



Current Global Scenario of Trachoma With Special Emphasis on the ‘SAFE’ Strategy: A Review

Diptarup Mallick¹

¹Post Graduate Department of Zoology, Barasat Government College, 10, KNC Road, Barasat, Kolkata-700124 ,
West Bengal, India

Corresponding Author: E-mail address: diptarupmallick3@gmail.com

ABSTRACT

Trachoma is a Neglected Tropical Disease (NTD) and one of the most common ocular contagious diseases, caused by different serotypes such as A, B, Ba ,C of bacterium Chlamydia trachomatis that occurs recurrently. Most infants are adversely affected from chronic keratoconjunctivitis, leading to blindness in later life. Epidemiological studies in 2023 revealed that approximately 115.7 million people were at risk of trachoma, but presently it has been declined to almost 103.2 million. Basically this disease is predominant in least developed or developing nations with high poverty. Preventive measures being implemented by the World Health Organization (WHO) , popularly known as ‘SAFE’ strategy: S for surgery, A for antibiotic dissemination, F for facial cleanliness, and E for environmental improvements. Now-a-days it is effectively and extensively applied; that’s why number of active patients are reduced drastically, but trachoma-free world creation should be the principal and researches will make it possible.

Keywords: Trachoma, Chlamydia trachomatis, epidemiological studies, WHO, ‘SAFE’ strategy.

1. INTRODUCTION

Trachoma is one of the most prevalent ocular diseases and was listed as one of the twenty ‘Neglected Tropical Diseases’ (NTDs) by the World Health Organization (WHO) [1]. Trachoma adversely affect the eyes, resulting in conjunctival inflammation in infants, opaqueness in the cornea, and even blindness in adults. The causative agent of this disease is the bacterium *Chlamydia trachomatis* (Ct), which is found globally, and the disease is rapidly disseminated from person to person directly through contact with infected eyes or nasal discharge or indirectly through specific flies, especially in young children. In 2024, the WHO reported that 1.9 million people were blind or visually impaired due to trachoma worldwide. Epidemiological studies in 2023 revealed that approximately 115.7 million people were at risk of trachoma, but presently, the number of trachoma-susceptible individuals has declined to almost 103.2 million, and their habitats are positioned in trachoma-endemic regions [2].

In 2013, almost 125 million people resided in trachoma-endemic areas globally [1], so it is clear that, owing to economic development as well as the application of modern disease assessment tools and techniques and effective treatments, the number of trachoma-endemic areas and active cases have both started to decrease drastically, which ultimately promotes the sustainable development of each nation. However, many developed countries in Europe and North America were affected by trachoma, which is considered one of the major concerns for public health, but currently, trachoma is not an issue of concern elsewhere except for low-income nations, where poverty is too high, for example, few African countries.

In 1998, the WHO established the Alliance for the Global Elimination of Blinding Trachoma by 2020 (GET 2020) and implemented the ‘SAFE’ strategy for preventing *C. trachomatis*-induced infectious disease, of which four components imply four different meanings: ‘S’ for surgical treatments, ‘A’ for antibiotics, ‘F’ for facial cleanliness, and ‘E’ for environmental improvements. Later, the WHO updated the ‘SAFE’ strategy and rescheduled a target for eliminating trachoma worldwide by 2030.

2. DEVELOPMENT OF CHLAMYDIA TRACHOMATIS

Ct (gram-negative bacteria) can develop into two distinct forms, viz. Infectious elementary body and non-infectious reticulate body. The elemental body of Ct is mobile, enters host cells through cell surface receptors (endocytic pathway) and resides in vacuoles composed of the host cell membrane and chlamydial proteins, which subsequently develop into perinuclear inclusions [3]. Within this inclusion, the elementary body transforms into a replicative and relatively larger form (approx. 1.2 μm in size), and the reticulate body shows properties such as active metabolism and the inability to cause infection. Further transformation of the reticulate body led to the regeneration of enormous elementary bodies almost 3 days later, which moved outwardly after rupturing the cell surface. Intracellularly, *C. trachomatis* is able to evade recognition and effectively dampen the immune responsiveness of the individual.

3. PATHOGENESIS AND CLINICAL FEATURES

Four distinct serotypes of *Ct*, viz. A, B, Ba, and C (ocular) are mainly responsible for inducing blinding trachoma. Although other serotypes from D to K and L1—3 are also able to cause ophthalmological problems in children or conjunctival inflammation in adults, infections induced by these serotypes are generally nonrecurring, and as a consequence, blindness does not occur. Serotypes D-K can cause urogenital infections, and L1-3 can cause lymphogranuloma venereum. Diseases caused by these non-ocular serotypes are usually recognized as sexually transmitted diseases (STDs) and may occur concurrently with trachomatous conjunctivitis.

