Eye (2005) 19, 1067–1073

www.nature.com/eye

CAMBRIDGE OPHTHALMOLOGICAL SYMPOSIUM

Can blinding trachoma be eliminated by 20/20?

J Kumaresan

Abstract

Trachoma is the leading cause of preventable blindness in the world today. Long ago eliminated in North America and Europe, the disease is almost unknown, and indeed forgotten, in the West. Nevertheless, it continues to wreak havoc in the poorest parts of Africa, Asia, and other areas throughout the world. The World Health Organization (WHO) estimates that there are currently 7.6 million people who are visually impaired due to trachoma, and 84 million people with active infections. In 1998, WHO passed a resolution calling for member states to take action to eliminate blinding trachoma by the year 2020. The scale of what must be accomplished in order to reach this goal is daunting. However, the work of the International Trachoma Initiative together with national governments as well as other organizations in applying the WHO-recommended SAFE strategy for trachoma control has produced critical successes in challenging settings. This paper gives a brief history and description of trachoma, explains treatment options and the SAFE strategy, and discusses successes from two trachoma control programmes as examples of how to move forward in eliminating this devastating disease.
Eye (2005) **19,** 1067–1073. doi:10.1038/sj.eye.6701963

Keywords: trachoma; blindness; partnership; SAFE strategy; ITI

Introduction

Trachoma is an ancient scourge that was described in the Egyptian Ebers papyrus in 1900 BC and well known to Hippocrates.[1] It persists and even flourishes today as the world's leading cause of preventable blindness. Long ago eliminated in North America and Europe, trachoma is almost unknown, and indeed forgotten, in the West. Nevertheless, it continues to wreak havoc in the poorest parts of Africa, Asia, and other areas throughout the world. It is a disease associated with poverty, low income, poor hygiene, high numbers of flies, and lack of access to water are all implicated in prevalence.[1] Trachoma disproportionately affects women and children. Women are blinded up to three times more often than men, and sadly, the prevalence of infection is highest in 1–5 year olds. The World Health Organization (WHO) estimates that there are currently 7.6 million people are visually impaired due to trachoma, and 84 million people with active infections. Trachoma causes approximately $2.9 billion in productivity losses per year, blinding 10 times as many people as the better-known River Blindness.[2]

The need for action to address this devastating disease is clear. In 1998, WHO passed a resolution calling for member states to take action to eliminate blinding trachoma by the year 2020. Developments over the past 5 years have been highly encouraging, and if the resources, commitment, and political will can be mobilized, the goal of global elimination by 2020 will be within our grasp.[3]

History of trachoma

Descriptions of clinical signs of trachoma, including trichiasis—in-turned eyelashes—and surgery for their removal are found in Egyptian papyri. Galen is given credit for the first description of trachoma, the name deriving from the Greek word for rough and describing the lymphoid follicles of the upper lid that are considered pathognomic of the disease.[3] Trachoma was treated with Copper Sulfate from Egyptian times through the 1940s.[1]

The disease was first noted in Europe after the Napoleonic wars[4] when tens of thousands of troops returned with trachoma after fighting in Egypt. It spread rapidly through the armies of

International Trachoma Initiative, New York, USA

Correspondence:
J Kumaresan, International Trachoma Initiative, New York, NY 10017, USA
Tel: +1 212 490 6460;
Fax: +1 212 490 6461.
E-mail: jkumaresan@trachoma.org

Received: 14 April 2005
Accepted: 2 May 2005

Presented in part at the 34th Cambridge Ophthalmological Symposium, September 2004

Europe, where the troops lived in crowded and unsanitary barracks, and then into the general population. Trachoma quickly became a disease of the urban slums. As people left their relatively healthy rural homes and were crowded into the workhouses and tenements created by the Industrial Revolution, personal and community hygiene fell to an all-time low and the prevalence of trachoma surged. The disease spread to North America through immigrant populations, and by the 19th century, trachoma was a serious problem both in Europe and in North America.[5]

