14

TRACHOMA

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14.1 INTRODUCTION

Trachoma, a chronic bacterial keratoconjunctivitis, is the most common infectious cause of blindness. One hundred years ago trachoma was the most important cause of blindness of any etiology and the cause of the founding of many eye hospitals. Trachoma has always been linked to poverty, poor hygiene, and availability of water. Fortunately, with improving socioeconomic conditions, including especially access to water and improved hygiene, trachoma as a cause of blindness is absent from industrialized countries. It remains a significant cause of blindness in the poor, dry developing countries and the productivity costs of trachoma-related reduced vision and blindness have been estimated USD 5.3 billion annually in 2003 dollars (1). Population-based surveys provided recent information for 42 out of 57 endemic countries; 40.6 million people are estimated to be suffering from active trachoma and 8.2 million are estimated to have trichiasis, the trachomatous condition that leads to blindness (2). The current estimate of prevalence of trachoma is lower than the previous World Health Organization (WHO) estimates: This can be explained by the success in implementing a control strategy, by more accurate data, as well as by socioeconomic development in endemic countries. In the past 12 years, great changes in trachoma control have taken place as a result of the WHO's leadership in developing a comprehensive strategy for control (*SAFE*, described below) and the founding of the Alliance for Global Elimination of Trachoma by the year 2020 (*GET2020*). As a result, the chance for reducing or perhaps eliminating this debilitating cause of blindness is within reach (3, 4).

14.2 CAUSATIVE ORGANISM AND NATURAL HISTORY

Trachoma is caused by four serovars of *Chlamydia trachomatis* (A, B, Ba, and C); serovars D through K cause genital tract infection. This obligate intracellular gram-negative bacterium prefers the epithelial surfaces of the eye; the other serovars affect the epithelial surfaces of the genital tract, causing the most common form of sexually transmitted disease. Crossover of these serovars to the alternative site is rare. *C. trachomatis* is an obligate intracellular bacterium and cannot replicate outside eukaryotic host cells. The metabolically active *Chlamydia* reticulate body matures, enlarges, and finally erupts causing cell death and releasing spore-like elementary bodies, which are the infecting agent. The elementary body attaches to epithelial cells on contact through its major outer membrane protein (MOMP). The presence of these elementary bodies in the secretions from the eyes and noses of infected persons (children especially) facilitate further transmission to family or contacts.

The intracellular location of the organism leads to protection from antibody and complement and there is a downregulation of the host major histocompatibility complex or MHC class I molecules by infected cells, thereby reducing killing by cytotoxic T cells. Episodes of infection seem to fall in severity as the child ages, suggesting that there is some development of immunity. On the other hand, this may reflect a decreasing of frequency of reinfection that occurs with age. While the immunopathology of trachoma is not fully defined, it is accepted that more severe trachoma, scarring, and corneal damage occurs after repeated infections and that this is related to a delayed hypersensitivity reaction. Detailed

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reviews of immunity and immunopathology are available in two *Lancet* seminars on trachoma (5, 6).

14.3 CLINICAL MANIFESTATIONS

After a brief incubation period of 5–10 days, the initial infection will result in a mild conjunctivitis that heals without permanent damage. As little immunity exists, repeated infections result in an exaggerated response: intense inflammation and scarring of the upper subtarsal conjunctiva, distortion of the lid margin that results in a shortened upper lid pulling the eye lashes inward (trichiasis). The early signs of trachoma (follicular disease and intense inflammation) are seen in children; scarring and trichiasis is observed in the older population. The resulting abrasion of the cornea by inturned lashes causes pain and eventually leads to corneal opacity and blindness. The World Health Organization has devised a simplified grading scheme for assessment of trachoma in communities (Fig. 14.1), which demonstrates the progression of disease that may take place over years of infection and reinfection. The early signs of trachoma are detected by everting the upper eyelid and examining with a 2.5× loupe (preferably) for the follicular stage (TF): characteristic white or yellow follicles of 0.5–2.0 mm. As disease worsens, the intense inflammatory stage (TI) may be seen. Trachomatous scarring (TS) begins as small stellate scars that with time coalesce to form the dense scar tissue that distorts normal lid architecture. This is followed by frank trachomatous trichiasis (TT) and corneal opacity (CO). The WHO scheme shown in Fig. 14.1 has been taught to eye workers in