Where blinding trachoma is more prevalent, communities are generally expected to achieve the first episode of bacterial infection earlier; for example, where trachoma exhibits hyperendemicity and where acquisition of the first episode occurs at very beginning of life. However, in regions with trachoma mesoendemicity and hypoendemicity, acquisition age might be delayed.

Chlamydia trachomatis gradually affects the epithelial cells of the conjunctiva as a result of a combination of immune reactions that lead to the development of inflammation after the release of pro-inflammatory cytokines, causing conjunctivitis [4]. However, the clinical features of trachomatous conjunctivitis are simplified by the WHO as five grades that are simultaneously useful for trachoma assessment and management [5] as follows:

- Trachomatous inflammation – Follicular (TF): characterized by the appearance of 5 or more follicles that are greater than 0.5 mm in length and are found in the upper tarsal conjunctiva (Fig. 1A).
- Trachomatous inflammation – Intense (TI): characterized by pronounced tarsal conjunctival inflammatory thickening that leads to obscurity in more than half of the deep normal vessels. TF and TI are collectively called active trachoma (AT), i.e., Patients whose AT shows each or both clinical signs (Fig. 1A).
- Trachomatous scarring (TS): characterized by the appearance of tarsal conjunctival scarring (Fig. 1B).
- Trachomatous trichiasis (TT): at least one eyelash rub on the eyeball (Fig. 1C).
- Corneal Opacity (CO): characterized by an opaque cornea that is apparent from the outside, becomes opaque to the whole pupil (Fig. 1D).

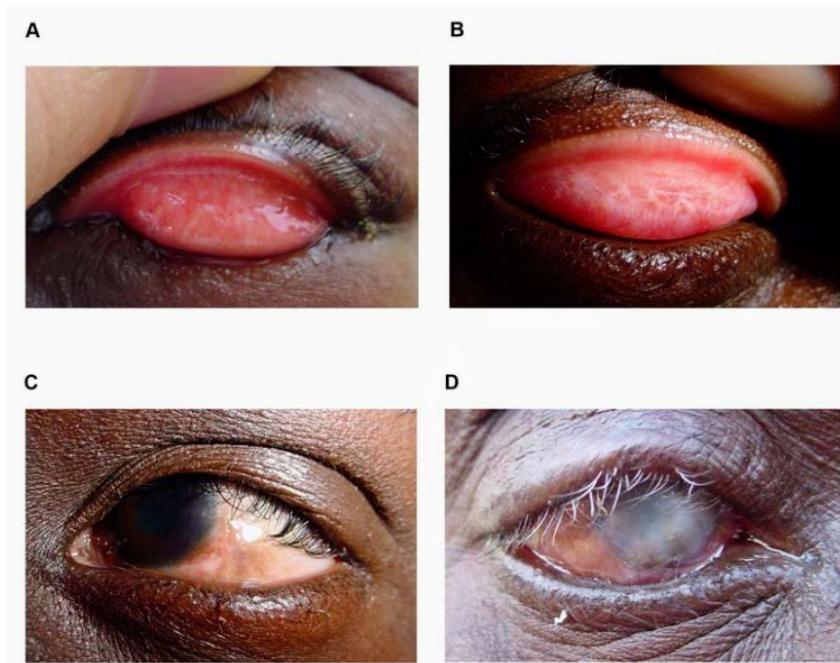


Figure 1. Clinical signs of trachomatous conjunctivitis. A. Child with active trachoma (AT) showing trachomatous inflammation – follicular (TF) and trachomatous inflammation – intense (TI) ; B. Trachomatous scarring (TS) in the tarsal conjunctiva; C. Trachomatous trichiasis (TT) with entropion; & D. Corneal Opacity (CO). Reproduced with permission from authors cited in [6].

The severity of both *Ct* infections and inflammatory responses are subsidized over time. It has been experimentally proven that chlamydial infections may be resolved possibly by the activities of immune cells, which produce mainly interferon-gamma (IFN- γ), after studying animals as model organisms and gathering information obtained from humans [7]. Community-based surveys regarding *C. Trachomatis* infection reported that infection is not prevalent and persists as low as age increases in areas with trachoma endemicity, which is probably due to the increased maturity of immune responsiveness after repeated exposures [8]. Whole organism-based vaccines were initially developed against chlamydial infection, providing insufficient protection with low durability and bacterial strain specificity. Therefore, despite receiving single or multiple doses of vaccine, individuals living in endemic regions fail to achieve the desired immunity against *C. Trachomatis*, rendering them susceptible to reinfection and subsequent chronic keratoconjunctivitis. Chronic conjunctival inflammatory responses occur in conjunction with trachomatous scarring in cases of prolonged recurrent infections, during which scar tissues develop within the conjunctiva (Fig. 1B) [9]. Owing to the accumulation of scar tissue, contraction causes eyelashes to roll up and move inwardly to the eye, referred to as entropion, after which these eyelids rub on the eyeball, causing trichiasis (Fig. 1C). The development of scar tissue may be dependent on the bacterial load, recurrence of infection, and individual immune status [10]. Weak immunological responses against *C. Trachomatis* infection may increase the severity of inflammatory responses and ocular histological damage (protease-mediated damage), resulting in deterioration of optical health. An extreme consequence of trachomatous conjunctivitis is blindness owing to corneal opacity, which is provoked mainly by trichiasis (Fig. 1D), although prolonged inflammation and intense contamination may also occur.