However, the disease was largely eliminated in Western nations in the early 1900s, due to improved living standards as well as eradication efforts. In the United States, the last Trachoma hospital, located in Kentucky, was closed in 1938. The US took several different approaches to the eradication of trachoma. The first was simply to keep the disease out of the country by denying entry and immigration for anyone showing visible symptoms. The 1891 Immigration Law forbade the entry of 'all idiots, insane persons, paupers or persons likely to become public charges, persons suffering from a loathsome or dangerous contagious disease.'[6] Trachoma, tuberculosis and typhus, among others, fell under this law's purview. As a second means of elimination, in 1913, the US Congress and President Woodrow Wilson authorized the Public Health Service to use money from its 'epidemic fund' to halt the progression of trachoma.[7] At that time trachoma was still a large public health threat in Appalachia: (Kentucky, Tennessee, and Missouri). The Public Health Service set up clinics in affected areas and placed 'traveling Trachoma clinics' on the backs of trains to fight the spread of the disease. These clinics used topical tetracycline and taught the importance of good hygiene as a method of combating the disease. These same methods are still employed in many countries around the world today.

The cause of trachoma was identified in 1907, when cytoplasmic inclusions in epithelial cells in Giemsa-stained scrapings from the conjunctiva of Indonesian children with trachoma were described. They called them *Chlamydozoa*, or cloaked animals, because of the way in which the inclusions were draped around the nucleus of the cell, however; it was not until 1957 that the organism was successfully isolated.[1]

The isolation and availability of lab-cultured specimens of the organism sparked interest in the possibility of a vaccine. After some limited success in preventing trachoma in subhuman primates, several large-field trials were undertaken in humans in the 1960s in Taiwan, Saudi Arabia, and Italy, and at the MRC trachoma unit in the Gambia. The vaccines were ultimately unsuccessful though the trials greatly advanced understanding of the natural history and pathogenesis of trachoma.[1]

The nature of the disease

Trachoma is a chronic kertoconjunctivitis caused by repeated reinfection with the ocular serovars A, B, Ba, and C of the intracellular bacterium *C. trachomatis* (the other serovars cause genital tract disease). Repeated infections with the ocular strains result in chronic inflammation of the tarsal conjunctiva of the upper lid. The chronic condition results in scarring and shortening of the upper lid with in-turning of the eyelashes (trichiasis). The painful abrading of the cornea, if not corrected, results in corneal scarring, opacity, and blindness.[3] Trachoma is spread by hands, clothing, or flies that have come in contact with discharge from the eyes or nose of an infected person. Hygiene is crucial in preventing the transmission of the disease, and as such it generally occurs in poor countries where people have limited access to water and health care.

Laboratory diagnosis of trachoma is possible using culture, immunofluorescent microscopy, enzyme-linked immunosorbent assay or polymerase chain reaction. However, laboratories are generally unavailable in poor communities where trachoma is endemic, so the diagnosis is usually made clinically. WHO has developed a simplified grading system based on signs and the extent of inflammation, conjunctival thickening and scarring, trichiasis, and corneal opacity.[8] According to this system, the *C. trachomatis* infection has five distinct stages:

The first stage of trachoma is Trachomatous Inflammation—Follicular. In this stage, the infection is just beginning and may not be particularly irritable. Usually five or more follicles, at least 0.5 mm in size, are visible on the 'flat' surface of the upper tarsal conjunctiva[9] (Figure 1).

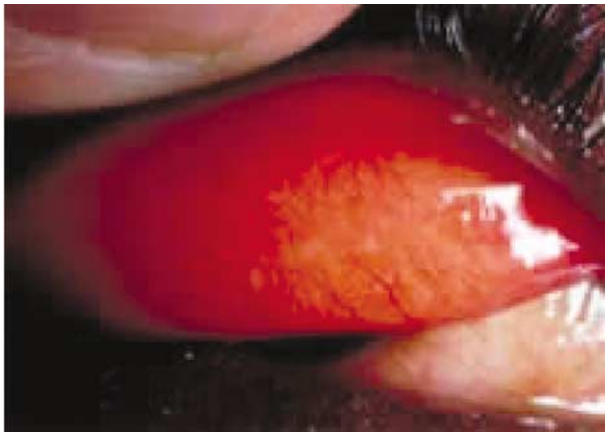

Figure 1 The first stage of trachoma is Trachomatous Inflammation.

