

Trachoma Matters



Somewhere in Africa, Photo credits: Doug Menez

Special Edition:

History of Trachoma

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international
trachoma
initiative

Dedicated to eliminating
the world's leading cause
of preventable blindness

Start

Trachoma is a **preventable** disease that affects the eye and can lead to blindness if left untreated. Repeated infections scar and distort the inner upper eyelid, causing the eyelashes to turn inwards and scratch the cornea, ultimately leading to blindness.

Trachoma has been causing blindness for several millennia. The history of trachoma cannot be pinpointed precisely because scientists have only gained a thorough understanding of the disease within the last several decades. However, the history of ophthalmias, eye diseases with visible symptoms, is frequently documented. Through these records and a modern understanding of trachoma, the history of this ancient disease can be constructed.

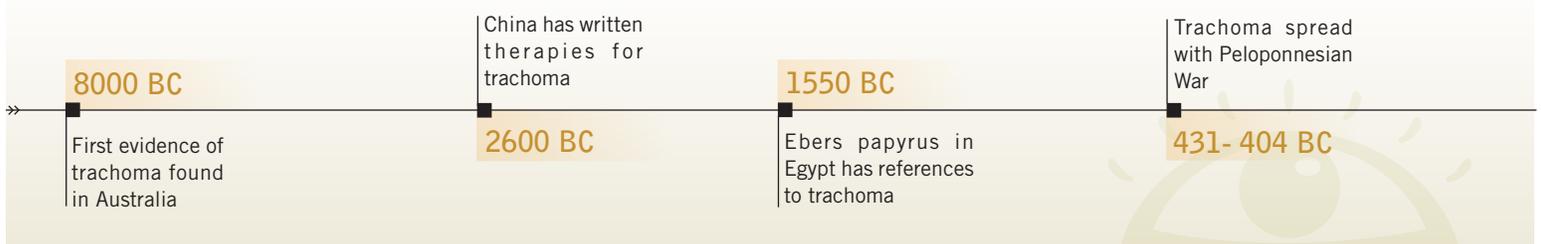
The struggle against trachoma began as early as 8000 B.C. Over these thousands of years, trachoma has blinded great thinkers, traveled across continents, and inspired a vigilant medical inspection process. Today, trachoma continues to blind millions in the developing world, but great progress has been made towards elimination. In the past 50 years, scientists cultured the agent, discovered antibiotics to treat active infection, and developed the SAFE strategy, which combines treatment and prevention. Although packaged as a comprehensive approach to trachoma control in the past several decades, the SAFE strategy is truly the culmination of a struggle against trachoma that began thousands of years ago.

Trachoma and the Ancient World

The most probable geographic origins of trachoma can be established by analyzing the prevalence rates among different racial groups. After looking at the distribution of trachoma among different races, researcher Taborisky determined that Central Asia is most likely the place where trachoma originated.^{55, 63} In the first half of the twentieth century, when Taborisky was conducting his research, people of Central Asian ancestry had a higher rate of trachoma than people whose origins lay elsewhere. The main tribes from Central Asia were the Mongols and the Finns. Groups of people who came into contact with the Mongols and the Finns had rates of trachoma correlating to the amount of contact. As Taborisky explains, “nearly always people who contracted the disease suffered from it less than those who propagated it.”⁵⁵ Taborisky was not alone in his assessment. Arthur MacCallan, who also conducted research on trachoma, agreed that the origins of trachoma were in Central Asia.^{39, 55} Perhaps trachoma did not only emerge in Central Asia, as diseases often emerge simultaneously in several areas, but the evidence suggests that Central Asia was one of the regions of origin.



Surgery preparation, Photo credits: Doug Menez



Trachoma and the Ancient World

The lesions were found frequently, which suggested the cause was common among Australians. The size and depth of the lesion varied slightly among skulls and based on these observations, scientists concluded that the lesion was caused by an infection of the tissue, which penetrated into the bone and not the reverse. Based on the lesion's proximity to different tissues, several eye infections were identified as possible causes. The scientists analyzed the presence of different diseases in Australia's history, as well as the geographic distribution of skulls containing the lesion. The lesion was found in the same areas of Australia where trachoma afflicts Australians today. After completing these analyses, the scientists concluded that trachoma was the most compatible disease. The skulls investigated date back to 8000 B.C. and, if the analysis is correct, it indicates trachoma's presence in Australia at that time.⁶⁷