4. DISEASE VS. INFECTION

Chlamydia trachomatis is the only causative agent for trachoma and cannot be identified firmly. This is because, since 1957, when this bacteria was first isolated, as many cases of active trachoma have been reported, few cases of chlamydial involvement have been detected after checking results obtained from highly sensitive nucleic acid amplification tests [11]. C. Trachomatis is apparent only in patients with AT rather than in individuals receiving antibiotics. Conditions regarding active disease confined by the WHO are still not fulfilled by all individuals living in trachoma-endemic areas; hence, infections are frequently recorded. However, the title of this discussion is not so much concise, yet it's necessary to know. Disease is a simple consequence of infection, but in some cases, the clinical manifestations of active disease may be reversed, and infection still persists, and vice versa. Hence, there is a subtle relationship between disease and infection that changes over time. Disease onset and progression are divided into three consecutive periods that are further assisted by infectiveness:

- The short latent period, where clinical symptoms are not visible after the infective agent enters the body; the incubation period is ongoing.
- During the patient period, both infection and clinical manifestations are fully fledged.
- During the recovery period, infection clearance occurs, and clinically identifiable features that might be long-lasting may be present.

Like other infectious diseases, all these episodes occur step-by-step in trachoma [12]. Importantly, the incubation period of trachoma is approximately 5–10 days, but frequent reinfections occur even in diseased infants. An infected person will be able to spread infections within 2–3 months, which fully depends on the status of infectivity.

5. TRANSMISSION OF CT

Trachoma is a communicable disease that spreads directly by establishing close contact with the infected person (touching one's eyes through one's fingers) or indirectly through the use of infected face cloths or eye-seeking flies; hence, it is also a vector-borne disease. The transmission of C. Trachomatis may be environment specific, especially in the case of eye-seeking flies. *Musca sorbens* (female) is a prominent eye-seeking fly that is able to transmit bacteria and is caught on the faces of Ethiopian children, and its chlamydial appearance was proven in approximately twenty percent of flies via polymerase chain reaction (PCR) [13]. Additionally, the number of patients with active trachoma decreases with decreasing fly population, as reported by Gambian studies [14]. However, *M. Sorbens* cannot transmit bacteria uniformly throughout the world and is high in one place but less so in another. Animal reservoirs of Ct are still not found, and eye-seeking flies play roles just as vectors. Although it is still unknown whether infection caused by Ct may affect flies or how bacterial replication occurs, the latest study on *Musca domestica* [15] confirmed the presence of live bacteria within the fly for up to two days since the feeding of infected human exudates consisting of proteins was helpful for fly ovulation. However, bacteria are also visible in nasal discharges, which are nasopharyngeal secretions that may lead to the initiation of systemic reactions along with severe conjunctivitis.

Worryingly, a single dose of an antibacterial drug cannot cure fatal trachomatous conjunctivitis; moreover, infected secretions pass via the nasolacrimal ducts and continue to damage. A genotype-based study of samples obtained from the conjunctiva and nose of the same person with active trachoma revealed that both infected samples are genotypically distinct, indicating that different variants of *C. Trachomatis* may be responsible for inducing site-specific infections [16]. Hence, the three ‘Fs’ that best summarize the transmission of Ct are Fingers, Fomites (face-cloths/towels) & Flies.

6. GLOBAL PREVALENCE

Ct-induced blindness to trachoma is irreversible and poses significant threats to the least developed countries, especially those where poverty is too high. According to the latest reports (2024) of the WHO, many regions of Africa, Asia, Australia, Central and South America and the Middle East exhibit hyperendemicity, possibly because the poorest and rural communities are populated there and their unhealthy lifestyle massively facilitates the transmission of Ct. Ethiopia is the most affected and prevailing country, with approximately 61 million people residing in areas with trachoma endemicity, representing the largest burden (59%) of trachoma globally, and worryingly, they secured first rank consecutively over many years, which continues. The next most prevalent country is Sudan, where the percentage of infantile trachoma recorded is approximately 60%, still posing one of the major problems for public health. Worldwide, almost 40% of trachoma-endemic communities are located in various nations of Africa except Ethiopia [17].

