. *Soc Sci Med.* 1983;17:1715–1721.

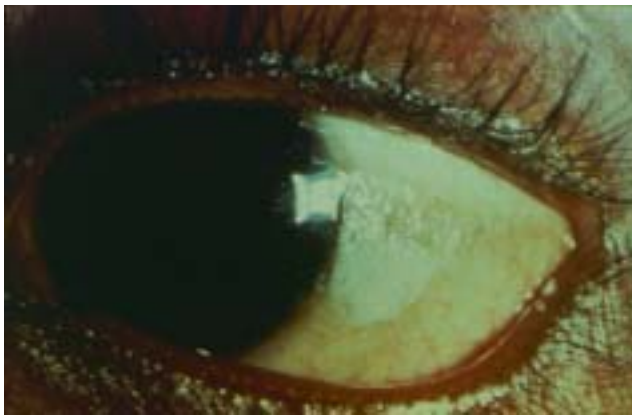

Fig. 27-7. Bitot's spots are small, white, cheeselike patches that have a foamy appearance and do not wet easily. This finding is often associated with a punctate keratopathy. Reproduced with permission from Spalton DJ, Hitchings RA, Hunter PA. *Atlas of Clinical Ophthalmology.* Philadelphia, Pa: JB Lippincott; 1984: Figure 5.42.

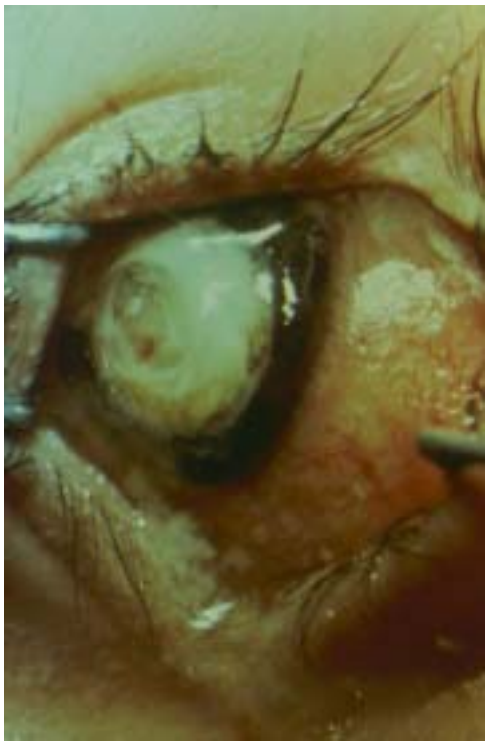

Fig. 27-8. Advanced keratomalacia associated with vitamin A–deficient xerosis can cause the entire cornea to become opacified and can also be complicated by secondary infection, perforation, and endophthalmitis. Reproduced with permission from Spalton DJ, Hitchings RA, Hunter PA. *Atlas of Clinical Ophthalmology*. Philadelphia, Pa: JB Lippincott; 1984: Figure 5.44.

be wetted. These patches are almost always seen temporally; when they are found nasally, they usually suggest vitamin A deficiency. If there is more than 180° of conjunctival xerosis, the conjunctivae take on a thickened appearance, appearing more prominent with circumferential folds. Bitot's spots are foamy, cheesy aggregations of desquamated keratin and saprophytic bacilli (Figure 27-7). They overlie areas of xerosis and will remain even after adequate vitamin A therapy.

The earliest corneal manifestation of vitamin A deficiency is xerosis, and this may present in the pattern of superficial punctate keratitis. Although the quadrant most commonly involved is the inferonasal, xerosis can be progressive with larger areas of involvement, commonly involving the interpalpebral zone. There may be stromal edema as well as keratinization. Xerosis tends to respond to vitamin A therapy. Vitamin A deficiency can also lead to xerophthalmic ulcers, which are small, sharply demarcated, punched-out lesions. The ulcers may be partial or full thickness and are most commonly found nasally and peripherally. They may advance and become complicated by secondary bacterial infection and stromal destruction and keratomalacia (Figure 27-8).

The posterior segment findings manifest as small, white blisters, appearing as intraretinal dots. These are more commonly found in the periphery and respond to vitamin A therapy.