In addition to the conclusions drawn from these modern observations, there are many written records of trachoma dating back several thousand years. Written therapies for trachoma from 2600 B.C. were found in China.²⁸ Another reference is contained in the Ebers papyrus from the 16th century B.C., which is a collection of medical prescriptions found in Egypt.⁶³ Trachoma was also present in Ancient Greece and Rome. Several written records of the disease have been found from this era (1200 B.C. to 400 A.D.). The Hippocratic Corpus, the collection of work from Hippocrates' school of medicine (5th century B.C.), contains sections about trachoma. Several doctors, including Celsus (1st century A.D.), Discorides (40-91 A.D.), Galen (129-216 A.D.), Grassus (12th century A.D.) and Chauliac (1300-1368 A.D.), mention trachoma in their works.^{2, 7} Discorides was the first person to use the word "trachoma" around 60 A.D. in his work *Materia Medica*.⁴ In addition to references in medical texts, trachoma was also part of popular discourse. Several of the plays by Aristophanes, including *Plutus*, contain allusions to trachoma. In this particular play, *Plutus*, god of riches, has been blinded by Zeus. This blindness is believed to be a reference to the widespread trachoma in Greece at the time.⁶³ Scholars also believe the biblical passage about Leban's eldest daughter, which states "Leah was tender eyed,"⁵⁸ is describing trachoma.⁶³ Through these texts and others, the history of trachoma can be traced back thousands of years.

Did you know St. Paul, Cicero, Horace and Galileo all had **trachoma**?

By reading these documents, historians have learned not only the long history of the disease, but also the extensive record of treatments. Around 1550 B.C. the Ebers papyrus suggested that in order to treat trichiasis, the turning inwards of the eyelashes and scratching of the cornea, one should "pull hairs and apply mixture of myrrh, lizard's blood, and bats blood until healed or a mixture of fly's dirt, red ochre and urine or a mixture of frankincense, lizard dung, ox blood, ass blood, pig blood, hound blood, goat blood, stibium and malachite."² Other treatments included scraping of the eyelid with various tools and surgeries to secure the eyelashes away from the eyeball. The principle of removing or curing the infected tissue and of physically fixing the eyelashes away from the eyeball to prevent scarring are a common theme of trachoma treatment.



Surgery, Photo credits: Liz Gilbert

200 BC

Hippocratic Corpus mentions trachoma

Discorides first uses the word trachoma

60

1095

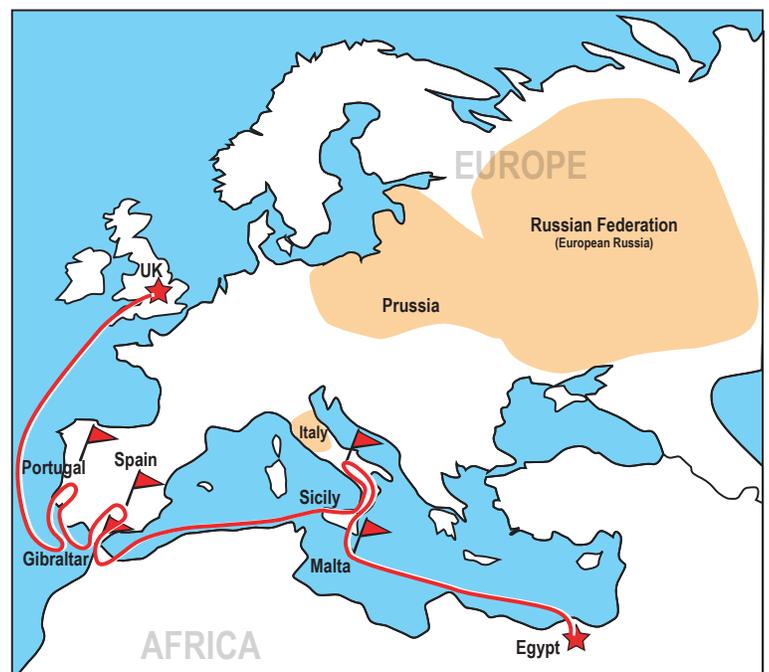
Crusades begin – trachoma spreads with them