To date, almost 1.9 million people are blind or visually impaired due to trachoma worldwide; the percentage of blindness globally is 1.4%. Epidemiological studies in 2023 revealed that approximately 115.7 million people were at risk of trachoma, but currently, the number of trachoma-related cases has declined to almost 103.2 million, and trachoma-related cases are located in trachoma-endemic regions [2]; 10 years ago, the number of people localized in trachoma-endemic regions was 125 million [1]. However, despite the reduced risk of trachoma, the economic burden on infected persons and their families has increased enormously worldwide. Recent studies on the economic loss of global productiveness revealed that the calculated amount is approximately US\$ 2.9—5.3 billion per annum in the case of blind and visually impaired people, which further increased to US\$ 8 billion when TT was added.

Recently, 18 nations have been able to eliminate trachoma as a public health issue, as validated by the WHO, such as Benin, Cambodia, China, Gambia, Ghana, the Islamic Republic of Iran, Iraq, Lao People’s Democratic Republic, Malawi, Mali, Mexico, Morocco, Myanmar, Nepal, Oman, Saudi Arabia, Togo, and Vanuatu [2]. The goal of ten other countries is also to achieve prevalence targets for eliminating trachoma—Botswana, Burundi, Guatemala, India, Mauritania, Namibia, Pakistan, Papua New Guinea, Tunisia, and Vietnam [2]. Countries where no current histories regarding trachoma prevalence have been estimated by the WHO, such as European nations and two other countries, the Congo [18] and Timor-Leste [19], are not marked with colour, as depicted in Fig. 2. Trachoma is considered a hazard of public health in almost 39 countries, as the dataset was prepared from the GET 2020 database after the latest district-based prevalence studies. Thorough surveillance for trachoma prevalence may be needed for three other countries, but sufficient inspections have not yet been completed effectively for checking suspicious regions with trachoma endemicity.

The global survey for trachoma prevalence undertaken by the WHO is quite complicated, as the survey solely depends on district-wise information provided by different countries while organizing national programs, and gradual limitations in data or data-gapping frequently occur in such a way. Global validation by the WHO suggests that any district may be able to record up to three consecutive estimations per the respective temporal settings within a single calendar year. In the case of isolated reports, actual fluctuations in zonal prevalence rates and the number of patients with AT, increases in the severity of clinical features (the amount of time required to develop from TF to TT or CO if untreated or treated with antibiotics), and so many cannot be obtained properly, which misleads the agenda for eliminating trachoma globally. However, efforts are needed for interventions, and the point prevalence snapshot for 15 April 2024 can be compared with that of 25 April 2023, which was prepared and validated by the WHO.

7. RISK FACTORS ASSOCIATED WITH TRACHOMA

Several factors associated with trachoma incidence have been identified to date, as reported by earlier studies, and these factors can significantly increase the risk of developing trachoma; however, interpretation of these factors is very complicated, as they act differently on the basis of the environment, socioeconomic status, and individual behaviour. In addition, inadequate controllability of these factors might also be responsible for the increase in active cases. Poor hygiene is frequently considered one of the most important risk factors, as unclear faces play significant roles in the transmission of trachoma. It may be manipulated environmentally, socioeconomically or behaviourally. In regions where drought is frequent, rural and poorest communities cannot sanitize themselves properly due to water deficiency or pure water unavailability, especially in sub-Saharan countries. In addition, those who are financially stable and have access to clear water may also become infected, possibly because they have the least education or awareness of facial cleanliness. Crowded sleeping arrangements also increase the risk of developing trachoma [20], which doubles when individuals share the same bedding. As mentioned above, flies, especially eye-seeking flies, can actively transmit infection and increase risk many-fold.

Age-related risks are very common in trachoma; in regions with trachoma endemicity, communities generally achieve the first stage of infection at the very beginning of life, probably the first month after birth. Here, disease occurrence was highest in children, and greater bacterial loading was observed in infected young individuals than in other individuals [21]. Owing to their lack of effective acquired immunity, they are affected much more, so they are at high risk, although the immune response will mature after exposure to repeated infections as age increases. The risk of trachoma may differ according to sex, as evidenced by previous studies. Prepubertal children (males and females) are infected in equal proportions, but the rate/risk of infection predominantly increased in the case of adult females, almost 2—4 times higher than that of males, and it seems to be controlled by occupational status (for those who are directly associated with health services), genetic makeup, hormonal factors, etc.

8. ‘SAFE’ STRATEGY

In 1998, the WHO established the Alliance for the Global Elimination of Blinding Trachoma by 2020 (GET 2020) and implemented the ‘SAFE’ strategy for preventing *C. Trachomatis*-induced infectious disease, of which four components imply four different meanings: ‘S’ for surgical treatments, ‘A’ for antibiotics, ‘F’ for facial cleanliness, and ‘E’ for environmental improvements.