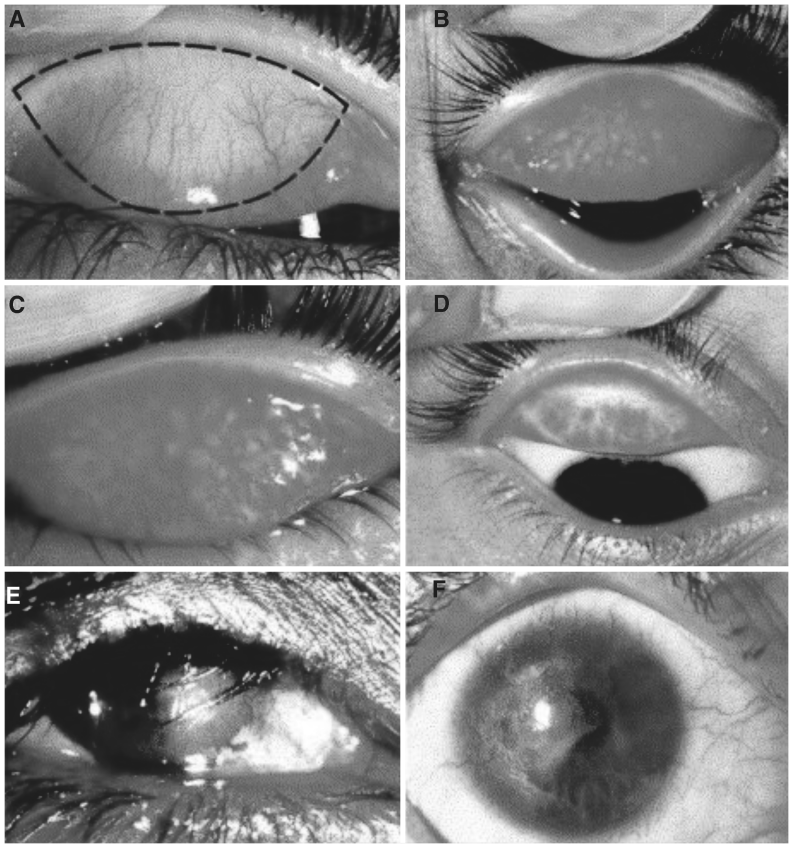

FIGURE 14.1 Clinical appearance of trachoma and the WHO trachoma grading scheme. (a) Normal everted upper tarsal conjunctiva; pink, smooth, thin, and transparent. Large deep-lying blood vessels that run vertically are present over the tarsal conjunctiva. The dotted line shows the area to be examined. (b) Trachomatous inflammation-follicular (TF). Five or more follicles of >0.5 mm. (c) Trachomatous inflammation-follicular and intense (TF + TI). Inflammatory thickening obscuring >1/2 the normal deep tarsal vessels. (d) Trachomatous scarring (TS). (e) Trachomatous trichiasis (TT). (f) Corneal opacity (CO). These photographs are reproduced with permission from the WHO Programme for the Prevention of Blindness and Deafness. (*See insert for color representation of this figure*.)

many trachoma endemic countries as a means of assessing the burden of disease within communities.

14.4 DIAGNOSIS

Diagnosis is generally a clinical diagnosis made by the examination described above. Giemsa stain of the intracytoplasmic inclusions and or culture of the organism are difficult and laborious and generally unavailable in endemic areas. Although both are specific, they are not sensitive. Four nuclei acid amplification tests are commercially available for the diagnosis of *C. trachomatis* infection. All were developed primarily for diagnosis of urogenital chlamydial infections and only two (Amplicor (Roche) and LCx (Abbott)) have been tested in ocular chlamydial infections. It is clear that the positive predictive value of clinical exams falls with falling prevalence and it is postulated that in persons who have had trachoma, any ocular infection or irritation may stimulate the typical follicular response seen in early trachoma. In at least one study, while clinical exams continued to find a few active cases, no infection could be detected by PCR tests done simultaneously with clinical exams in a control program in Tanzania (7, 8). Therefore, for practical public health purposes, the available and cost-effective method is the clinical examination. Should the cost and ease of application of the PCR tests be reduced and their role with respect to prevention of blindness be clarified, these tests could add an increased measure of accuracy to the current public health control programs—possibly allowing the discontinuation of antibiotic treatment sooner than reliance on clinical grading would dictate.

14.5 EPIDEMIOLOGY

Trachoma remains highly endemic in many parts of Africa and continues to persist in a number of countries in the Middle East, Asia, and Latin America (9). As noted above, 57 countries are known or considered endemic for the disease and more than 40 million people have active trachoma. Another 8.2 million have trichiasis and therefore at high risk of irreversible and severe visual impairment. Population-based surveys provided recent information for 42 out of 57 endemic countries. Globally 1.2 billion people live in endemic areas, 40.6 million people are suffering from active trachoma, and 8.2 million have trichiasis. In addition, 48.5% of the global burden of active trachoma is concentrated in 5 countries: Ethiopia, India, Nigeria, Sudan, and Guinea. On the other hand, 50% of the global burden of trichiasis is concentrated in only three countries: China, Ethiopia, and Sudan. Overall, Africa is the most affected continent—27.8 million cases of active trachoma (68.5% of all) and 3.8 million cases of trichiasis (46.6% of all) are located in 28 of the 46 countries in the WHO African Region, with an estimated population of 279 million living in endemic areas (2).

