Corneal blindness: a global perspective
John P. Whitcher,¹ M. Srinivasan,² & Madan P. Upadhyay³

Diseases affecting the cornea are a major cause of blindness worldwide, second only to cataract in overall importance. The epidemiology of corneal blindness is complicated and encompasses a wide variety of infectious and inflammatory eye diseases that cause corneal scarring, which ultimately leads to functional blindness. In addition, the prevalence of corneal disease varies from country to country and even from one population to another. While cataract is responsible for nearly 20 million of the 45 million blind people in the world, the next major cause is trachoma which blinds 4.9 million individuals, mainly as a result of corneal scarring and vascularization. Ocular trauma and corneal ulceration are significant causes of corneal blindness that are often underreported but may be responsible for 1.5–2.0 million new cases of monocular blindness every year. Causes of childhood blindness (about 1.5 million worldwide with 5 million visually disabled) include xerophthalmia (350,000 cases annually), ophthalmia neonatorum, and less frequently seen ocular diseases such as herpes simplex virus infections and vernal keratoconjunctivitis.

Even though the control of onchocerciasis and leprosy are public health success stories, these diseases are still significant causes of blindness — affecting a quarter of a million individuals each. Traditional eye medicines have also been implicated as a major risk factor in the current epidemic of corneal ulceration in developing countries. Because of the difficulty of treating corneal blindness once it has occurred, public health prevention programmes are the most cost-effective means of decreasing the global burden of corneal blindness.

Keywords: Corneal diseases/epidemiology; Blindness/etiology; Eye injuries/epidemiology; Ocular/prevention and control; Trachoma/drug therapy; Onchocerciasis; Leprosy/prevention and control (source: MeSH).

Mots clés: Kératopathie/épidémiologie; Cécité/étiologie; Traumatisme oculaire/épidémiologie; oculaire/prévention et contrôle; Trachome/chimiothérapie; Onchocercose; Lèpre/prévention et contrôle (source: INSERM).

Palabras clave: Enfermedades de la córnea/epidemiología; Ceguera/etiología; Traumatismos oculares/epidemiología; Ocular/prevenición y control; Tracoma/quimioterapia; Oncocerciasis Lepra/prevencción y control (fuente: BIREME).


Introduction

Using the World Health Organization (WHO) definition of blindness as a visual acuity of 3/60 or less (1), it is estimated that currently there are 45 million individuals worldwide who are bilaterally blind and another 135 million who have severely impaired vision in both eyes (2). The fact that there are 180 million people in the world today who are in some way severely visually disabled is a tragic, unacceptable situation in both social and economic terms, but this number does not even begin to address the additional hundreds of millions who are disabled by monocular visual loss. In recent years the epidemiology of blindness has changed, shifting away from traditional infectious causes, such as trachoma, onchocerciasis, and leprosy, to other important causes, such as cataract (3). Indeed, so much emphasis has been placed on managing the backlog of cataract surgery in many developing countries that programmes dealing with other causes of blindness have in some cases been neglected (4).

The importance of corneal disease as a major cause of blindness in the world today remains second only to cataract, but its epidemiology is complicated and encompasses a wide variety of infectious and inflammatory eye diseases. In addition, the prevalence of corneal blindness varies from country to country and even from one population to another, depending on many factors, such as availability and general standards of eye care (3). For instance, corneal disease, especially corneal ulceration, is in many regions of Africa the most common cause of monocular
Review: corneal blindness

Specific causes of corneal blindness

Trachoma

At present trachoma is still the world’s leading infectious cause of blindness and the leading cause of ocular morbidity (11). It is estimated by WHO that at present there are 146 million people worldwide with trachoma: 10 million suffer from trichiasis and need surgery to prevent corneal blindness from developing, and another 4.9 million are totally blind from trachomatous corneal scarring (2, 12). Trachoma, therefore, remains the leading cause of preventable blindness in the world today (see Frick et al. in this issue, pp. 201–207). The emphasis on prevention is essential because the outcome of penetrating keratoplasty in trachoma patients is often disappointing due to extensive corneal vascularization, ocular surface problems, and the invariable presence of entropion and trichiasis (13). To make matters worse, eye-bank facilities, modern operating rooms and equipment, and adequately trained surgeons and nurses are rare in areas where severe trachoma is endemic. It is essential, therefore, to prevent corneal blindness from occurring by instituting trachoma prevention programmes in areas where the disease is endemic.