Trachoma, Soldiers and Civilians

AS treatments have changed over time, so too has the prevalence and distribution of trachoma. When civilizations were isolated from one another without extensive interaction, trachoma affected segments of society, but the extent of disease was limited. When mass movements of people occurred, trachoma spread beyond the isolated populations it affected. Prior to the 19th century, these mass movements were mainly the result of war. Both the Peloponnesian War (431-404 B.C.) and the Crusades (beginning 1095 A.D.) contributed to the spread of trachoma, and Napoleon's campaigns across Europe and Africa caused trachoma's prevalence to increase rapidly.⁶³

When Napoleon began his quest into Egypt in 1798, he not only had to fight the Egyptian army, but also blinding eye diseases that would incapacitate thousands of his soldiers. Military or Egyptian ophthalmia, as the disease was called, infected three thousand of Napoleon's troops in two and a half months, blinding many.⁶³ Although military ophthalmia was viewed as a single disease, the affliction was actually a combination of several eye infections, including Koch-Weeks conjunctivitis (known today as *Haemophilus influenzae* biotype III), gonococcal conjunctivitis, and trachoma.² The combination of these infections often aggravated the symptoms of each and most likely the gonococcal infections were responsible for the rapid onset of blindness.²⁹ When Napoleon's troops withdrew from Egypt they spread the ophthalmia, including trachoma, from Egypt, where the disease was endemic, across Europe, where trachoma was only present sporadically. The British soldiers were also infected with trachoma as a result of their military campaigns in Egypt. The British troops spread trachoma on their way home and trachoma became a public health problem in the United Kingdom after their return.¹¹ Contact between Europe and Egypt through the Napoleonic Wars facilitated the rapid spread of trachoma.

Napoleon's campaigns, however, did not introduce trachoma into Europe. Trachoma had been present in Europe between 1200 A.D. and 1700 A.D. but had remained largely unnoticed. Military activities allowed trachoma to expand quickly because many people from different areas were coming into contact with one another. The presence of trachoma in Europe at the end of the 18th century is indicated by the troubles faced by other armies. Infected soldiers were recruited into the ranks of the Italian, Russian and Belgian armies, and the infection spread within the cramped military quarters. If infected soldiers were allowed to remain in the army, they spread the infection to their fellow soldiers, yet if these soldiers were discharged, they brought the infection home with them and began civilian epidemics.



1798

Napoleon begins his quest into Egypt

Sir Ralph Abercromby's troops return from Egypt and begin epidemic in England

1801

1803

Trachoma epidemic begins in Paris

John Vetch makes sustained case of contagiousness

1807

Gentlemen's Magazine publishes article about troops faking trachoma

Trachoma, Soldiers and Civilians

Confusion over how trachoma was transmitted and lack of effective treatment also allowed trachoma to spread rapidly. The concept of contagiousness and the idea of each disease having a unique cause were still topics being debated by doctors in the 19th century. Various environmental factors were often blamed for disease and the idea of person-to-person transmission of disease was not widely accepted.⁶⁶ A common belief was that only soldiers who served in Egypt could be afflicted with trachoma. However, when civilians and soldiers who had never been to Egypt began contracting the infection, the contagious nature of trachoma became clear. In 1810, England appointed a team of professionals to investigate trachoma. The team recommended that infected people should be isolated and emphasized cleanliness, including frequent washing of persons and clothing and not sharing towels or linens. These new guidelines resulted in an improvement in the standard of living for many British soldiers.¹¹ Treatments also included removal of granulations, various eyewashes, and bloodletting, which involved making cuts near the eye and allowing the blood to flow from these cuts until the patient fainted. While physicians were largely unsuccessful at treating trachoma, they did understand how to prevent the spread of trachoma.

The ophthalmic schools created in England are an example of successful trachoma control. Trachoma was a serious problem in the poorer schools in the late nineteenth and early twentieth centuries in London.¹¹ The British government created special schools, including Hanwell Ophthalmic School and Swanley, where infected children were isolated.^{11, 36} Strict sanitary measures were enforced according to the expert committee's guidelines. The schools had the joint success of stopping the transmission from infected to healthy children and helping the infected children recover from infection without progressing to blindness. The fact that the nurses and staff at the schools did not become infected also helped prove that trachoma was not airborne. Recognizing sanitation as a key to trachoma control helped eliminate trachoma as a problem in England.