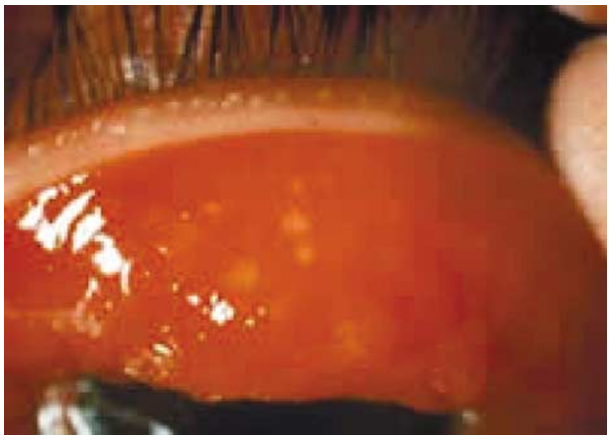

Figure 2 The second stage of trachoma is Trachomatous Inflammation.

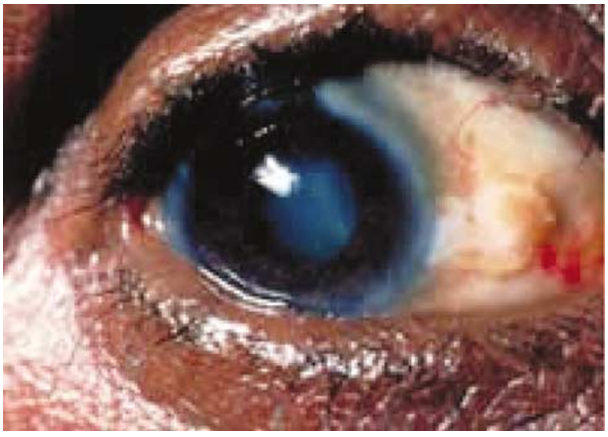

Figure 4 The fourth stage of trachoma is Trachomatous Trichiasis.

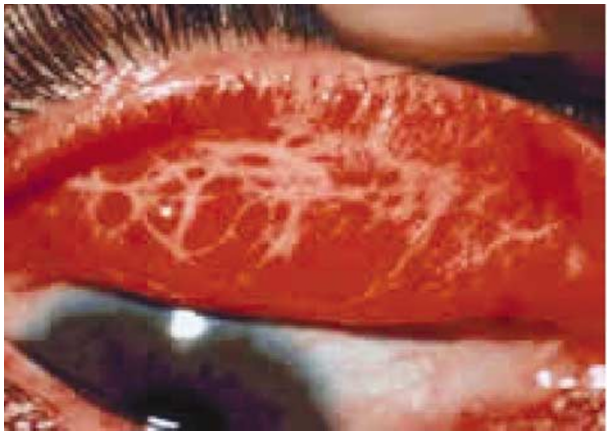

Figure 3 The third stage of trachoma is Trachomatous Scarring.

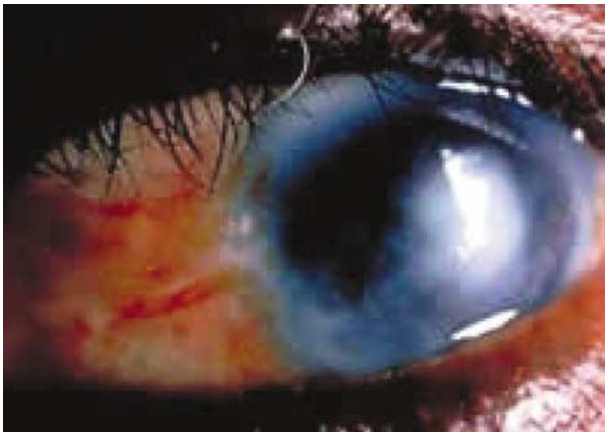

Figure 5 The fifth and final stage of trachoma is Corneal Opacity due to trachoma.