Trachoma is one of the oldest recorded diseases of mankind. First described in the Egyptian Eber’s papyrus in 1900 BC, it was the major cause of blindness worldwide until the twentieth century. Until the advent of sulfonamides in the late 1930s, the treatment of choice for trachoma was still copper sulfate scarification of the conjunctiva — identical to the treatment described by the ancient Egyptians. Trachoma has always been associated with poverty, poor sanitation, and low socioeconomic status. The infection is transmitted from eye to eye by contaminated fingers, clothes, eye make-up, flies, and aerosolized nasopharyngeal secretions (14). For transmission to become commonplace, however, certain environmental conditions must also be present. Numerous studies have demonstrated that limited access to water supplies, low water consumption by the household, the presence of flies, and poor hygiene — especially with regard to facial cleanliness — are all risk factors for becoming infected with Chlamydia trachomatis (15). In a recent study in Nepal, it was found that villages without tube wells had a higher prevalence of trachoma, but lower rates of infection were seen in families who lived in cement houses with fewer people per room, and had more servants, more household goods, more animals, and more land (16). In south-western Ethiopia, where 24.5% of the population was shown to have clinically active trachoma, Zerihun found that both active and cicatricial trachoma were significantly associated with females; living in rural areas; having illiterate parents; and not having a latrine (17). The fact that females seem to be especially at risk has been confirmed by studies in Kenya (18) and the United Republic of Tanzania (19). Whether this is because they have a lower status in their society or spend more time with young children — who are the main source of clinically active infection — has not been clearly delineated. It is clear, however, that individuals who are marginalized, impoverished, and at the bottom socioeconomic level of society are most likely to have the disease. As general conditions improve, the prevalence of trachoma...
ma declines. For example, Dolin et al. found that from 1986 to 1996 the prevalence of blindness resulting from trachomatous corneal opacities in a study population in the Gambia fell from 0.10% to 0.02%, a relative decline of 80% (20). At the same time the prevalence of clinically active trachoma decreased by 54%. During this 10-year period primary health care services expanded, access to water increased, and sanitation improved, and there was a general improvement in the public health infrastructure, all in spite of a rapid growth in population.

Recent studies from the Gambia (21), Saudi Arabia (22), and Egypt (23) have demonstrated that a single dose (20 mg/kg) of azithromycin is effective in eradicating Chlamydia trachomatis from more than 70% of an infected population. Schachter et al. have shown that multiple doses of the antibiotic (once a week for three weeks) may be even more effective for treating communities (24). Lietman has developed a mathematical model using epidemiological data from a variety of countries which suggests that a much more cost-effective method of eradicating trachoma would be to treat populations based on the prevalence of the disease: prevalence less than 35% in children should be treated annually; more than 50% prevalence in children should be treated biannually (25). This innovative approach has called into question the recommendation for empirical mass drug administration in endemic trachoma areas — a goal of the WHO Alliance for the Global Elimination of Trachoma by the year 2020. Studies carried out by Baral et al. in Nepal have shown that an intensive trachoma control effort is unnecessary when the prevalence of clinically active disease falls below 10% in children (26).

In spite of the efficacy of azithromycin as a treatment for clinically active cases of trachoma, more than antibiotic treatment is needed to prevent the progression to corneal blindness of those previously infected individuals. To meet this challenge, WHO has developed an integrated plan of attack on trachomatous blindness — the SAFE strategy. This approach includes Surgery for trichiasis, Antibiotic treatment of clinically active chlamydial infection, the promotion of Facial cleanliness, and the improvement of Environmental conditions (27). Antibiotic treatment is but one of the four critical components in the SAFE strategy. Ultimately, to eliminate trachoma, as well as blindness resulting from the disease, each of the four components must be successfully implemented (11). The cost-effectiveness of an approach that incorporates multiple strategies has been documented by Evans et al. in Burma (28). Thirty years of trachoma control, promoting both surgical and non-surgical programmes, has led to a remarkable decline in trachomatous corneal blindness.