8.1. Surgical Treatments

Surgical treatments for TT are principally applied to limit the progression to CO and blindness due to continuous scratching of the cornea by the eyelids. Surgery is comfortable for patients with TT, as it provides better improvement in vision and decreases in discharge from the eyes. In this context, the WHO suggests that surgeries should be performed regularly through several outreach programs, especially in regions with trachoma endemicity for trichiasis patients. However, a number of methods are employed for the treatment of trichiasis, including the method of making a full-thickness incision via the tarsal plate in combination with some evertting sutures to turn the distal portion of the eyelashes outwardly [22]. However, the WHO-recommended method for successful trichiasis treatment is bilamellar tarsal rotation (BLTR), which also incises the skin and yields the best outcomes.

Nevertheless, the number of patients receiving surgery is significantly low, especially in trachoma-endemic areas, possibly due to fear and expensiveness of surgery, transport difficulties, lack of knowledge regarding the necessity of treatment, etc. Despite the insufficiency of properly trained surgeons/healthcare practitioners, sterilized surgical kits are also considered barriers to low-level surgeries. Individuals can actively participate in community-based programs for trichiasis surgery when efficient surgeons, nurses, sterilized surgical equipment, etc., are in high demand and when there is no or little demand from patients’ families. This is possible only when governments take initiative in mass surgery. In addition, postsurgical complexities associated with trichiasis are frequently reported, and the major drawback of trichiasis surgery is its high recurrence rate (rate: 20%-60%). Postsurgical trichiasis recurrence depends on various factors, including the type of method applied, expertise level of the surgeon, intensity of infection and status of disease before the operation. Importantly, many studies have reported that Ct-induced recurrent trichiasis after surgery is generally not common; bacteria other than Ct may infect and cause recurrence, although further studies are needed.

8.2. Antibiotic Treatment

Two kinds of antibiotics are used to control Ct infection: tetracycline for external use and azithromycin for internal use. Either 1% tetracycline eye ointment can be used two times per day for up to six weeks, or a single oral dose of azithromycin can be used; however, both of these options have been shown to be effective. Notably, azithromycin is more efficacious than tetracycline in operative cases. There are many complexities associated with the application of tetracycline ointment, such as an inaccurate duration of dosage administration (doctor-to-doctor may vary), frequently reported side effects (stinging and blurred vision are most common), etc.

A comparable oral dose of azithromycin poses very few side effects and is widely accepted and prescribed for both infants and adults. In addition, it is able to reduce the case fatality and death rates of infants significantly and effectively prevent extra-ocular Ct infections.

Weight-based dosages of azithromycin are administered to infants (20 mg/kg body weight), whereas adults may receive 1 g of azithromycin. Height is also considered a determining factor for dosage administration and is successfully applied instead of weight, as weight-based methods require regular calibrations, and carriage difficulties may persist. However, oral medication is not allowed for infants younger than six months or pregnant mothers; hence, tetracycline ointment can be used. As per the recommendations of the Centre of Disease Control (CDC), children (< 1 month), those infected with pertussis and pregnant mothers suffering from urogenital infections caused by extra-ocular Ct can take a single oral dose of azithromycin.

If the oral drug may be converted into eye drops that are more specific in action with minimal side effects, azithromycin eye drops could be developed. Mass treatment through 1.5% azithromycin eye drops in districts of Cameroon was found to be effective, as the percentage of prevalent communities decreased from 31.5% to 6.3% within one year [23]. Antibiotic-resistant strains of Ct have not been developed even after multiple administrations of azithromycin.