The second stage of trachoma is Trachomatous Inflammation—Intense.[10] In this stage, the eye becomes more irritable and is highly infectious. An inflammatory thickening of the upper tarsal conjunctiva with more than half of the normal deep tarsal vessels obscured is seen (Figure 2).

The third stage of trachoma is Trachomatous Scarring.[11] Repeated infection leads to scarring of the tarsal conjunctiva. At this stage, the eyelid starts to distort and turn in (entropion) and trichiasis begins (Figure 3).

The fourth stage of trachoma is Trachomatous Trichiasis.[12] In this stage, the scarred inner lining deforms the lid margin causing the eyelid to fold inwards. Inversion of the upper eyelid brings the eyelashes in contact with the cornea of the eye, thereby scratching the surface of the eye with each blink or movement of the eyelid. This painful condition is called trichiasis (Figure 4).

The fifth and final stage of trachoma is Corneal Opacity due to trachoma. In this stage, the scarring of the cornea that has occurred will be sufficient to partially or wholly blind the patient (Figure 5).

Progress in the last decade

GET 2020 Alliance

On a scientific basis, the case for elimination of blinding trachoma was outlined at a WHO global scientific meeting in 1996. To facilitate action, WHO founded the Alliance for Global Elimination of Trachoma by 2020 (GET 2020) in 1997. In 1998 a World Health Assembly resolution called for member states to take steps to eliminate blinding trachoma by 2020 using the WHO recommended SAFE strategy. These developments contributed to the decision by Pfizer Inc to donate azithromycin in support of national programmes implementing SAFE and, with the Edna McConnell Clark Foundation, to found the International Trachoma Initiative as a public charity organization dedicated to the elimination of blinding trachoma by 2020.

Vision 2020

In 1999, the WHO, with the International Agency for the Prevention of Blindness (IAPB), a partnership of eye care organizations, launched the VISION 2020: The Right to Sight initiative, under whose umbrella the GET Alliance now falls. VISION 2020 aims 'to eliminate avoidable blindness in the world by 2020' and targets the world's leading causes of avoidable visual impairment: cataract, trachoma, onchocerciasis, childhood blindness (including vitamin A deficiency), and refractive error and low vision. In areas of the world where these focal conditions have been controlled, glaucoma and diabetic retinopathy are included among the targeted conditions.[13]

SAFE

Given that the quarantine methods of the 19th century were no longer practical in the 20th a new angle of attack for combating trachoma was needed. Therefore, based on extensive research and evidence from studies and intervention projects, the 'SAFE' (or 'CHANCE' in French) strategy was developed by WHO in the 1997 and mandated in January of 1998. The SAFE strategy consists of:

Surgery for trichiasis
Antibiotics for active treatment of active (inflammatory) trachoma
Face washing
Environmental change

Surgery

Trachomatous trichiasis (stage TT) can be corrected surgically through a quick and simple procedure called bilamellar tarsal rotation, which involves division of the upper eyelid tarsal plate with external rotation of the distal margin by use of three or four sutures.[8] This allows the eyelashes to be rotated away from the eye to prevent further scarring of the cornea. Ophthalmic assistants and nurses can be trained in 2 weeks to perform the surgery using local anaesthetic. The procedure itself takes about 15 min, and long-term success rates are around 80%.[14]

Antibiotics

Active or inflammatory trachoma can be treated with antibiotics. For many years, a topical preparation of tetracycline has been used to treat trachoma. However, the ointment must be applied in the eyes twice a day for 6 weeks, and as such is irritating and difficult to use. Moreover, ocular *Chlamydia serovars* have been recovered from rectal and nasopharyngeal tissue in 28% of children in communities with trachoma. Extraocular reservoirs of infection are not amenable to topical therapy and may have a role in transmission of the organism even after successful treatment of the conjunctiva.[3]