Children are the main reservoir of infection with *C. trachomatis* and trachoma is a family-based disease with clustering in households and communities as a result of the ease of transmission of infected ocular secretions between people, especially other family members as noted above and in Fig. 14.2 (6). While children below 10 years of age account for the preponderance of active infections, the severe stages are seen in adults. Women are three times as likely to be

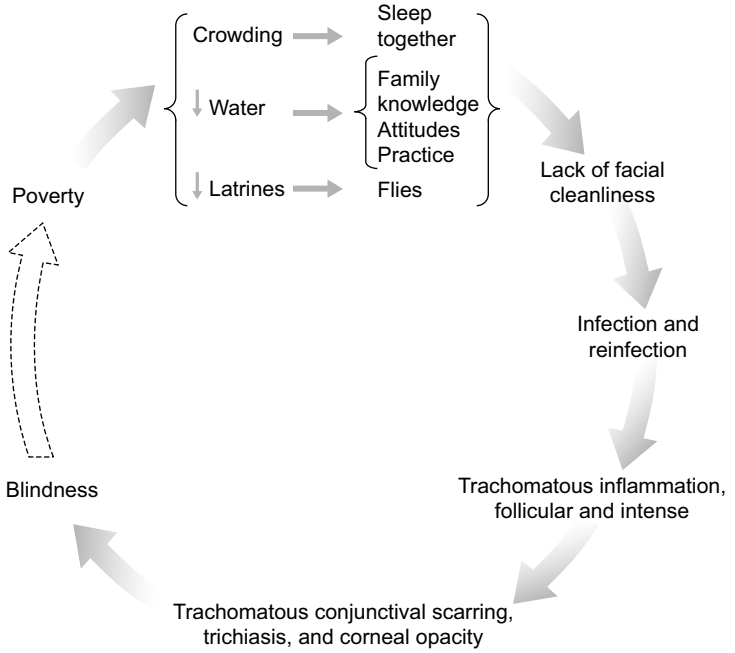

FIGURE 14.2 Interaction of risk factors for trachoma. Lancet reproduced with permission (6).

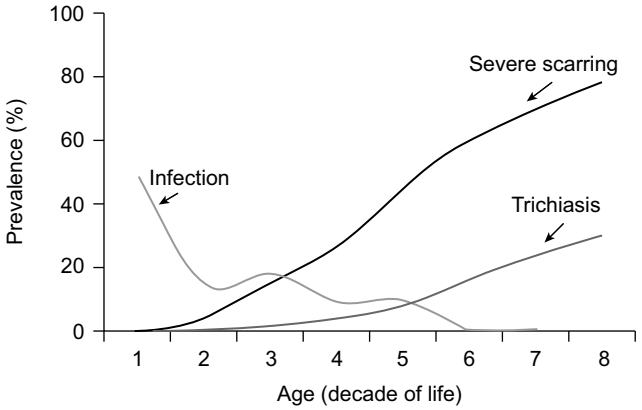

FIGURE 14.3 Schematic presentation of trachoma infection and disease based on community control programs in Ethiopia (courtesy of Dr. Bruce Gaynor, University of California San Francisco).

blinded by trachoma as are men; the cause of this is thought to be the frequent reinfection they acquire in child care. Figure 14.3 is a schematic demonstration of the sequence of early infection in childhood, but trichiasis and corneal opacity occurring in the older ages drawn from data collected in control programs in Ethiopia. This pattern to a greater or lesser level has been seen in all areas where trachoma is endemic.

Infection is easily transmitted from eye to eye by fingers, flies, and fomites (shared cloths, clothes, towels). Households with young children with eye discharge and external nasal exudates, posterior pharyngeal infection or drainage through the nasolacrimal duct are the greatest source of infection (10). Risk factor studies for trachoma have repeatedly shown the association of young children, poor sanitation, poor facial cleanliness, and inadequate access to water with trachoma (11, 12).

14.6 TRACHOMA: WATER AND SANITATION

The importance of water in the epidemiology of this disease is intuitively obvious when one considers the modes of transmission. But, water's link to trachoma is perhaps more complex than it would seem. In a detailed review of available studies of water and trachoma, Prost and Negrel concluded that there was a general reduction in trachoma rates as water access improved (13). However, it is also not clear whether water availability/access should be measured in terms of distance to source or time to fetch water. Cairncross has noted that a "water use plateau" exists in areas of scarce water supplies throughout the world. The amount used may vary, but the plateau of use exists from a few minutes from the house to 30 min away (14). After 30 min, water use declines from the plateau and hence, those beyond 30 min of a water source are likely to benefit most from a new and closer water source. In a rigorous study of children ages 1–9 years in Tanzania involving 99 randomly selected households, active trachoma increased with increasing water collection time but was unrelated to amount of water collected. In a smaller sub-study in the same area, active trachoma prevalence was substantially lower in children from households where more water was used for personal hygiene independent of the total amount of water used (15). The allocation of water to hygiene was directly associated to shorter water collection time. Similarly in Gambia trachoma-free households used more water for washing children than households with trachoma cases (16). The key issue affecting trachoma in households is then the use of water in personal hygiene, especially in children.

