Trachoma

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Lancet 2014; 384: 2142–52
Published Online July 17, 2014
http://dx.doi.org/10.1016/S0140-6736(13)62182-0

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Trachoma is the most common infectious cause of blindness. Repeated episodes of infection with *Chlamydia trachomatis* in childhood lead to severe conjunctival inflammation, scarring, and potentially blinding inturned eyelashes (trichiasis or entropion) in later life. Trachoma occurs in resource-poor areas with inadequate hygiene, where children with unclean faces share infected ocular secretions. Much has been learnt about the epidemiology and pathophysiology of trachoma. Integrated control programmes are implementing the SAFE Strategy: surgery for trichiasis, mass distribution of antibiotics, promotion of facial cleanliness, and environmental improvement. This strategy has successfully eliminated trachoma in several countries and global efforts are underway to eliminate blinding trachoma worldwide by 2020.

Introduction

Trachoma is a blinding infection caused by an ancient organism. *Chlamydia trachomatis* evolved with the dinosaurs, and all vertebrates have evolved with their own chlamydial strains.[1,2] Trachoma remains the most common infectious cause of blindness.[3] The intense conjunctival inflammation with follicles recognised as active trachoma (TF) is sustained by repeated episodes of reinfection and reflects a sustained immune-mediated response to chlamydial antigens.[4] This inflammation causes scarring, distortion of the lid, and inturning of the lid (entropion), with the eyelashes touching the cornea (trichiasis) that leads to blindness (figure 1). The key to trachoma is that repeated episodes of reinfection and inflammation lead to the blinding complications.[4]

As human beings evolved, occasional chlamydial conjunctivitis did not apparently lead to blindness. However, after the last Ice Age (about 8000 years BCE), when people were crowded in growing communities and hygiene was poor, the frequency of reinfection increased and blinding trachoma resulted.[6] Crowding and poor hygiene lead to outbreaks of chlamydial infections in a range of birds, mammals, and marsupials.[7] Trachoma rates increased greatly as crowding and poor living standards increased at the end of the Agricultural Revolution and the start of the Industrial Revolution, but waned in the 20th century as living standards improved.[6] The disappearance of trachoma from more developed countries was hastened with the introduction of sulpha drugs in the 1930s and antibiotics in the 1940s.

However, trachoma still affects millions of people in the least developed countries. In recognition of the likelihood that spontaneous improvement in living conditions and disappearance of trachoma could take many decades, a specific global commitment has been made to eliminate trachoma. A resolution of the World Health Assembly in 1997 established the Global Alliance for the Elimination of Blinding Trachoma by the year 2020 (GET 2020) and much progress is being made to eliminate the disease. Some successes have led to increased resources and effort as set out here.

Epidemiology

Trachoma is still endemic in many of the poorest and more remote areas of Africa, Asia, Australia, and the Middle East (figure 2). Active trachoma affects an estimated 21 million people with about 2·2 million blind or severely visually impaired. A further 7·3 million have trichiasis[3] (table 1). An intensive global trachoma mapping effort is underway at present. WHO classes 53 countries as endemic for trachoma[10,11] and estimates that 229 million people live in endemic areas, with most blinding trachoma in Africa.[12,13] Although few up to date prevalence data are available from China and India, with their large populations even a low prevalence could substantially alter global estimates.

Active trachoma (follicular or severe inflammatory trachoma) is most common in children younger than 5 years and the prevalence can reach 60% or more.[14–16] The greatest load of infection is also in young children.[17] The prevalence of active trachoma decreases with age, few adults have signs of active trachoma, and even fewer have evidence of infection.[14,17–19] As active inflammation wanes, conjunctival scarring becomes more apparent; rates increase with age so that at over 25 years, up to 90% of people could have scarring.[20] Rates of active trachoma are generally similar by sex at young ages, but scarring trichiasis and loss of vision are generally more common in women than in men.[14,20] This difference is attributed to longer exposure of women to infection because they are more likely than men are to care for young children.

The prevalence of scarring, trichiasis, and corneal opacities in older people relates to their exposure to trachoma when they were young. This concept is important because even when active trachoma has disappeared, the late sequelae, including trichiasis, can still occur for decades.[21,22] Persisting episodes of infection with *C trachomatis* or other ocular infections can contribute to progressive scarring, so reduction of these exposures benefit adults.

Many cross-sectional and longitudinal studies have linked clean faces to lower risk of trachoma.[6,23] Improvement in facial cleanliness also decreases the severity of active disease, probably by lowering the likelihood of transmission.[24]

Water is necessary for face washing, and trachoma often occurs in communities or households without an adequate

water supply. Several studies have identified a positive association between the distance to the water source and the prevalence of active trachoma.[23] However, the provision of water to communities does not necessarily ensure that infection or active trachoma rates will decline.[25] The decision to use water for hygiene is complex and is a very important factor.[26]

Within communities, trachoma clusters both by neighbourhood and by household.[14,27,28] Studies of the re-emergence of infection after mass azithromycin treatment show that it reappears in households within 6 months, but takes up to a year to be evident in neighbouring households.[29]

Overcrowding is a risk factor for trachoma; the risk of children having active disease increases with the number of people per sleeping room.[28] Crowded conditions and close contact enable exchange of infected secretions among children especially if they have unclean faces and share a bed. Although a large family in itself is not a risk factor, the increased risk of contact with potentially infected children is. In Nathan Congdon and colleagues' study,[30] mothers of children with trachoma were more likely to have active disease than women who did not take care of children or whose children did not have trachoma.