By contrast, azithromycin is a single-dose oral systemic antibiotic that results in high tissue to serum concentrations; its concentration in phagocytes ensures delivery to infected tissues, and it provides high, sustained tissue levels as well as high concentrations in tears. Field trials in Africa, Asia, and the Middle East have shown that administration of a single dose of azithromycin clears infection by *C. trachomatis* as well as or better than the 6-week course of tetracycline ointment.[3]

Face washing

Face washing breaks the cycle of reinfection and helps to stop the transmission of disease, especially among children. Studies have shown that small amounts of water can keep children's faces clean, and that children with clean faces are much less likely to get or spread trachoma infection. A single litre of water can keep up to 30 faces clean.[15]

Environment change

Environmental improvement is an essential part of trachoma elimination. Poor living conditions contribute to high rates of blinding trachoma in communities around the world—and trachoma, in turn, exacerbates and perpetuates those problems. Overall rates of active disease are therefore closely related to larger environmental and economic concerns. Reducing fly populations, enhancing the management of animal and human waste, and improving access to water are all critical in addressing the problem of trachoma.[14]

International trachoma initiative

In 1998, the Edna McConnell Clark Foundation and Pfizer Inc. founded the International Trachoma Initiative or ITI. As a vital member of the GET 2020 Alliance and VISION 2020, ITI's goal is to achieve global elimination of blinding trachoma by putting the SAFE strategy into action, including donated Zithromax, from Pfizer Inc The ITI supports country programmes to ensure that surgical services are available to patients with advanced disease, that antibiotics are distributed, that face washing is widely publicized, and that communities are working to improve access to clean water and sanitation. Pfizer's Zithromax (azithromycin) donation is a central element of the ITI's support for the SAFE strategy. Zithromax has been proven to be more effective and easier to administer

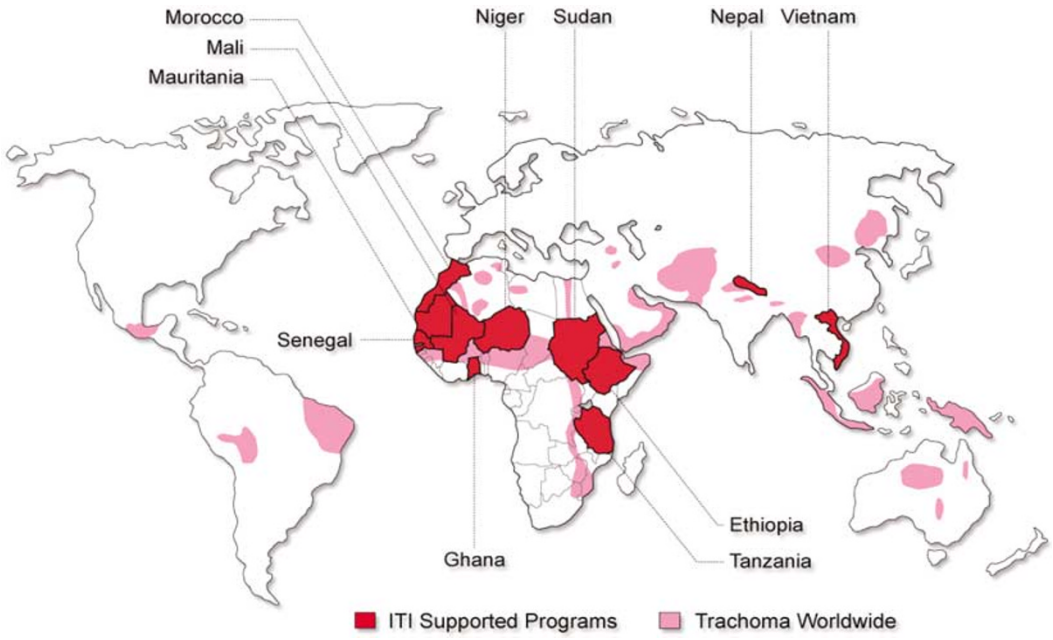

Figure 6 Trachoma worldwide and ITI programmes.

and ensure compliance than the previously recommended regimen of tetracycline eye ointment twice daily for 6 weeks.[3]

Working on an independent basis, the ITI catalyses partnerships among international agencies and governmental and nongovernmental organizations. It seeks to build on growing international momentum to support the WHO's goal of eliminating trachoma by 2020, and to maintain high scientific and management standards in the pursuit of its mission.[14] ITI supports national trachoma programmes in nine countries, and an additional two more in 2004 (Figure 6).