The increase in prevalence of trachoma that accompanied the Napoleonic Wars created an atmosphere in which trachoma could no longer be ignored. These epidemics raised awareness and brought money and scientific expertise to the field of ophthalmology. In Britain these epidemics influenced the establishment in 1805 of the Central London Ophthalmic Hospital, which is still an active ophthalmological hospital (Moorfields Eye Hospital) today.^{4, 21} In 1903, Sir Ernest Cassel, who financed the Aswan Dam, donated £40,000 to train Egyptian ophthalmologists. Sir Cassel hoped free ophthalmology services would become available to those in need.³⁹ The Egyptian camel drivers during World War I benefited from Sir Cassel's donation. The high prevalence of trachoma spurred these developments in the field of ophthalmology.

Trachoma's impact on society reached beyond the physician's office. When trachoma struck France in 1803, the epidemic began in Paris and spread from there. The prevalence of trachoma was extremely high in Paris and all social classes were affected. Trachoma was labeled a fashionable disease because it was so widespread.⁶³ In Britain, soldiers attempted to fake ophthalmia to avoid military service. Knowledge of this ploy was widespread and *Gentlemen's Magazine* published an article in 1807 about troops from the 28th regiment of foot soldiers using an ointment to fake trachoma in an attempt to be discharged. The soldiers' plot was exposed when surgeons were sent to investigate by authorities concerned at the high rate of ophthalmia in this region.⁶³

When Lewis and Clark were traveling on the Columbia River in the United States they encountered native tribes suffering from ophthalmia, which may have been trachoma. **trachoma?**

England appoints experts to investigate trachoma

1810

1815

Belgian troops create epidemic in Belgium

Wilhelm Werneck demonstrates that the disease can be transmitted person to person through pus

1823

1870

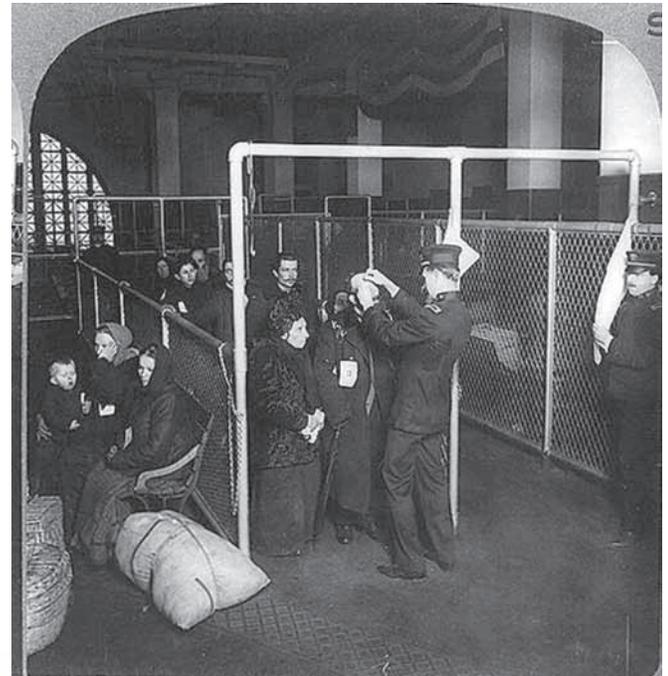
England begins isolating students with trachoma into separate schools

Trachoma, and Immigration

At the end of the 19th century and beginning of the 20th century, many immigrants left their homes in Europe and set out for a new life in America. Immigrants infected with trachoma carried the disease with them on their long journey and were a source of infection for the people they encountered. Anxiety about diseases transported by immigrants led to legislation being passed in 1891 by the U.S. Congress that stated, “[t]hat the following classes of aliens shall be excluded from admission into the United States [...] persons suffering from a loathsome or a dangerous contagious disease.”¹² The concern about trachoma was so great that in 1897, trachoma was the first disease classified as a loathsome or dangerous contagious disease by the U.S. government.³¹ From 1898 until 1905, immigrants exhibiting symptoms were examined for trachoma, and after 1905, all immigrants wishing to enter the United States were examined.^{30, 41} Trachoma was viewed as a serious threat by many governments and this threat guided decisions regarding immigration legislation. As a result of the strict American laws, steamship companies decided to conduct trachoma inspections in Europe before embarkation. Companies refused to transport infected passengers because of the expense of transporting rejected immigrants back to Europe. Many immigrants traveled to the U.S.A. through Canada, the United Kingdom, Germany and other countries. Immigrants who were suffering from trachoma were refused passage to the U.S.A. and remained in port cities where they created trachoma outbreaks. These outbreaks caused several countries, including Canada who passed legislation in 1902, to exclude immigrants with trachoma.¹¹