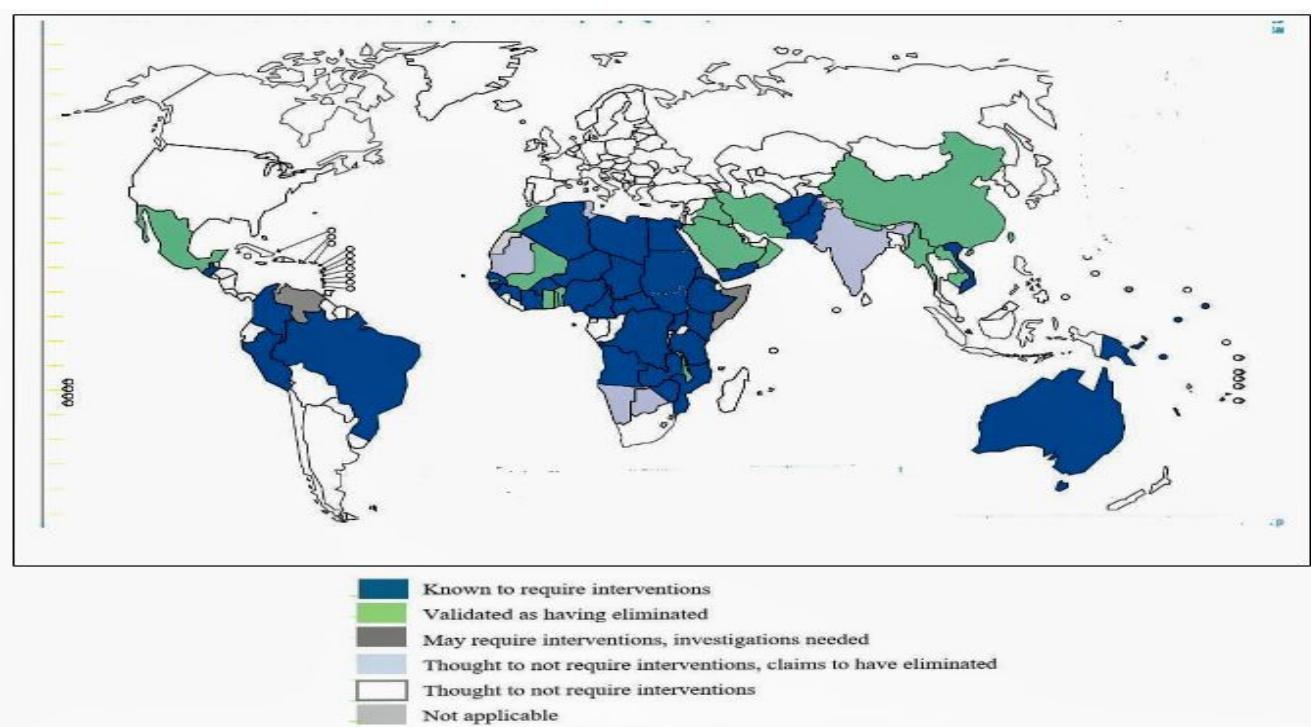


Figure 2. Global Prevalence and Elimination of Trachoma. The boundaries and names shown, and the designations used on this map don't imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city, or area or of its authorities ,or concerning the delimitation of its frontiers or boundaries. Adapted with permission from WHO [2].

8.3. Facial Cleanliness

Cleaned faces have been shown to minimize the risk of autoinfection and infection. Facial cleanliness refers to the proper removal of exudates from the eyes and nose of an infected person, which is generally achieved once awareness or basic knowledge about health and hygiene is developed and when clean water also plays an important role. However, very few confidential documents regarding the role of facial cleanliness in reducing the prevalence of trachoma have been reported. Face cleaning largely depends on individuals' own choices, and naturally, questions arise in the case of self-validated reports, as they may be self-biased. A study conducted at the end of the 20th century revealed a strong correlation between frequent face clean up and decreased infection among Mexican infants. However, the validity of this study has been further validated by many researchers, and in most cases, only face washing, even in combination with tetracycline ointment, does not effectively reduce active trachoma.

8.4. Environmental Improvements

The fourth component of the 'SAFE' strategy encourages hygienic development with respect to the person and environment against Ct infection. Since World War II, Europe and North America have been able to eliminate disease by improving the environment sustainably, and since 1950, there have been no requirements for interventions [24]. The transmission of Ct is significantly reduced by improving the surrounding environment, such as by increasing the accessibility of pure water and latrine, decreasing the population of flies, minimizing overcrowding and educating people about health and hygiene. Although mass antibiotic treatment provides superior protection to the 'F' and 'E' components under the 'SAFE' strategy, sustainable improvement of the environment can reduce case fatality and mortality accordingly and provide passive protection. Very few studies on decreases in the fly population suggest a reduction in prevalent communities as a result of insecticidal sprays for declining populations of eye-seeking flies.

9. IMPLEMENTATION OF THE 'SAFE' STRATEGY BY THE WHO

On the basis of the WHO's implementation of the 'SAFE' strategy, the latest datasheet on trachoma elimination worldwide was prepared. In this context, it is important to know which criteria should be considered for eliminating trachoma as a public health problem, and these criteria are as follows:

- The prevalence of trichiasis should be less than 0.2% among people whose age is either equal to or greater than 15 years.
- The prevalence of TF should remain below 5% among infants aged 1—9 years living in districts with former endemicity (each district consists of 100,000—250,000 individuals).
- Each health system should play a role in the consecutive identification and management of cases of trichiasis.

According to the current WHO weekly epidemiological record (WER), the prevalence of trichiasis remains equal to or greater than 0.2% among individuals aged ≥ 15 years in 1726 districts globally.

In addition, the prevalence of TF remains equal to or greater than 5% among 1—9-year-old infants living in 984 districts during 2023 and in the majority of their habitats in African countries, especially Ethiopia.

However, the last three components of ‘SAFE’ viz. A, F and E are not applicable for districts of European and Southeast Asian countries, as they eliminate trachoma (Table 1). The WER suggests that 130,746 individuals were operated on for trichiasis globally in 2023, which is slightly greater than in the previous year (2022): 129,224. Surgical treatments for trichiasis are progressing, as almost 75% of global surgeries occurred in 2023 in Ethiopia only. In addition, 70% of patients were females who received surgical treatments, as reported by 37 nations globally, indicating sex bias.

Table 1. Prevalence of Trachoma and Implementation of ‘SAFE’ strategy in WHO regions (2023-24).
Adapted with permission from WHO [2].