14.7 PREVENTION AND CONTROL

It is water's link to poverty and poor hygiene that makes its role crucial in halting trachoma transmission. Water is essential but not sufficient to control trachoma. That is, access to water is usually less among the poor and likewise, poor hygiene cannot improve without water. This was the clear intention of the WHO in developing a strategy that incorporated the three major elements of public health improvement: primary, secondary, and tertiary preventive measures. In 1997, WHO founded an alliance (of ministries of health as well as nongovernmental organizations) for the global elimination of trachoma by 2020 (*GET2020*), and in 1998, a World Health Assembly resolution called for the 57 countries where trachoma remains endemic to take steps to eliminate blinding trachoma by implementing the "*SAFE*" strategy: WHA Resolution 51.11, *Global Elimination of Blinding Trachoma* (17). This strategy was devised by WHO and includes four proven elements leading to control. *SAFE* entails: (*S*) trichiasis surgery to halt corneal damage (tertiary prevention); (*A*) antibiotic treatment (single-dose azithromycin, 20 mg/kg of body weight for children and 1 g for adults (secondary prevention); (*F*) face washing or improved facial hygiene (primary prevention); and (*E*) environmental change including access to water and improved sanitation (primary prevention) was first described in the WHO manual, *Achieving Community Support for Trachoma* (see Section 14.7.2).

14.7.1 Surgery for Trichiasis—S

In untreated trichiasis, corneal opacity may develop in around one third of individuals whose trichiasis remains untreated for more than a year (18) and trichiasis itself is a cause of severe pain and reduced vision. Surgical treatment (tertiary prevention) is the only means of halting further

damage. The WHO recommends the use of the bilammellar tarsal rotation procedure or one of the two other similar procedures in use in endemic countries, depending on the experience of the eye care community in the country and ensuring that quality of service is carefully respected. Reacher and colleagues undertook a randomized controlled trial of this procedure in Oman and obtained at least a 70% success rate 6–24 months after surgery (19). The upper-eyelid tarsal plate is incised with external rotation of the distal margin by insertion of 3–4 sutures from the external surface to the incision to the internal surface of the upper part of the tarsal plate. This rotates the lashes up and away from the cornea. Recurrence of trichiasis has been a major concern and no doubt affects the acceptability of patients to have this procedure carried out. These rates have varied from as low as 8% at 1 year to 47% in a 17-year follow-up in Oman (20). The continuing trachomatous process of lid shortening around scarring, coupled with the possibility of reinfection, may explain the wide differences in recurrence rates. The other possibility could be less attentive eye surgeons with less experience with the procedure. In a trial under field conditions lid surgery by well-trained and well-equipped eye nurses has been shown to be as good as surgery provided by ophthalmologists (21) and has been successfully carried out in villages in national control programs in many countries. Moving this needed surgery to the villages improves acceptability, reduces costs, and is more direct in dealing with the need to halt further vision impairment. To assure improved performance of surgery, the WHO has made available two manuals for teaching and evaluating performance (quality control) of this procedure (see Section 14.A.1).

14.7.2 Antibiotics—A

From 1952 until the early 1990s, the recommended treatment for trachoma had been topical tetracycline ointment four times a day at first, later reduced to twice a day—for 6–8 weeks. While results could be good in the case of programs where therapy was observed or administered, in fact, when tubes of ointment were simply given to children or patients, the results were often poor because the ointment disturbed vision and because it is also irritable, it was discontinued as soon as any improvement in symptoms was obtained. Later doxycycline, an oral tetracycline with long half-life, was found to be effective if given once daily for 2 or 3 weeks. However, since the target population is young children, it was not suitable for wide use (or use at all) because of the dental damage in children as well as photosensitivity caused by doxycycline.

In the mid-1990s, three randomized trials of azithromycin showed that azithromycin in a single oral dose was at least as effective as tetracycline ointment (22–24). Community use of azithromycin in trachoma control was successfully carried out using 3 weekly doses in three countries: Egypt, Tanzania, and Gambia (25). Having an oral antibiotic that is effective in a single dose has revolutionized the control programs for trachoma. Additionally, this systemic antibiotic has the benefit of treating extraocular sites of chlamydial infection, especially the posterior pharynx not reached by ocular ointments. Azithromycin, a macrolide antibiotic with few side effects, has the unusual quality of concentration in macrophages, polymorphonucleocytes, and epithelial cells—where the intracellular *C. trachomati*s resides. Studies in conjunctival biopsies of uninflamed eyes showed that the inhibitory concentrations were maintained in these tissues for at least 15 days after a single treatment (26).