Achievements

Reports of the early programme scope and impact are encouraging. In 11 national programmes currently underway (constituting about 50% of the global burden) more than 143 000 lid surgeries have halted further corneal damage and prevented blindness, and more than 19 million treatments with azithromycin have been given with reductions in acute infections of around 50% in children (Figure 7).[3]

(a) Morocco: The improvement of the standard of living of the majority of the Moroccan population in the last decades has resulted in a notable decline in trachoma infection. However, before the start of the programme, areas of high trachoma prevalence still afflicted many provinces in the arid southeast regions of Morocco. With the support of ITI and other partners, the country has been able to effect a dramatic reduction in trachoma prevalence.[16]

Country	Surgeries	Antibiotic Treatments
Morocco	21 888	4 186 186
Tanzania	10 864	2 760 990
Vietnam	46 561	1 315 104
Ghana	2001	637 100
Nepal	7745	799 270
Niger	15 954	2 770 654
Mali	11 318	4 614 277
Ethiopia	21 017	1 504 441
Sudan	5217	1 041 233
Mauritania	451	103 103
Senegal	437	0

Figure 7 ITI supported programmes 1998–2004.

Figure 8 demonstrates how rapidly and effectively a trachoma control programme using Zithromax can scale up antibiotic treatment. By treating trachoma with azithromycin instead of tetracycline ointment, population coverage has reached more than 90% since 1999. It is clear how much more could and can be achieved with an increased arsenal of antibiotics. With Pfizer's commitment of Zithromax® of 135 million treatments over the next 5 years, 40 million more people

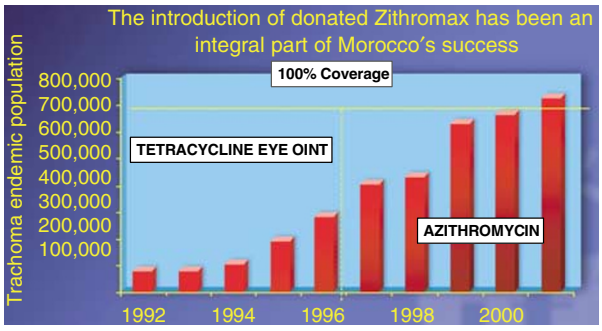

Figure 8 Azithromycin *vs* tetracycline.

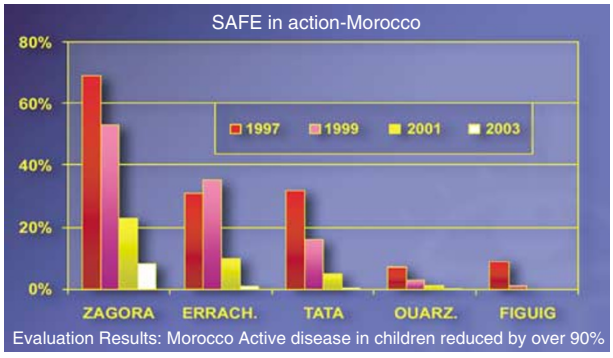

Figure 9 SAFE in action – Morocco.

can be treated.[17] Use of Zithromax results in improved compliance rates and vastly enhanced trachoma control.

As can be seen from Figure 9, Morocco, one of the first countries to implement SAFE with azithromycin, has achieved remarkable results and expects to eliminate blinding trachoma by 2005. Already in 2003, active disease in children had been reduced by over 90%. With sustained efforts, Morocco will be one of the first countries to achieve elimination of blinding trachoma utilizing the SAFE strategy.