Diagnosis

Vitamin A deficiency can be diagnosed in various ways, although these modalities may not be available in underdeveloped countries. Serum vitamin A levels may be determined with high-pressure liquid chromatography. A vitamin A level higher than 20 μg/dL is considered adequate. A second test is the determination of the level of total retinal binding protein (RBP) via an immunoassay for circulating RBP. A relative dose response may also be done; this records the changes in serum vitamin A–RBP after an oral or intravenous vitamin A test dose is administered. Lastly, conjunctival impression cytology may be evaluated. With this method, the specialist looks for evidence of squamous metaplasia, loss of goblet cells, irregularly shaped cells, enlarged cells, and keratinized epithelial cells.

Management

With nutritional blindness, the treatment goal is

to replenish vitamin A stores.[24] The patient may be administered oral vitamin A in an oil- or water-miscible form. If ocular disease does occur, the goal is to prevent blinding complications: protect the eye against secondary bacterial infection, and protect the globe when the structural integrity has been disrupted.

Prevention, once again, is an important aspect of the management of nutritional blindness (Table 27-3). The populations at risk should be identified, and treatment should begin with periodic administration of vitamin A. Within the at-risk population, the overall absorptive ability of the patient must be considered, and the patient should accordingly be dosed with vitamin A. Educational programs have been developed but as yet have not been shown to be very effective.

TABLE 27-3

WORLD HEALTH ORGANIZATION RECOMMENDATIONS FOR VITAMIN A PROPHYLAXIS

Population	Dose and Frequency
Pregnant and lactating women	20,000 IU/wk or 5,000 IU/d
Newborns	50,000 IU at birth
Children < 1 y old	100,000 IU every 4–6 mo
Children > 1 y old	200,000 IU every 4–6 mo

IU: international unit
Source: Steinkuller PG. Nutritional blindness in Africa. *Soc Sci Med*. 1983;17:1715–1721.

HANSEN'S DISEASE

Hansen's disease (leprosy) is a chronic granulomatous inflammation caused by *Mycobacterium leprae*. Worldwide, there are approximately 10 million to 12 million ocular cases, but only about half of these cases are registered.[2] Hansen's disease may be more widespread than some of the other ophthalmic diseases that have been discussed in this chapter. Areas in which ocular leprosy occurs include tropical climates, North and South Korea, Argentina, central Mexico, central Africa, the Middle East, Southeast Asia, India, and Indonesia.

Classification

Various classification schemes have been developed with a variable degree of overlap. The primary forms of disease are tuberculoid, lepromatous, borderline, and intermediate. In the tuberculoid pattern, the clinical findings may resemble those of tuberculosis. Lesions tend to be well demarcated, hypopigmented, and hypoesthetic. The histopathological findings include epithelioid cells, giant cells, and lymphocytes—findings that are commonly seen in specimens obtained from tuberculosis patients.

Multiple diffuse, less-well-defined lesions characterize the lepromatous form. The dermatological manifestations are heralded by thickening of the skin, producing leonine facies. The lepromatous form of Hansen's disease has more systemic involvement, compared with the tuberculoid form, and is also associated with a cell-mediated immune defect. Histopathological examination reveals numerous intracellular and extracellular acid-fast bacilli, lipid-laden macrophages, and histiocytes.

The borderline and intermediate categories of Hansen's disease represent mixes of the tuberculoid and lepromatous forms and will not be discussed further.

Ocular Leprosy

The ocular manifestations of Hansen's disease can involve any portion of the eye, but most findings are related to the periorbital skin region and the anterior segment. The orbicularis may be involved, particularly the pretarsal fibers, producing dermatochalasis. Similarly, there may be eyebrow loss with subsequent ptosis that typically begins temporally and may progress nasally. Atrophic changes involving the canthal tendons, the tarsal plates, or both can cause ectropion or entropion, which may further be complicated by trichiasis. In this population, tear dysfunction may develop secondary to infiltration of the meibomian glands, resulting in inadequate lipid production. The lacrimal gland may also be involved, producing dry eyes. Lacrimal gland involvement can be further complicated by recurrent dacryocystitis. Various eyelid nodules have also been reported[2] to occur.

Hansen's disease may also cause polyneuropathy. Involvement of the seventh cranial nerve typically results in lagophthalmos and ectropion, potentially compromising the ocular surface. Fifth cranial nerve involvement results in an anesthetic cornea, which, when combined with a seventh nerve palsy, greatly increases the chance that a corneal ulcer will develop.