**Ocular trauma and corneal ulceration**

Until recently, ocular trauma and corneal ulceration were not considered as important causes of corneal blindness. Both trauma and ulceration are usually monocular and affected individuals are, therefore, not characterized as totally blind but only as visually disabled. However, as public health programmes have become more effective in reducing the prevalence of traditional causes of corneal blindness, such as trachoma, onchocerciasis, and leprosy, so ocular trauma and corneal ulceration have become relatively more important. In 1992, Thylefors drew attention to the fact that trauma is often the most important cause of unilateral loss of vision in developing countries and that up to 5% of all bilateral blindness is a direct result of trauma (29). The implication is that well over half a million people in the world are blind as a result of eye injuries (30). A careful analysis of the world literature by Negrel & Thylefors in 1998 brought to light a global epidemic of ocular trauma with some 55 million eye injuries occurring annually, of which 750,000 cases required hospitalization and 200,000 were open-globe injuries (31). They further estimated that approximately 1.6 million people were blind from their injuries, 2.3 million had bilateral low vision, and 19 million were unilaterally blind or had low vision.

Even though ocular trauma is a global problem, the burden of blindness from eye injuries falls most heavily on developing countries, especially those where war and civic unrest have left a legacy of eye trauma from weapons such as land mines (32). A country-wide population-based survey in Nepal — a country with a peaceful history — reported that trauma was responsible for 7.7% of all monocular blindness (33). A more recent population-based prospective study in Bhaktapur District in Kathmandu valley, Nepal, revealed that the annual incidence of ocular injury is 1788 per 100,000 people, with 789 of the injuries due to corneal abrasions (34). In other words, 1.8% of the residents of Bhaktapur District experience some form of ocular injury every year. In Nepal and other developing countries, injuries are usually associated with agricultural work, but a much higher rate of ocular trauma can occur in specialized situations, such as foundries: an 11% eye-injury rate was reported in foundry workers in Saudi Arabia (35).

Corneal ulceration in developing countries has only recently been recognized as a “silent epidemic” (36). Gonzales et al. found that the annual incidence of corneal ulceration in Madurai District in South India was 113 per 100,000 people (37) — 10 times the annual incidence of 11 per 100,000 reported from Olmsted County, Minnesota, in the United States of America (38). By applying the 1993 corneal ulcer incidence rate in Madurai District to all of India, there are an estimated 840,000 people a year in the country who develop an ulcer. This figure is 30 times the number of corneal ulcers seen in the United States (37). Extrapolating the Indian estimates further to the rest of Africa and Asia, the number of corneal ulcers occurring annually in the developing world quickly approaches 1.5–2 million, and the actual number is probably greater. Invariably corneal blindness is the end result in the majority of these infections, or the
Childhood corneal blindness
Currently, it is estimated that there are about 1.5 million blind children in the world, of whom one million live in Asia (41). Each year there are half a million new cases, 70% of which are due to vitamin A deficiency which leads to xerophthalmia (42). The burden of childhood blindness globally is staggering. It is estimated that a child goes blind somewhere in the world every minute.

Xerophthalmia. Xerophthalmia, caused by vitamin A deficiency, is still the leading cause of childhood blindness. Of the approximately 1.5 million children blind and 5 million visually disabled worldwide, 350,000 are blinded every year as a result of vitamin A deficiency. The subsequent high mortality in these children, initially documented by Sommer et al. (43), explains the relatively low prevalence of xerophthalmia in developing countries in spite of its high incidence. In other words, the majority of children who have vitamin A deficiency severe enough to cause the bilateral corneal melting, perforation, and blindness associated with xerophthalmia, die within the first year. An even more tragic aspect of xerophthalmia is its close association with measles epidemics. Malnourished children who are on the edge of developing xerophthalmia frequently do so after contracting measles from a sibling or a classmate (44). Prevention programmes, therefore, must include widespread immunizations, the regular distribution of high-dose vitamin A capsules to children at risk, nutritional education for families, and dietary fortification for populations with poor nutrition. The populations that are most affected are often the poorest of the poor, living in areas where other diseases such as trachoma and onchocerciasis are epidemic and public health programmes are overwhelmed by the diversity of diseases causing corneal blindness.