(b) Niger: The African country of Niger, in which the national trachoma programme is currently ramping up its population coverage, represents an example of the SAFE strategy in action in a highly challenging setting. Niger is one of the poorest countries in the world. The 2004 UNDP Human Development Index ranked it 176th out of 177: only Sierra Leone ranked lower. In 2004, UNDP also ranked Niger as having the lowest GDI or 'Gender Development Index' in the world. (GDI is an indication of the degree of gender inequity in development between men and women, which is of concern because trachoma disproportionately affects women and children).[18] The country is landlocked and extremely dry, 80% of the country's population lives in rural areas, and the economy is dominated by subsistence agriculture. Trachoma is hyperendemic throughout Niger. A study in 2000 suggested that more than 1 million children under the age of 10 have active infection, and 68 000 adults suffer from severe infection.[19]

Trachoma has long been on the health agenda in Niger; with national trachoma prevalence surveys having been carried out in 1997 and 1999/2000. The PNLCC (Programme National de Lutte Contre le Cecite) was formed by the government in 1987 as part of the Ministry of Health. It is responsible for leading national efforts against blinding diseases. Following the trachoma prevalence survey of 1999/2000, with the help of NGO partners, the PNLCC instituted a national trachoma control programme active in the three regions with highest prevalence: Zinder, Diffa, and Maradi. In 2001, following a request from the Niger Government, ITI became involved as a partner, together with other NGOs and supports the PNLCC, implementing the full SAFE strategy.

At its inception in 2002, ITI provided strategic support for all aspects of the SAFE strategy, training healthcare workers to perform bilamellar tarsal rotation, organizing mobile surgery teams and camps, organizing antibiotic distribution, providing support for a large BBC-developed IEC radio project and managing community-based IEC programmes, water provision and latrine building activities. In 2004, all of the above activities were expanded based on experiences of the first 2 years of the programme, with a new focus on S and A activities, and accelerated efforts to mobilize partners to conduct F and E activities.

The trachoma program in Niger has shown dramatic success in the short time that it has been in operation. Population coverage with Zithromax scaled up swiftly from 91 723 doses distributed in 2002, to over 700 000 in 2003. In 2004, coverage reached yet another dramatic expansion: 1.77 million doses by the end of the year, approximately 20% of Niger's population (Figure 10). An evaluation of the programme in areas in which the full

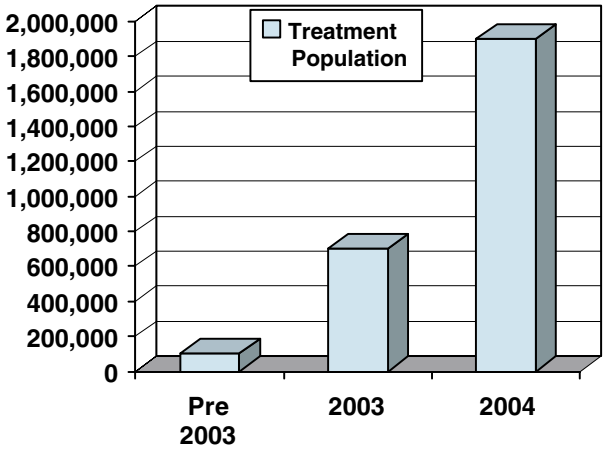

Figure 10 Niger treatment population.

SAFE strategy, including Zithromax distribution, is being implemented, has shown that trachoma prevalence in children under 10 years of age has been reduced by around 40%.[20] It is clear from this country's example that positive partnerships developed with each country can help to rapidly grow and support strong trachoma programmes.

Conclusion

Where there is political will there is a way for success of programmes: strong government involvement and support was critical to progress both in the Morocco and the Niger programmes. ITI recognizes this and therefore seeks to build government ownership and participation in trachoma control programmes. To this end, it has been helping to prepare national 5-year plans in each of its programme, countries that involve various sectors as health education, water, and sanitation. By the end of 2004, around 2 000 000 doses of Zithromax will have been distributed in Niger, 2 800 000 doses in Mali, and over 15 000 trichiasis surgeries will have been performed in Vietnam. It is this type of country-by-country progress that lies at the heart of the future success of 20/20.