WHO Regions	2024			2023					
	Districts with prevalence of trachiasis $\geq 0.2\%$ in ≥ 15 -year-olds	Population in areas that warrant treatment with antibiotics, facial cleanliness, and environmental improvement for eliminating trachoma as a public health problem	Number of people managed for TT	Population in areas that warrant treatment with antibiotics, facial cleanliness, and environmental improvement for eliminating trachoma as a public health problem	Number of individuals were treated with antibiotics	Total number of districts that warranted treatment with antibiotics, facial cleanliness, and environmental improvement for eliminating trachoma as a public health problem	Geographical coverage (%)	Proportion of treated districts reporting $\geq 80\%$ antibiotic coverage (%)	National coverage (%)
African	1543	93,127,397	125,431	103,320,820	31,996,279	837	33.9	82.4	31.0
America s	7	333,519	4	333,519	29,548	8	37.5	75.0	8.7
Eastern Mediterranean	131	6,570,595	1014	7,305,517	895,241	53	11.3	83.3	12.3
South–East Asia	0	0	499	0	0	0	0	0	0
Western Pacific	45	3,211,760	3,798	3,211,760	10,649	86	3.5	16.7	0.3
Global	1726	103,243,271	130,746	114,171,616	32,931,717	984	30.1	81.1	28.8

Approximately 32,931,717 people previously received antibiotic treatments for trachoma globally, with 33.9 million administered doses of antibiotics (Table 1); comparatively, the number of individuals receiving antibiotic treatment was 36.2 million in 2022 and 64.6 million in 2021. These individuals were able to receive antibiotic treatments during the time of surgery for trichiasis/after the diagnosis of active trachoma/during the mass antibiotic treatment programs. A total of 32,931,717 individuals were treated with antibiotics, representing 29% of 114,171,616 individuals living in 984 districts in which mass drug administration programs had been taken as a part for eliminating trachoma in 2023.

The relevant donation of antibiotics was performed by the International Trachoma Initiative (ITI) to nations with trachoma endemicity, and the majority of antibiotics of interest were azithromycin. A similar figure is visible in Ethiopia as that of mass surgical treatments, i.e., overall, 65% of total antibiotic treatments globally occurred in the previous year in this country only. Additionally, sex-unbiased data concerning the treatment of trachoma with antibiotics have also been collected from 17 countries, suggesting that 52% of all patients who received treatments in 2023 were females. The first two components of 'SAFE' viz. 'S' and 'A' provide better protection than 'F' and 'E' do and have much information, as it is possible to apply them uniformly and widely documented. The evidence of successful applications of the last two components is relatively low, and the results depend on many factors that cannot directly protect against active trachoma but are known to reduce transmission. Importantly, the success of these two methods is promoted by awareness programs undertaken by allied agencies of governments and ministries of health.

Hopefully, the number of individuals at risk of trachoma was 204.4 million in 2014, but now, in 2024, it has decreased to 103.2 million, i.e., a 49% reduction within 10 years, which makes continuous interventions by different countries possible. The global burden of trichiasis has significantly decreased from 2.8 million individuals (2016) to 1.5 million (2024), indicating an almost 47% reduction. To date, 18 countries are able to eliminate trachoma as a public health problem by applying the 'SAFE' strategy, and other countries are attempting to achieve the goal of eliminating trachoma.

10. CONCLUSION

Trachoma, an NTD, becomes more severe if untreated, causing blindness, as seen in many poor and rural communities living in trachoma-endemic regions, but continuous interventions make it less prevalent. Through the sustainable application of the 'SAFE' strategy, European and North American countries were able to prevent disease, and many new strategies are then developed and continue.

In 2021, the WHO fixed a roadmap for eliminating all NTDs, including trachoma, worldwide by 2030. The identification of suspected trachoma-endemic regions, modifications, and region-specific applications of four components of SAEs, etc., are specifically emphasized in this roadmap. Further studies with this purpose are needed, and if all initiatives and/or programs regarding trachoma elimination and optical health improvements are successful, then we can expect a trachoma-free world in 2030.