This extraordinary means of treating trachoma was enthusiastically supported by the trachoma control community and at least four large cohort studies have been carried out in Tanzania (8, 27), Ethiopia (28), and Gambia (29), showing reduced prevalence of chlamydial infection or signs of active trachoma after community-wide treatment with single-dose oral azithromycin. In a region of Gambia where the disease is hypoendemic a sustained reduction in the prevalence of chlamydial infection was achieved in 12 of 14 villages receiving oral azithromycin (29). The results of a single treatment in a village hyperendemic to trachoma in the Kongwa district of Tanzania showed a reduction in the prevalence of chlamydial infection from 57% to 12% 2 months after treatment. In another Tanzania district, Rombo, trachoma prevalence showed a sustained reduction after a single treatment; however, in this case, all children with active disease at 6, 12, and 18 months were offered tropical tetracycline treatment. In this district of low prevalence (pretreatment prevalence = 9.5%) no evidence of *C. trachomatis* DNA was detected in the community at 24 months (7, 8).

Many areas in Ethiopia are hyperendemic for trachoma and prevalence of infection, although initially decreased, was found to increase after treatment, in absence of the other transmission control measures included in the SAFE strategy. Theoretical models suggested that biannual treatments may be required when the initial prevalence of trachoma is >50%. In a study of 16 adjacent villages 14,897 of 16,403 eligible individuals (90.8%) received their scheduled treatment. In the eight villages in which residents were treated annually, the prevalence of infection in preschool children was reduced from a mean of 42.6% (range, 14.7–56.4%) to 6.8% (range, 0.0–22.0%) at 24 months. In the eight villages in which residents were treated biannually, infection was reduced from 31.6% pretreatment (range, 6.1–48.6%) to 0.9% (range, 0.0–4.8%) at 24 months. Biannual treatment was associated with a lower prevalence at 24 months ($P = 0.03$, adjusting for baseline prevalence). At 24 months, no infection could be identified in six of eight of those treated biannually and in only one of eight of those treated annually ($P = 0.049$, adjusting for baseline prevalence) (28). Following the same

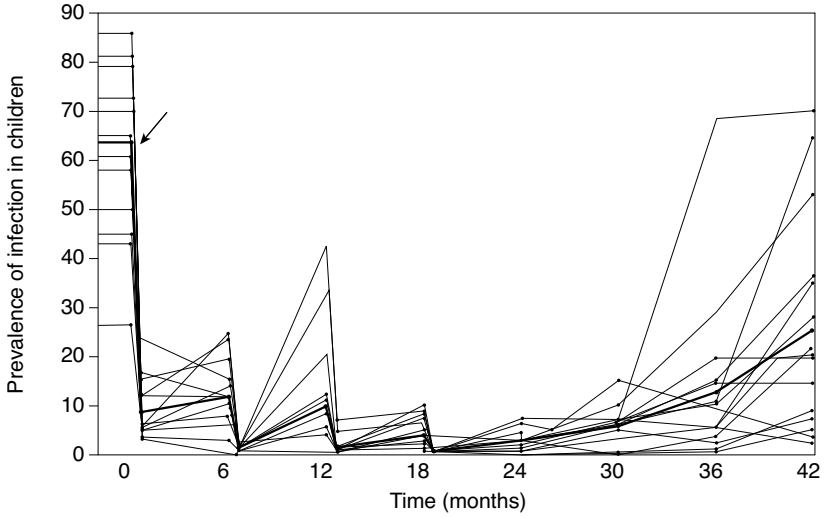

FIGURE 14.4 The mean prevalence of infection (black) and the prevalence in each of the individual 16 study villages (gray) in Ethiopia based on estimates of the prevalence of infection in 1–5 year-old children at a single village visit. After the fourth treatment at 18 months after the study began, infection returned to the 16 villages as shown (30).

16 villages, the same group of investigators found in a much larger study but with only four mass treatments 6 months apart, mean prevalence in 1–5 year-old children began a steady rise in the 24 months following the last treatment. The initial prevalence was 63.5%, falling to 2.6% 6 months after the last treatment. But in the next 18 months prevalence had increased to 25.2% (Fig. 14.4) (30). This was a steady increase after the last treatment but still was 40% less than the original prevalence. Also in Ethiopia, these investigators conducted a smaller study of two villages with a total population of 768 who were offered six biannual mass treatments with oral azithromycin. At 12 months after the final treatment, each village member was examined clinically and swabs were taken for testing for evidence of *C. trachomatis* RNA. The average antibiotic coverage was high, >90% in both villages. Clinical activity in children aged 1–5 years decreased from 78% and 83% in the two villages before treatment to 17% and 24% at 42 months. But, PCR evidence of infection in the same age group decreased from 48% to 0% in both villages at 42 months (31). These important studies are indicative of both the power and limitations of effective antibiotic treatment. That is, if mass antibiotic treatment is offered at 6-month intervals, prevalence will remain low even in areas of the highest transmission. However, this is untenable in terms of public health delivery, costs, and bacterial resistance issues. This is especially true in light of what is known about the importance of water and behavioral change for facial cleanliness.