A multisectoral approach and cooperation between partners, both international and domestic, is vital. ITI provides expertise and strategic support for surgery and antibiotic distribution, including Pfizer's generous donation of Zithromax towards the elimination of trachoma. It is also committed to providing targeted support to catalyse, mobilize, and leverage partners and national sources to carry out and build capacity for F and E activities. It seeks to develop human resources, scale up grassroots education and improve knowledge of SAFE programmes. New initiatives, such as the recently instituted coalition of blindness prevention NGOs, aim to strengthen cooperation and coordination.

Despite all of the gains made in the fight against trachoma, however, there are still many more challenges that lie ahead. Advocacy is needed to raise awareness of trachoma and the SAFE strategy. Effectively fighting the disease will require better estimates of disease burden, studies on Disability-Adjusted Life Years and more cost–benefit/effectiveness analyses. Integrated approaches to community-based interventions and links with other Public Health programmes are also necessary. Creative collaboration between health, education, and water/sanitation sectors is critical to reducing the disease burden. More applied research to improve SAFE is also warranted.

In the next 5 years ITI will continue to raise awareness and advocacy for the disease through education efforts as well as researching and developing cost-effective tools to combat the disease.

Given the sheer burden of the disease, the task is daunting. However, key accomplishments in countries implementing the SAFE strategy, and strikingly successful examples such as Morocco and Niger are extremely encouraging. If political will and public health support can be mobilized, the goal of eliminating trachoma by 2020 can be achieved.

References

1 Mabey DCW, Bailey R. Eradication of trachoma worldwide. *Br J Ophthalmol* 1999; **83**: 1261–1263.
2 WHO. www.who.int
3 Mecaskey JW, Knirsch CA, Kumaresan JA, Cook JA. The possibility of eliminating blinding trachoma. *Lancet J Infect Dis* 2003; **3**: 728–734.
4 Timothy Tan. *Medical Ecology*. http://medicalecology.org/water/w_trachoma.htm
5 Taylor H. Trachoma in Australia. *Med J Australia* 2001; **175**: 371–372.
6 National Library of Medicine. National Institutes of Health. *http://www.nlm.nih.gov/exhibition/phs_history/20.html*
7 National Library of Medicine. National Institutes of Health. *http://www.nlm.nih.gov/exhibition/phs_history/26.html*
8 Weir E, Haider S, Telio D. Trachoma: leading cause of infectious blindness. *Canad Med Assoc J* 2004; **170**: 1225.
9 International Centre for Eye Health. http://www.iceh.org.uk/files/tsno7/text/10.htm
10 International Centre for Eye Health. http://www.iceh.org.uk/files/tsno7/text/11.htm
11 International Centre for Eye Health. http://www.iceh.org.uk/files/tsno7/text/12.htm
12 International Centre for Eye Health. http://www.iceh.org.uk/files/tsno7/text/13.htm
13 Pizzarello L, Abiose A, Ffytche T, Duerksen R, Thulasiraj R, Taylor H *et al*. VISION **2020**: the right to sight: a global initiative to eliminate avoidable blindness. *Arch Ophthalmol* 2004; **122**: 615–620.
14 International Trachoma Initiative: SAFE strategy. http://www.trachoma.org/safe.asp
15 McCauley AP, Lynch M, Pounds MB, West S. Changing water-use patterns in a water-poor area: lessons for a trachoma intervention project. *Soc Sci Med* 1990; **31**: 1233–1238.
16 International Trachoma Initiative. Program Reports.
17 International Trachoma Initiative. Trachoma Presentation Pfizer Board Meeting March 2004
18 UNDP statistics. http://hdr.undp.org/statistics/data/
19 International Trachoma Initiative. http://www.trachoma.org/niger.asp
20 International Trachoma Initiative, evaluation reports.