Eye-seeking flies have been presumed to be physical vectors for *C trachomatis*. Although *C trachomatis* has been identified in trapped flies,[31,32] whether they can transmit infection is not known. The presence of a functional latrine near the house has been associated with lower trachoma prevalence.[14] How the presence of a latrine would decrease trachoma is not clear, although latrines might reduce breeding sites for the eye-seeking fly *Musca sorbens*,[33] or could be simply a marker for families with better overall hygiene.[34]

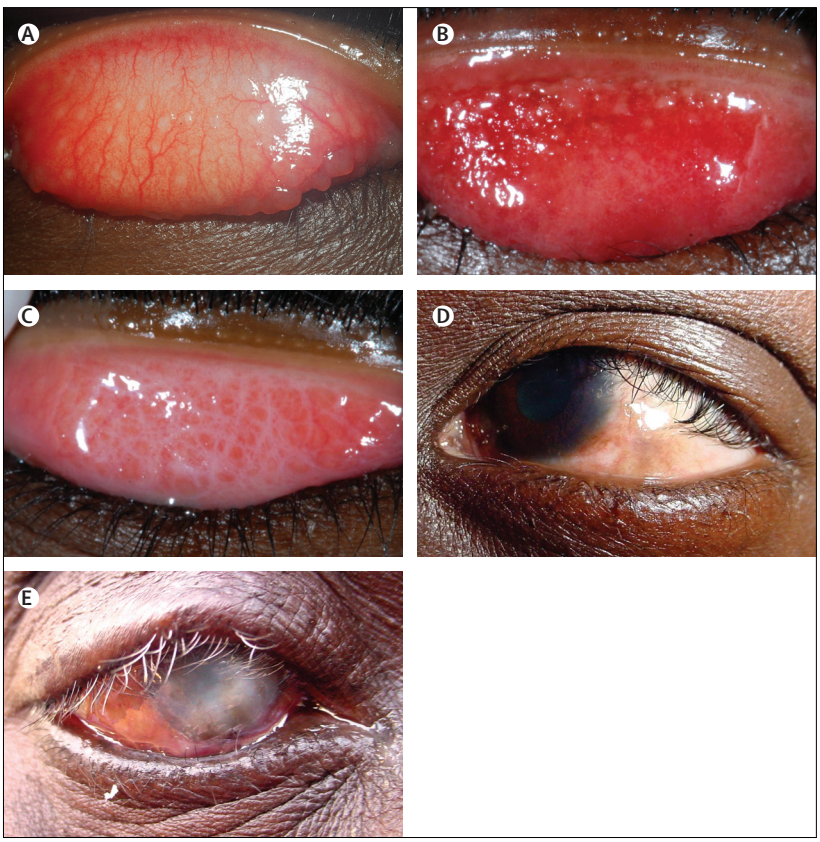

Figure 1: **Clinical features of trachoma and the WHO simplified grading[5]**
(A) Trachomatous inflammation–follicular (TF); the presence of five or more follicles in the upper tarsal conjunctiva. (B) Trachomatous inflammation–intense (TI); pronounced inflammatory thickening of the tarsal conjunctiva that obscures more than half of the normal deep tarsal vessels. (C) Trachomatous scarring (TS); scars are easily visible as white lines, bands, or sheets in the tarsal conjunctiva. (D) Trachomatous trichiasis (TT); at least one eyelash rubs on the eyeball; evidence of recent removal of inturned eyelashes should also be graded as trichiasis. (E) Corneal opacity (CO); easily visible corneal opacity over the pupil.

Pathogenesis

The causative organism

Trachoma is caused by the obligate intracellular Gram-negative bacterium *C trachomatis*, which has a single chromosome of about 1 Mbp and a multicopy plasmid that functions as a virulence factor.[2] This unusual organism has a biphasic developmental cycle. Initially the small, hardy, metabolically inactive elementary bodies attach to and enter epithelial cells. Once inside, elementary bodies transform into the larger, metabolically active reticulate bodies within an intracytoplasmic vacuole, the inclusion body, and replicate by binary fission. The reticulate bodies transform into elementary bodies before host-cell lysis and their release—the elementary body is the transmissible form. No non-human reservoir for the human strains of chlamydia is known.

Endemic trachoma is caused by *C trachomatis* serotypes A, B, Ba, and C. *C trachomatis* infection of the genital tract is generally caused by serotypes D to K, which can also infect the eye, causing ophthalmia neonatorium in infants or inclusion conjunctivitis in adults. The basis for the tissue tropism of the serotypes has not been fully elucidated.

	Active trachoma	Blindness	Trichiasis
1956	400	NA	NA
1971	400–500	1–2	NA
1981	500	6–7	NA
1985	360	6–9	NA
1994	146	5·9	NA
1996	NA	NA	10·6
2003	84·0	1·6	7·6
2007	40·6	NA	8·2
2011	21·4	2·2	7·3

Data are millions of individuals. NA=not available.

Table 1: **WHO estimates of the global burden of trachoma, by year[3,6,9]**

However, the ocular serotypes have lost the capacity to synthesise tryptophan; and there is polymorphism in the *tarp* and *pmp* genes.[35] Whole-genome analysis of *C trachomatis* suggests that extensive recombination between different strains is possible and that typing based on *ompA* might not be as reliable as previously thought.[36]