If an immigrant did pass the preliminary inspections in Europe, they still faced the scrutiny of the United States Public Health Service (USPHS) physicians at Ellis Island or other similar facilities across the country. The physicians had approximately six seconds per immigrant to determine if he or she had any physical or mental ailments which should bar entry to America. The exam included a physician examining the underside of the immigrants’ eyelids using either his fingers or a buttonhook to evert the eyelids, a process which was frightening for the immigrants. If an immigrant failed the eye exam, he was sent to a special committee that decided whether or not he could enter the country. Occasionally, if the board thought the immigrant could be cured and had sufficient financial backing to pay for medical treatment, the immigrant was sent to the trachoma ward in one of the immigrant hospitals, and was admitted to the U.S.A. after treatment. The more likely outcome of the committee hearing was that the immigrant would be sent back to his port of origin.^{30, 49} The U.S. government did not change the rules for special immigrants and detained two sons of a Chinese government official in 1923 at the Angel Island immigration station in California. Both men had trachoma and the U.S. government ignored their complaints that they deserved better treatment.¹⁹

While steerage passengers encountered a rigorous inspection ashore, first and second-class travelers were inspected onboard the ship. Only those showing symptoms were sent with the steerage passengers to be inspected more thoroughly. An ill first or second class passenger had a much better chance of slipping through the inspections than an ill steerage class passenger. This became known as the second-class scam, and any immigrant who was able to purchase the more expensive ticket did so.⁴⁰ The medical exam was an involved process that created apprehension for the immigrants.



Sir Ernest Cassel donates £40,000 for combating eye disease in Egypt

1897

Trachoma classified as a loathsome and contagious disease

1902

Canada passes laws excluding immigrants with trachoma

1903

1905

All immigrants entering the US examined for trachoma

Trachoma, and Immigration



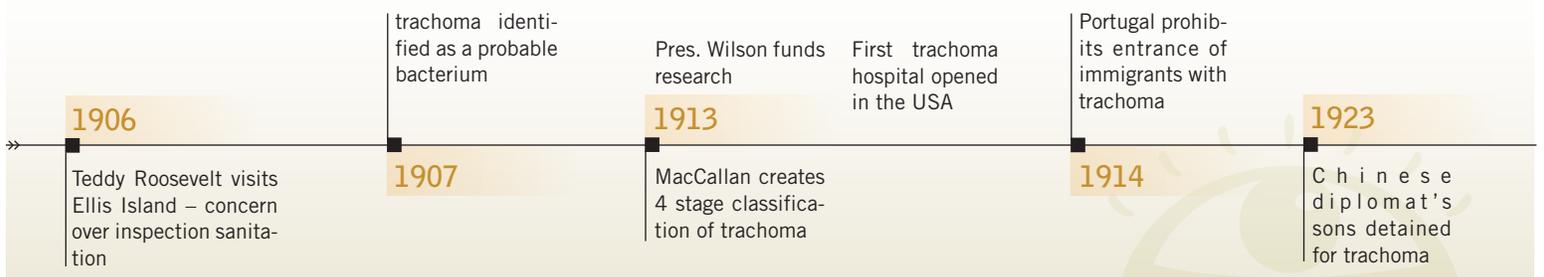
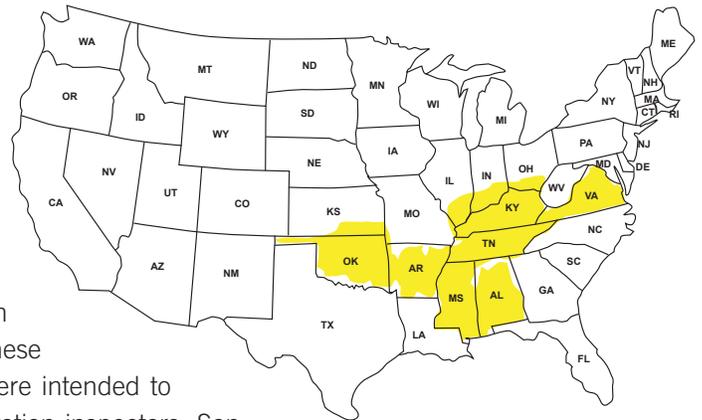
Buttonhook, short description of purpose