A topical azithromycin topical eye drop has been prepared, but is in preliminary trials and not yet available under a drug donation framework. In a trial in Cameroon in children between 1 and 10 years, prevalence of active infection (TF and TI) fell from 31.5% before treatment to 6.3% at 12 months after the treatment and the drops were reported to be well accepted (32). This preliminary report will require comparison with oral and therefore systemic treatment with azithromycin, or define its role in trachoma elimination campaigns that use the MDA approach.

While oral azithromycin has proved effective for trachoma, there are additional community benefits observed in those receiving mass treatment. Beneficial effects on mortality rates have been observed in a large study in Ethiopia (33). Mortality rates in children 1–9 years of age in two large groups of villages of 15,902 and 14,716 participants. The control group of villages received biannual treatment with oral azithromycin 1 year after the first group. In the treated communities, the estimated overall mortality rate during this period for children in the untreated group was 8.3 per 1000 person-years, while among the treated communities, the estimated overall mortality rate was 4.1 per 1000 person-years. It is likely that this mass treatment had beneficial effects on gastrointestinal and pulmonary disease reducing mortality in the treated group. With the broad use of any antibiotic, the specter of antibiotic resistance must be considered. No evidence of azithromycin resistance has been reported in *Chlamydia* species. However, azithromycin resistance in other pathogens, particularly pneumococci has been shown to develop after mass treatment. Fortunately the prevalence of macrolide-resistant strains generally returns to pretreatment levels between 6 and 12 months (34, 35).

In 1996 at its Global Trachoma Scientific Meeting, the World Health Organization endorsed the use of azithromycin in trachoma control programs (36). In the following year, the WHO founded the Global Alliance for the elimination of

blinding trachoma by the year 2020—GET2020. WHO's endorsement of the use of azithromycin for trachoma led to a generous decision by Pfizer Inc. to donate azithromycin for this purpose. Pfizer joined the Edna McConnell Clark Foundation to found the International Trachoma Initiative, a nongovernmental organization, to advance this elimination program. Since 1998, 18 countries have begun national trachoma control programs using the SAFE strategy and donated mass treatment with azithromycin. The WHO recommends mass treatment for at least 3 years if the prevalence of trachoma in children aged 1–9 years in greater than 10%, and then reassessment of prevalence. Recent experience suggests that trachoma is unlikely to be eliminated in a single year and a delay of 2 or 3 years for reassessment would be saving in public health resources. While the impact of this long-acting antibiotic is truly remarkable, it is clear that long-term elimination requires the full SAFE strategy.

14.7.3 F and E—Facial Cleanliness and Environmental Change

The F and E of this strategy translate into the role of water and sanitation in the transmission and control of blinding trachoma. Mass antibiotic treatment alone is unlikely to eliminate ocular chlamydial infection especially in areas such as Ethiopia where infection is clearly hyperendemic (Emerson and Ngondi, 2009) (37). And, the efficacy of access to water and improved hygiene has been shown even in the absence of antibiotics in western Europe and North America by the mid-twentieth century. On the other hand, Rabiu and colleagues assessing evidence for the effectiveness of environmental sanitary measure on the prevalence of active trachoma in endemic area for the Cochrane Database concluded that there was a dearth of acceptable data to determine the effectiveness of all aspects of F and E (38). In this case, the absence of randomized trials in this area is not surprising as it involves the difficult areas of cultural/behavioral change and whole communities assigned to an intervention. Also, in the face of the ease of providing a single dose drug, behavioral change/health education and/or water supplies/latrine building is much more labor intensive and expensive. Still, it is obvious that these measures have benefits far beyond trachoma control, both in terms of disease control as well as better quality of life and expenditure of time and energy in obtaining water. Water, and therefore the link to sanitation, affects trachoma transmission by access and use of water (behavioral factors), sanitation/latrine availability, and fly control.

There is, however, evidence outside of rigid strictures of randomized controlled trials that F and E are effective. A randomized control trial on facial cleanliness was undertaken by West and her colleagues in six villages of central Tanzania (West, 1995) (27). In this case, all members of the villages received topical tetracycline daily for 30 days. Three villages also received an additional program focusing on facial cleanliness in children. At the end of 1 year, clean faces in children in the intervention villages had increased by 60% and the rate of active trachoma was reduced by 42%; the rate of intense trachoma (TI) fell by 65%. That is, there was greater reduction in severe disease before reduction in the milder first stage of infection. These results were obtained in addition to a benefit seen in both arms of the study as a result of the use of the tetracycline ointment. Using an adult village participatory learning program, the same investigators were able to increase the rate of clean faces in children from 9% to 33% in 1 year (39, 40).