References

- [1] WHO (2022) Trachoma, *factsheet*. World Health Organization ,Geneva.
- [2] WHO (2024) WHO Alliance for the Global Elimination of Trachoma: progress report on elimination of trachoma,2023. *Weekly epidemiological record* 99(28), 363-380.
- [3] Gitsels A, Sanders N and Vanrompay D (2019) . Chlamydial infection from outside to inside. *Front. Microbiol.* 10 ,2329.
- [4] El-Asrar AM, Van den Oord JJ, Geboes K, Missotten L, Emarah MH and Desmet V(1989). Immunopathology of trachomatous conjunctivitis. *Br J Ophthalmol.* 73 (4), 276-282.
- [5] Thylefors B, Dawson CR, Jones BR, West SK and Taylor HR (1987). A simple system for the assessment of trachoma and its complications. *Bull World Health Organ.* 65 ,477-483.
- [6] Burton MJ and Mabey DC (2009). The global burden of trachoma: a review. *PLoS Neglected Tropical Diseases* 3, e460.
- [7] Rottenberg ME, Gigliotti-Rothfuchs A and Wigzell H (2002). The role of IFN-gamma in the outcome of chlamydial infection. *Curr Opin Immunol.* 14,444-451.
- [8] Grassly NC, Ward ME, Ferris S, Mabey DC and Bailey RL (2008). The natural history of trachoma infection and disease in a Gambian cohort with frequent follow-up. *PLoS Neglected Tropical Diseases* 2 ,e341.
- [9] West SK, Munoz B, Mkocha H, Hsieh YH and Lynch MC (2001) . Progression of active trachoma to scarring in a cohort of Tanzanian children. *Ophthalmic Epidemiol.* 8 ,137-144.
- [10] Natividad A, Hanchard N, Holland M J, Mahdi O S M, Diakite M, Rockett K, Jallow O ,Joof H M, Kwiatkowski D P, Mabey D C and Bailey R L (2007). Genetic variation at the TNF locus and the risk of severe sequelae of ocular Chlamydia trachomatis infection in Gambians. *Genes Immun.* 8 (4), 288-295.
- [11] Miller K, Schmidt G, Melese M, Alemayehu W, Yi E, Cevallos V, Donnellan C, Olinger L, Fantaye D, Gaynor B, Whitcher JP and Lietman T(2004b). How reliable is the clinical exam in detecting ocular chlamydial infection? *Ophthalmic Epidemiol.* 11(3), 255-262.
- [12] Wright HR, Turner A and Taylor HR (2008) . Trachoma. *Lancet* 371, 1945-1954.
- [13] Lee S, Alemayehu W, Melese M, Lakew T, Lee D, Yi E, Cevallos V, Donnellan C, Zhou Z, Chidambaram JD, Gaynor B, Whitcher JP and Lietman T(2007). Chlamydia on children and flies after mass antibiotic treatment for trachoma. *Am. J. Trop. Med. Hyg.* 76 (1), 129-131.
- [14] Emerson P, Lindsay SW, Alexander N, Bah M, Dibba SM, Faal HB, Lowe KO, McAdam K P W, Ratcliffe AA, Walraven G E L and Bailey RL (2004). Role of flies and provision of latrines in trachoma control: cluster-randomized controlled trial. *Lancet* 363 , 1093-1098.

- [15] Brewer N, McKenzie MS, Melkonjan N, Zaky M, Vik R, Stoffolano JG and Webley WC (2021). Persistence and significance of Chlamydia trachomatis in the housefly, *Musca domestica* L. *Vector Borne Zoonotic Dis.* 21(11), 854-863.
- [16] Andreasen AA, Burton MJ, Holland MJ, Polley S, Faal N, Mabey DC and Bailey RL (2008). Chlamydia trachomatis ompA variants in trachoma : what do they tell us? *PLoS Neglected Tropical Diseases* 2, e306.
- [17] Gebre T, Kello A and Emerson P (2020). Current status of trachoma elimination in Africa. *International Journal of Infectious Diseases* 101, 383
- [18] Missamou F, Marlhand H, Dzabatou-Babeaux A, Sendzi S, Bernasconi J, D'Souza S, Bakhtiari A, Millar T, Willis R, Bengraïne K, Resnikoff S and Solomon AW (2018). A population-based trachoma prevalence survey covering seven districts of Sangha and Likouala departments , Republic of the Congo. *Ophthalmic Epidemiol.* 25, 155-161.
- [19] Correia M, Brunner D, Sharma M, Andrade V, Magno J, Müller A, Pereia BM, Thumann G, Verma N, Bangert M, Kreis AJ and Solomon AW (2018). A search for trachoma in Timor-Leste: no evidence to justify undertaking population-based prevalence surveys. *Ophthalmic Epidemiol.* 25, 131-137.
- [20] Taylor HR (2001). Trachoma in Australia. *Med. J. Aust.* 175, 371-372.
- [21] Taylor HR, Siler JA, Mkocha HA, Munoz B and West S (1992). The natural history of endemic trachoma: a longitudinal study. *Am. J. Trop. Med. Hyg.* 46, 552-559.
- [22] Yorston D, Mabey DC, Hatt S and Burton MJ (2006). Interventions for trachoma trichiasis. *Cochrane Database of Systematic Reviews* 3, D004008.
- [23] Huguet P, Bella L, Einterz E, Goldschmidt P and Bensaid P (2010). Trachoma mass treatment with azithromycin 1.5% eye drops in Cameroon: feasibility, tolerance and effectiveness. *The British Journal of Ophthalmology* 94, 157-160.
- [24] Mabey DC, Solomon AW and Foster A (2003). Trachoma. *Lancet* 362, 223-229.