The sanitation of the inspections at Ellis Island remains a debated topic. When Theodore Roosevelt visited in 1906 he commented that “the Line,”⁴¹ as the inspections were referred to, was unsanitary and appeared to be a way to spread disease to healthy people. The inspectors were supposed to wipe the buttonhooks with Lysol soaked towels and wash their hands between each inspection, yet, with limited time and facilities for sanitation, this did not always happen. Fortunately, however, no outbreaks were reported among immigration inspectors or among newly arriving immigrants.^{31, 74}

While the USPHS spent 80% of its resources on medical inspections at the borders, on average less than 1% of incoming immigrants suffered from trachoma each year.⁴¹ However, trachoma did represent the leading medical cause for rejection of immigrants at the U.S. border.^{16, 19} Although preventing immigrants from entering the country with trachoma certainly helped avoid new cases, immi-

grants were not the only people suffering from trachoma in the United States. The rates of trachoma were much higher than 1% in some areas of the United States. A survey in Kentucky in 1912 found more than 12% of those surveyed suffered from trachoma.³ Trachoma rates were high in Virginia, Kentucky, Tennessee, Missouri, Arkansas, Alabama, and Oklahoma, which became known as the Trachoma Belt. Additionally, the prevalence of trachoma reached 90% on some Native American reservations, while surveys of the students in New York City public schools found that about 10% of students suffered severe or mild trachoma.^{3, 31, 41}

Despite the attention given to identifying cases of trachoma, little was known about effective treatments. Although no effective remedy was available, many different treatments were being administered. Those immigrants who were placed in hospitals were given a variety of therapies including removal of infected tissue, rupturing of the granules, rinsing the eye with different washes, and rubbing the eyelid with a “bluestone” which was made of copper sulfate crystals.⁴⁰ A large market for medications flourished, in spite of the fact that they were ineffective. Some of these treatments were aimed at curing the disease, while others were intended to cover the symptoms of trachoma in order to trick the immigration inspectors. San Francisco newspapers documented the topical use of adrenaline by Chinese and Japanese immigrants to mask the signs of trachoma and fool immigration officers.¹⁹ Some immigrants also rubbed their eyelids with sugar cubes for six weeks before embarking to cure themselves of trachoma symptoms.¹⁶



Trachoma, and Immigration

With immigrants and travelers moving around the world, health and disease control became something to address on a global level. Between the first and second World Wars La Ligue Contre Le Trachome was organized and worked with the International Organization Against Trachoma, which was founded in 1929.

Additionally, the World Health Organization was formed in 1948 and immediately identified trachoma as an important disease to combat. In 1949 the WHO collected all the available statistics on trachoma rates worldwide and put together a report. A summary of this information is found below.⁷²

who map or chart should be here

The Discovery of *Chlamydia trachomatis* and Elimination of Trachoma

The twentieth century brought many scientific advances that aided efforts to eliminate trachoma. In 1907, Halberstaedter and Prowazek found cytoplasmic inclusion bodies, small structures in the cytoplasm of cells, in samples from apes and humans suffering from trachoma. As research continued, scientists discovered that these inclusion bodies were found in non-gonorrheal ophthalmia neonatorum, male urethritis, and female genital epithelium. This began linking trachoma, newborn conjunctivitis, and non-gonorrheal sexually transmitted infections. Studies continued to determine the nature of the Halberstaedter-Prowazek inclusion bodies and around 1930 these inclusion bodies were accepted as the cause of trachoma. In 1954 T'ang and his colleagues in China cultured *Chlamydia trachomatis* in the yolk sac of chick eggs. In addition to T'ang, many other scientists were attempting to cultivate the agent of trachoma and were producing a variety of results. This prompted the WHO to create criteria for acceptance of an attempt as successful. T'ang's work met the guidelines and in 1957 his accomplishment was recognized. Throughout the first half of the 20th century, the agent of trachoma was thought of as a virus because it was so small and could only be grown within living cells. By the 1970's, however, *Chlamydia trachomatis* was acknowledged as a bacterium because it possessed both DNA and RNA and was susceptible to antibiotics.^{7, 16, 37, 60, 65}