Water is clearly linked to two other risk factors for trachoma: sanitation (latrines) and flies. A case-control study in almost 1000 households in 8 Tanzanian villages examined the association between use and quality of latrines and the risk of trachoma. Use of latrines was significantly associated with a decreased risk of trachoma. The condition of the latrine or quality was not a determining factor. Latrines then need not be expensive or elaborate to provide health benefits (41). In a community-based study of 507 children 1–9 years of age in 232 Ethiopian households, lack of access to a latrine increased the risk of having active trachoma by 4.36-fold but perhaps more important, absence of a clean face (defined simply as only absence of discharge from eyes or nose) increased the odds of having trachoma by 7.59-fold (42). The prevalence of trachoma in this community was 53%.

It is clear from studies in Gambia (43) and Ethiopia (44) that *Chlamydia* DNA can be found by polymerase chain reaction (PCR) on flies caught on children's faces. These flies are water-seeking flies: largely, *Musca sorbens*, a species that preferentially breeds in human feces, hence, the link to latrines. However, trachoma transmission has been found to exist in areas where flies are *not* a problem. This was observed in Kentucky in the United States in 1911 where the basic lack of hygiene and sanitation was felt to be the major cause of continuing transmission (45). It has been shown that in a trial in Gambia of use of fogging with insecticides that the fly population was reduced and fly populations remained so long as insecticides were continued. Similarly, the expected rate of new cases of trachoma rates was shown to fall concomitantly (46). In a larger study in Gambia, villages were randomized to receive fly control, the provision of new latrines, or no additional activities. Persons with intense trachoma were treated with either tetracycline or azithromycin. After 6 months the number of *M. sorbens* on children's faces had decreased by 88% with fly control and 30% in the villages with new latrines. At 6 months, the prevalence of trachoma in children in the fly control villages fell from 14% to 7%, in the latrine villages from 11% to 8%, and increased in the control villages from 9% to 10% (47). However, studies in Tanzania using the same fly control techniques did not show any benefit from fly control when

used in conjunction with antibiotic treatment in this hyperendemic area (48). Similarly and perhaps more definitively, studies in Ethiopia where transmission is extraordinarily high, studies have shown that in the presence of mass treatment with azithromycin, fly control may not add to reducing transmission of trachoma through fly–eye contact. Flies were collected in a village that had received mass oral azithromycin distribution and were compared with flies in an untreated village. Polymerase chain reaction (PCR) was performed to detect chlamydial DNA on the flies. Conjunctival swabs were also taken to assay for chlamydial prevalence in the children. Chlamydia was found on 23% of the flies in the untreated villages but only 0.33% in the treated villages. Therefore, mass treatment of children with antibiotics would seem to drastically reduce the role of flies as a disease vector without controlling the fly population (44).

In Vietnam a public health intervention study was conducted between 2002 and 2005 to assess the impact of improved water and sanitation compared with villages that received only the S and A components of SAFE (49). Two villages of 1300–1500 population, separated by 10 km and five other villages were studied. The F and E components applied to the village receiving the full SAFE strategy included health education (through the Women's Union and school authorities), as well as 284 latrines, 241 bathrooms, 273 dug wells, and 252 water tanks. The comparison village received only SA. The SA village prevalence fell from 10.2% to 6.7%, while the SAFE village fell from 13.3% to 1.4%. The additional decline of active trachoma due to the addition of health education and water/sanitation was responsible for 58.7% of the decline at all ages and 37.4% in children under the age of 15 years.

14.8 THE PATH TOWARD ELIMINATION BY 2020

Since the founding of the WHO's GET 2020 alliance and the Pfizer donation of azithromycin though ITI, 18 countries have embarked on national trachoma control programs using mass treatment with azithromycin in the SAFE strategy (Box 14.1). Of these, Morocco and Ghana have informed the WHO that they have reached their target for elimination of blinding trachoma. In addition, Mexico and Saudi Arabia are in the process of assessing the situation and inform the WHO of having achieved the elimination of blindness from trachoma.