Ophthalmia neonatorum. Ophthalmia neonatorum, or conjunctivitis of the newborn, refers to any conjunctivitis with discharge that occurs in the first 28 days of life (45). If the infection is caused by Neisseria gonorrhoeae the risk of blindness is high, especially since ocular gonorrhoea in the newborn is frequently bilateral. If the infection is caused by C. trachomatis or other less virulent pathogens, the risk of blindness is low. In the past century there has been a significant change in the spectrum of organisms causing ophthalmia neonatorum as the incidence of chlamydial infections has risen dramatically in relation to gonorrhoeal infections, especially in industrialized countries (46). In developing countries the prevalence of chlamydial infection in pregnant women ranges from 7 to 29% (47). One-third of infants exposed at birth will develop a chlamydial infection. Similar studies of gonorrhoeal infection in Africa indicate a maternal infection prevalence of 3–22%, with gonorrhoeal ophthalmia developing in 30–50% of exposed neonates (47). Laga et al. reported gonorrhoeal ophthalmia in 3 to 4% of live births in Nairobi, Kenya (48). Although the worldwide incidence of ophthalmia neonatorum is not known, it represents a significant cause of childhood corneal blindness, especially in developing countries.

Efforts to decrease the incidence of ophthalmia neonatorum include prevention of sexually transmitted diseases in adults, antenatal screening of pregnant women, ocular prophylaxis at birth (see Schaller & Klauss in this issue, pp. 262–263), and early diagnosis and treatment of ocular infections in

neonates. Studies have shown that a 2.5% solution of aqueous povidone-iodine applied to the eyes of neonates is just as effective and cheaper than erythromycin ointment or 1% silver nitrate (Credé’s prophylaxis) in preventing the majority of cases of chlamydial and gonorrhoeal ophthalmia neonatorum (49). Tetracycline ointment may also be used. If prophylaxis fails, a single intramuscular injection of cefataxime (100 mg/kg) is effective against gonorrhoea in the newborn, and a two-week course of erythromycin orally (50 mg/kg daily in four divided doses) is recommended for the treatment of chlamydia.

Other causes of childhood corneal blindness. Even though herpes simplex virus (HSV) infections are rare in the newborn, they should be considered as a potential cause of ophthalmia neonatorum. HSV infections may also play a significant role in complicated cases of xerophthalmia. It is known that dendritic keratitis frequently occurs in conjunction with febrile episodes such as those that occur in measles (50). Infections with HSV should be considered in any unusual corneal infection occurring in childhood, especially if the corneal sensation is diminished or absent.

Tabbara has reported visual loss among children with severe vernal keratoconjunctivitis in Saudi Arabia (51). Visual loss occurs secondary to corneal complications including corneal scarring, astigmatism and keraatoconus, as well as from complications of the unsupervised use of topical corticosteroids. Tabbara emphasizes that vernal keratoconjunctivitis in developing countries is a potentially serious cause of childhood blindness.

Chemical keratitis is also a rare but disastrous cause of blindness in children. For instance, in South India where lime is sold on the streets in small plastic packets to be taken with betel nut, the residual powder is occasionally blown into the eyes of children who play with the discarded bags. The prognosis in such cases is invariably poor. Exposure to chemicals and caustic agents in the household as well as in the environment also places the unsupervised child at potential risk from injuries leading to blindness.

Traditional eye medicines
The use of traditional eye medicines (TEM) is an important risk factor for corneal blindness in many developing countries. Chirambo & Ben Ezra reported that 26% of childhood blindness in Malawi was associated with the use of TEM (52), and Yorston & Forster in a one-year prospective study in the United Republic of Tanzania showed that 25% of corneal ulcers were associated with TEM use (53). The main problem is that traditional medicines are often contaminated and provide a vehicle for the spread of pathogenic organisms. Lewallen & Courtright interviewed traditional healers in Malawi and found that most TEM consisted of dried plant material crushed into a powder and dissolved in an non-sterile aqueous medium (6). Such medications, as well as those using animal or human products such as urine, saliva, or breast milk, offer excellent opportunities for introducing pathogenic organisms into eyes already compromised by injury or infection. The use of TEM is a public health problem that exists throughout the developing world. Educating traditional healers and eliciting their cooperation in directing patients to appropriate health care facilities is a first step in preventing complications leading to blindness from the use of traditional medicines.