Multiple corneal findings have been reported.[2] Individuals with these findings are at high risk for developing an exposure keratitis, particularly when there is an associated fifth and seventh cranial nerve palsy. The keratitis may subsequently become complicated by corneal ulcer, globe perforation, phthisis, and, ultimately, blindness. Affected individuals may develop an avascular or a punctate keratitis, or both, which typically begins in the superior temporal quadrant as well-defined, chalky white opacities. In time, the lesions become less-well-defined, resulting in a confluent haze with later development of a neovascular pannus.

Histopathologically, the corneal lesions represent miliary lepromas and demonstrate macrophages, lymphocytes, *M leprae* organisms, calcium deposition, and destruction of Bowman's membrane. The avascular or punctate keratitis, or both, may also be associated with an interstitial keratitis.

Ocular leprosy is one of the conditions that is associated with prominent or enlarged corneal nerves. They appear as focal beadlike swellings but are accumulations of *M leprae*. Within the Asian population, corneal lepromas may be identified. They occur more commonly at the limbus and may extend onto the cornea.

A principal cause for blindness in Hansen's disease is uveitis. The patients tend to have a chronic, low-grade uveitis in which they present with a very quiet-appearing eye. Clinically, it may be possible to identify corneal keratic precipitates, iris stromal atrophy with a moth-eaten appearance (which can progress to iris holes), hypopyon, synechiae, hyphema, elevated intraocular pressure, and small, poorly reactive pupils. The uveitis is believed to represent an antigen-antibody–mediated hypersensitivity reaction. Interestingly, this hypersensitivity may arise as a response to treatment. Iris pearls may also be identified near the papillary border. These may migrate posteriorly, producing what have been called[2] "retinal pearls."

Patients with Hansen's disease may also present with evidence of scleral inflammation. This inflammation may manifest as an episcleritis or a scleritis, which may be further subdivided into nodular and diffuse. The etiology for this inflammation is not certain. It could represent direct invasion of *M leprae*. It could be an immune-complex-mediated process, similar to the uveitis previously discussed. Scleral inflammation may be complicated by scleromalacia, staphyloma, and globe disorganization, all of which may compromise visual function. Rare posterior segment findings have been reported[2] and include uveal effusions, choroiditis, and retinal pearls.

Management

The management of Hansen's disease must focus on prevention as well as treatment of the active disease, as was also the case with onchocerciasis and vitamin A–deficiency blindness, above. Research into a vaccine is currently in progress. The treatment of active disease can be divided into medical and surgical approaches. For years, dapsone had been the treatment of choice. However, resistance to dapsone has been developing, and the treatment is beginning to incorporate other agents used in conjunction with dapsone. The other agents include rifampin, clofazimine, ofloxacin, and minocycline. Clofazimine, however, is very costly and can cause hyperpigmentary changes of the skin.

WHO's treatment recommendations divide patient groups into multibacillary and paucibacillary leprosy. The paucibacillary group is further divided into single or multiple skin lesion subtypes. In multibacillary leprosy, the medical treatment is for 12 months and consists of rifampin, dapsone, and clofazimine. Paucibacillary patients with multiple skin lesions are treated with rifampin and dapsone for 6 months. The final subtype, paucibacillary with a single skin lesion, is treated with a single dose of rifampin, ofloxacin, and minocycline.

From a surgical standpoint, eyelid deformities need to be corrected in an effort to protect the cornea. A peripheral iridectomy may be useful in patients who present with angle closure glaucoma. A sector iridectomy may be useful in patients with small pupils; it will result in a larger pupil, which may improve the patient's visual function. Patients with small pupils tend to develop cataracts at an earlier age and, therefore, require surgical correction to improve their vision.

SUMMARY

Although the ocular diseases associated with blindness and visual impairment are too numerous—and the geographical distribution of ocular disease too extensive—to be reviewed in a single chapter, a brief overview of the leading causes of preventable blindness worldwide has been presented. Military medical personnel may encounter these conditions while on deployments or in a theater of operations.

WHO has been instrumental in promoting awareness of Third World ophthalmology. This organiza-

tion has been able to recruit many other organizations to work toward the goal of reducing the incidence of worldwide blindness, with the goal of reducing blindness prevalence globally to less than 0.5% and in any country to less than 1%.

Because we military ophthalmologists are not part of the ophthalmic community in Third World locations, we can easily remain ignorant of global issues that need to be addressed. Industrialized nations have tremendous resources that can help troubled and underdeveloped countries, however, including developing medications and vaccinations. Military ophthalmologists might also consider humanitarian missions that offer opportunities for engaging in ophthalmological care in the developing world.

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