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Trachoma is mentioned in *The Godfather* by Mario Puzo, *In a Sunburned Country* by Bill Bryson and in *The Innocents Abroad* by Mark Twain

Sulfonamides used to successfully treat trachoma

1937

1940

Penicillin used to treat trachoma

1943

Streptomycin used to treat trachoma

Francis I Proctor Eye Research Labs opened at UCSF

1947

The Discovery of *Chlamydia trachomatis* and Elimination of Trachoma

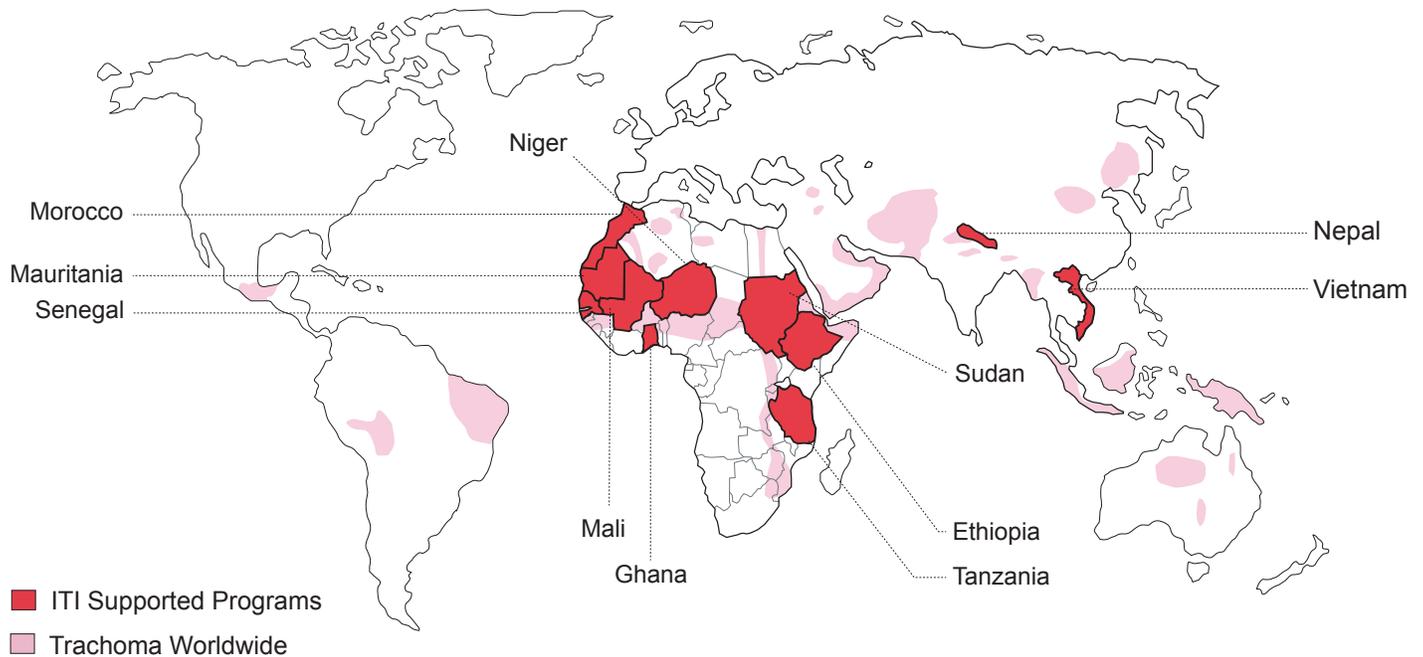
Along with identification of the agent came several new therapies for treating trachoma. The discovery of antimicrobials in the mid-20th century aided the progression of trachoma treatment even more than the identification of the agent.¹⁶ In 1937, scientists discovered that sulfanilamide was effective for treating trachoma.³ However, many people were allergic to sulfa antibiotics and experienced a severe skin reaction, so efforts continued to find an alternative treatment. In the early 1950's, both topical and oral tetracyclines were investigated. Oral or systemic tetracyclines were found effective, but slowed bone growth and damaged the teeth of young children, the primary group to receive therapy.¹⁷ Topical tetracyclines were chosen as the most effective therapy with the fewest side effects. Topical tetracyclines remained the treatment of choice until the 1990's when oral azithromycin therapy, which requires only one dose, was developed and became the preferred treatment for trachoma. With these new therapies available, trachoma control became a more manageable task.