Public health success stories
Onchocerciasis
Although onchocerciasis (river blindness) is currently a major cause of blindness in the world, eradication of the disease is a modern public health triumph. There are still 18 million people infected with *Onchocerca volvulus*, the parasite that causes the disease — over 95% of them in Central Africa and the rest in Central America. Of this 18 million, 6.5 million have severe skin disease and 270,000 are blind. In a recent survey by Schwartz et al. in the Central African Republic, onchocerciasis was found to be responsible for 73.1% of all blindness in the population (10). Even though *O. volvulus* causes destructive chorioretinitis it also produces severe blinding keratitis that develops as the result of an inflammatory response to dead and degenerating microfilaria in the corneal stroma. The end result is severe corneal scarring and vascularization (54).

Until 15 years ago the outlook for eradicating onchocerciasis was dismal. Public health projects that focused on reducing the habitat of the vector of the parasite, a small black fly that breeds in fresh-water streams and rivers, were frustratingly ineffective and destructive to the environment. The development of ivermectin in the 1980s and its widespread distribution since 1987 has led to a remarkable decrease in number of new cases of onchocerciasis in endemic areas. Ivermectin not only kills microfilaria, it also sterilizes the adult worms in infected individuals, producing a dramatic decline in the overall numbers of microfilaria in a treated population. With the administration of one tablet of ivermectin twice a year to all individuals in endemic areas, it is estimated that there will be no new cases of onchocerciasis by the year 2020.

Leprosy
There has been remarkable progress in the treatment of leprosy in the past 20 years, but corneal complications from the disease still remain a significant cause of blindness worldwide. Leprosy affects 10–12 million people, the majority of whom are in Africa and the southern portion of the Indian subcontinent (55), and there are approximately 250,000 blind from the disease.
Infections with *Mycobacterium leprae* rarely affect the posterior portion of the eye; the organism proliferates in the cooler parts of the body (the skin, extremities, face, and anterior segment of the eye), as well as in the nerves. Most of the complications leading to blindness are due to chronic uveitis and associated cataract formation, or are secondary to the development of lagophthalmos (facial motor-nerve palsies) associated with the loss of corneal sensation. Patients develop exposure keratitis, repeated corneal ulcers, and eventually corneal scarring and vascularization. Interstitial keratitis may also occur as a result of direct corneal infiltration by *M. leprae*.

Today the prevalence of leprosy is rapidly declining in most countries around the world as a direct result of widespread public health efforts, especially the administration of multidrug therapy (MDT), a combination of rifampin, dapsone, and clofazimine. The introduction of MDT by the World Health Organization in 1982 for the treatment of multibacillary leprosy has led to a shortened treatment time of two years and a high degree of bacteriological cure (99.9%). It is felt that the administration of MDT for two years in almost all cases is adequate for producing a complete bacteriological cure of the disease and for preventing the emergence of drug-resistant strains of the organism (36). Even as leprosy patients are cured bacteriologically, related ocular complications must be treated on an individual basis. With the success of MDT, however, there is now hope that the disease will be eradicated worldwide within the next few decades and the ravages of leprosy will be consigned to history.

**Résumé**

*Cécité cornéenne : tableau mondial*

Les maladies affectant la cornée sont partout une cause majeure de cécité, et ne le cèdent qu’à la cataracte quant à leur importance mondiale. L’épidémiologie de la cécité cornéenne est complexe et recouvre une gamme étendue de maladies oculaires infectieuses et inflammatoires à l’origine des cicatrices cornéennes qui conduisent à la cécité fonctionnelle. De plus, la prévalence des affections cornéennes varie d’un pays à un autre. Alors que la cataracte est responsable de près de 20 millions de cas de cécité sur les 45 millions que l’on compte dans le monde, le trachome vient ensuite avec 4,9 millions de cas de cécité essentiellement dus aux cicatrices et à la vascularisation cornéennes. Les traumatismes oculaires et les ulcérations de la cornée sont des causes importantes de cécité cornéenne qui sont souvent sous-diagnostiquées mais qui peuvent être à l’origine de 1,5 à 2,0 millions de nouveaux cas de cécité unilatérale chaque année. Parmi les causes de cécité de l’enfant (environ 1,5 million de cas dans le monde et 5 millions d’enfants atteints de déficience visuelle) figurent la xéroitalmie (350 000 cas par an), la conjonctivite gonococcique du nouveau-né, et des affections oculaires plus rares comme les infections herpétiques et la kératoconjunctivite printanière.