In April 2007, WHO launched its new approach to the control of neglected tropical diseases (NTDs). These diseases have a number of common features that are all associated with impoverished settings, and industry donations of the antibiotics needed for mass treatment are available. Control of these diseases is now considered to be part of the global drive to reduce poverty and to attain the United Nations Millennium Development Goals. The NTDs affect one third of the global population, especially poor populations living in remote rural areas. Trachoma is one of the "major five" NTDs; the others are onchocerciasis, lymphatic filariasis (LF), three soil-transmitted helminths (STH), and schistosomiasis. For trachoma and the first three of these, there are drug donation programs by major pharmaceutical companies: ivermectin (Merck) for onchoceriasis; albendazole (GlaxoSmithKline) along with an inexpensive generic, diethyl carbamazine for LF; and mebendazole (Johnson & Johnson) for STH. For schistosomiasis, the major generic drug, praziquantel, has fallen in price so that adults can be treated for as little as USD 0.25—children much less. These five diseases kill large numbers of people: 20% of deaths and 24% of disability-adjusted life years (DALYs) lost as a result of communicable diseases are due to these NTDs. Because of the availability of cheap or donated effective drugs for these diseases, they can be treated for as little as USD 0.40–0.79 per person (50). A major thrust for countries where there is overlap of these diseases is to integrate control programs wherever possible. This includes opportunistic synergy with programs focused on the "big three" (HIV, malaria, and tuberculosis) (51). Such a program has been reported in the Amhara region of Ethiopia where treatment and health education were combined in a joint trachoma and malaria effort under a Carter Center/Lions Club program with the Ministry of Health (52).

BOX 14.1 COUNTRIES WITH NATIONAL TRACHOMA CONTROL USING THE SAFE STRATEGY

- Burkina Faso
- Ethiopia
- Eritrea
- Gambia
- Ghana
- Guinea-Bissau
- Kenya
- Mali
- Mauritania
- Morocco
- Nepal
- Niger
- Nigeria
- Senegal
- Sudan
- Tanzania
- Uganda
- Vietnam

14.9 CONCLUSION

The evidence gathered from operational research studies cited here and from the experience of national control programs clearly supports the effectiveness of the SAFE strategy and the implementation of it in full as the path to secure elimination of blinding trachoma. The impact of mass treatment with azithromycin is remarkable; but alone it will not eliminate the irreversible consequences of the disease, with the potential exception of the areas of lowest transmission. The added benefits of access to water and hygiene (including availability of latrines, education on their use, and behavioral changes for personal hygiene) for general health and quality of life make this a needed inclusion in all NTD elimination programs. All programs that result in the behavioral change needed to increase clean faces in children will have a profound effect on transmission of trachoma. The SAFE strategy adds another benefit beyond simply mass drug administration (MDA). Since it is a complete public health strategy, it provides a linkage with chronic disease control programs and encourages development of a stable health care system. When and where trachoma elimination is/will be achieved, the people of those endemic areas will be left with a functional health care system, an increased education on the real benefits of public health and clinical care, and with first-hand evidence that prevention works and induces a higher quality of life, making the paradigm of primary health care a living truth.

14.A.1 APPENDIX: RESOURCES AVAILABLE FOR ELIMINATION OF TRACHOMA

The World Health Organization Program in Prevention of Blindness makes available the following invaluable resources for trachoma elimination programs.

These manuals can be obtained by writing: The World Health Organization, Prevention of Blindness Program, 1211 Geneva 27 Switzerland or they may be downloaded by accessing the WHO website: www.who.int/pdb/publications/trachoma/en.

14.A.1.1 Guides and Manuals

- *The SAFE Strategy: Preventing Trachoma*
- *Trachoma Control: A Guide for Program Managers*
- *Guidelines for Rapid Assessment for Blinding Trachoma*
- *Final Assessment of Trichiasis Surgeons*
- *Trichiasis Surgery for Trachoma*
- *Primary Health Care Level Management of Trachoma*
- *Achieving Community Support for Trachoma Control: A Guide for District Health Work*
- *Zithromax—Program Manager's Guide*
- *A Guide: Trachoma Prevention through School Health Curriculum Development*

14.A.1.2 Definitive Textbook on Trachoma

Hugh R. Taylor. *Trachoma: A Blinding Scourge from the Bronze Age to the Twenty-First Century*, Illustrated. East Melbourne, Australia: Centre for Eye Research Australia/Haddington Press, 2008, 282 pp. ($112 ISBN 978-0-9757695-9-1).

14.A.1.3 Information on Availability of Azithromycin for National Control Programs

The International Trachoma Initiative (ITI)
The Task Force for Global Health
325 Swanton Way
Decatur, GA 30030
Phone: 1 800 765 7173
Web: www.trachoma.org

14.A.1.4 Trachoma Information Service

In partnership with the ITI, the Kilimanjaro Centre for Community Ophthalmology (KCCO) in Tanzania manages a Trachoma Information Service—a bimonthly e-mailing of trachoma-related information including the latest trachoma research articles. Summaries provided by the authors pay particular attention to what the findings meant for people involved in trachoma control in developing countries.

Persons who wish to receive this material via e-mail may send name and e-mail address to KCCO, Dr. Paul Courtright at pcourtright@kcco.net.

14.A.1.5 Women and Trachoma

The Kilimanjaro Centre for Community Ophthalmology and the Carter Center make available a useful manual on *Women and Trachoma*. It can be downloaded from www.kcco.net or www.cartercenter.org; or, by phone to Carter Center 404-420-3830.

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