Several strains of *Chlamydia trachomatis* exist and some of the strains cause trachoma while genetically different strains cause a sexually transmitted infection. The research on *C. trachomatis* was initially useful for combating both diseases. In the 1970's and 1980's, however, the focus of research efforts shifted to the sexually transmitted infections. In 1973, work to eliminate trachoma by the WHO became part of the effort to prevent blindness, which gave trachoma importance in a larger context. Additionally, in the 1980's, the Edna McConnell Clark Foundation's (EMCF) continued support of research specifically targeting blinding trachoma was crucial to trachoma elimination efforts. Work funded by EMCF included the development by the WHO of a simplified scheme for diagnosing trachoma in the field, research investigating risk factors associated with trachoma, and the establishment of the value and feasibility of surgery.⁸

EMCF also worked to advance the comprehensive SAFE strategy, which is the basis for elimination efforts today. The SAFE strategy combines treatment (surgery and antibiotics) and prevention (face washing and environmental improvement). While the separate components of the SAFE strategy had been used throughout history, the packaging of the components into a four-part strategy offered a comprehensive approach to trachoma elimination that was adaptable to many different situations and could be implemented at the community level.

In 1996, the WHO, with support from EMCF, convened a global scientific meeting on trachoma. At the time of the meeting scientists had established that azithromycin was going to change trachoma control efforts. Participants at the meeting "identified 46 countries as having known areas of blinding trachoma" and created a list of 16 priority countries for trachoma control.⁷³ The following year, the WHO established the GET (Global Elimination of Trachoma) 2020 program in cooperation with national health programs, non-governmental organizations, research institutions and other partners, many of whom attended the scientific meeting in 1996. The GET 2020 alliance endorsed the SAFE strategy and has been working in endemic countries around the world to eliminate blinding trachoma with the goal of elimination by the year 2020. The GET 2020 alliance falls within the VISION 2020 program, which began work in 2000. These steps taken by the WHO aided the visibility and cooperation of the elimination efforts.





The Discovery of *Chlamydia trachomatis* and Elimination of Trachoma

The recognition of the effectiveness of a single, oral dose of azithromycin for the antibiotic component of the SAFE strategy was crucial to trachoma elimination progress. Pfizer's antibiotic Zithromax® (azithromycin), which is produced and used to treat many bacterial infections, was found effective for treating trachoma in clinical trials. Through the efforts of EMCF, Pfizer committed to join the fight against

trachoma by donating both Zithromax® and financial support to the International Trachoma Initiative (ITI), an organization formed by EMCF and Pfizer in 1998 to support the control efforts. As the only organization dedicated solely to trachoma, ITI has played an important role in working towards the goal of global elimination. The work completed by EMCF also motivated many other organizations to undertake trachoma control projects.

Today, national ministries of health, non-governmental organizations, and other partners are working together to ensure that surgical services are available to patients with advanced disease, antibiotics are distributed, face washing is widely publicized, and communities are working to improve access to clean water and sanitation.²⁷ The goal set by the WHO is elimination of blinding trachoma by 2020, although some countries, such as Morocco, may achieve this goal much sooner.



1978

WHO Program for the Prevention of Blindness established

EMCF publishes trachoma research plan

1985

1987

Simplified grading scheme adopted by WHO

1991

First discussions with Pfizer and EMCF

Conclusion, For the individuals suffering from advanced trachoma the disease has always been devastating, but with the continued success of ITI and other organizations, it is hoped that the long and complex history of blinding trachoma will soon come to a close. Trachoma disappeared from the United States and Europe with improved sanitation and limited public health efforts. People around the world, with help from the international community, can be free from blinding trachoma without waiting for the disease to disappear on its own. With elimination of blinding trachoma, millions of people will be spared the painful and disabling path towards blindness. Additionally, helping individuals retain their sight for the duration of adulthood will allow them to be more productive, and will help break the cycle of poverty. With hard work and continued commitment, the world can be free of the burden of blinding trachoma.