Même si les opérations de lutte contre l’onchocercose et contre la lèpre ont été largement couronnées de succès, ces maladies sont encore des causes importantes de cécité puisqu’elles touchent chacune environ 250 000 personnes. Les remèdes oculaires traditionnels jouent eux aussi un rôle majeur dans l’épidémie d’ulcérations cornéennes actuellement observée dans les pays en développement. Etant donné la difficulté de traiter la cécité cornéenne une fois installée, les programmes de prévention sont les moyens disposant du meilleur rapport coût-efficacité pour réduire la charge mondiale de cécité cornéenne.

**Discussion**

Eye diseases affecting the cornea are a major cause of blindness worldwide. In some areas of Africa as much as 90% of all blindness is a direct result of corneal pathology (10). Whether the underlying cause is trachoma, corneal ulceration, onchocerciasis, or any of the diseases discussed above, an eye that is blind from corneal scarring and vascularization usually remains blind throughout the individual’s life. It is a simple statement of fact that surgical intervention after corneal blindness has already occurred is rarely successful unless well-trained surgeons and nurses are available as well as modern operating rooms, good equipment, reliable eye-bank facilities, and well-established clinical services for long-term follow up and treatment of graft rejections and other post-operative complications that might occur (37). Even state-of-the-art medical treatment for trachoma, onchocerciasis, leprosy, and corneal ulcers may not prevent corneal scarring from occurring, especially if the disease has become established and ocular complications have already developed. The message is clear that medical and especially surgical intervention is not cost-effective in eliminating corneal blindness in developing countries. Prevention, in the case of almost every disease involved, is more cost-effective and ultimately more successful in decreasing the prevalence of blindness. Schwartz et al. estimated that 95.5% of all blindness in the population they studied in the Central African Republic was preventable or treatable (10). This is an astonishing fact, which should be a call to mobilize public health resources in countries worldwide, both in industrialized and developing economies, to decrease the global burden of visual disability through the initiation of innovative programmes for the prevention of corneal blindness.
Resumen

Ceguera corneal: una perspectiva mundial

Las enfermedades que afectan a la córnea son una importante causa de ceguera en todo el mundo, sólo superada por la catarata. La epidemiología de la ceguera corneal es algo compleja y abarca una amplia variedad de oftalmopatías infecciosas e inflamatorias que causan cicatrización corneal, proceso que acaba conduciendo a una ceguera funcional. Además, la prevalencia de enfermedad corneal varía de un país a otro, incluso de una población a otra. Aunque la catarata es responsable de casi 20 de los 45 millones de personas ciegas que hay en el mundo, la siguiente causa importante es el tracoma, que ha dejado sin vista a 4,9 millones de personas, sobre todo como consecuencia de un proceso de cicatrización y vascularización de la córnea. Los traumatismos oculares y la ulceración corneal son causas importantes de ceguera corneal que a menudo se subnotifican, pero que pueden dar lugar cada año a 1,5-2,0 millones de casos nuevos de ceguera monocular. Entre las causas de ceguera infantil (aproximadamente 1,5 millones en todo el mundo, con 5 millones de personas con discapacidad visual) cabe citar la xerofílalmia (350 000 casos anuales), la oftalmía del recién nacido, y otras enfermedades oculares menos frecuentes como las infecciones por el virus herpes simplex y la queratoconjuntivitis vernal.

Aunque las actividades de lucha contra la oncocercosis y la lepra han conducido a logros ejemplares en materia de salud pública, estas enfermedades son todavía una causa importante de ceguera, pues afectan cada una a un cuarto de millón de personas. Se considera también que las medicinas tradicionales para los ojos han constituido un destacado factor de riesgo en la actual epidemia de ulceración corneal registrada en los países en desarrollo. Dadas las dificultades para tratar la ceguera corneal una vez consumada, los programas preventivos de salud pública constituyen la opción más eficaz con relación al costo para reducir la carga mundial de ceguera corneal.

Referencias

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