Trachoma: An Ancient and Contemporary Scourge

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SUMMARY

Trachoma is an ancient yet contemporary scourge. It is a specific kerato-conjunctivitis caused by certain serovars of Chlamydia trachomatis. It affects an estimated 84 million people and remains the commonest communicable cause of blindness in 6 million people. WHO has introduced the SAFE strategy which needs to be implemented with more determination in Nigeria if the level of trachoma blindness is to be positively impacted. This is particularly in the area of identification of communities in need of intervention through more widespread application of Rapid assessment methods. The challenges in trachoma research remain to improve the accurate diagnosis of active disease, to monitor emergence of antibiotic resistance and to improve the understanding of transmission and reservoirs of the infectious agent.

Keywords: *Trac,' oma, SAFE strategy, blindness, communicable, Nigeria.*

INTRODUCTION

Trachoma(Greek=rough) is one of the oldest diseases known to man. There are records in the Egyptian Papyrus literature dating back to the 16th Century B.C.[1] and even earlier records in the Chinese literature, where in the time of Emperor Huang Ti Nei Ching, around the 27th century BC, trichiasis was reportedly treated. It was also a scourge in Mesopotamia (2000 BC). During the Egyptian campaigns of the Napoleonic wars (1789-1799), many soldiers succumbed to the blinding ravages of the disease which inevitably came to be referred to as 'Egyptian Ophthalmia' [2]. The famous Moorefield Eye Hospital in London was founded precisely because of the flood of soldiers infected with trachoma who in turn introduced the disease into the crowded tenements of Europe during the industrial revolution.

Definition: It is a chronic Kerato-conjunctivitis caused by various serovars of the organism, *Chlamydia trachomatis*. Chlamydiae are microorganisms which are obligate intracellular parasites. However, they are bacteria because they have both DNA and RNA nucleotides.

The serovars associated with trachoma are A, B, Ba and C. Other serovars are D, E, F, G, H, I, J, K, and L1, L2 AND L3. Serovars D to K are associated with the so called paratrachomas, including inclusion conjunctivitis; which is a milder kerato- conjunctivitis, sexually transmitted genital infections and some cases of ophthalmia neonatorum in newborns, a consequence of sexually transmitted cervicitis in the mothers. The serovars L1, L2 and L3 are associated with the Lymphogranuloma venerum series[3]. This is why the organism is sometimes called the TRIC agent, short for Trachoma Inclusion Conjunctivitis agent.

EPIDEMIOLOGY

Trachoma is associated with hot, dry climates, and with high fly populations and unsanitary conditions. At present it is endemic in parts of Africa, South Asia, Latin America, the Middle East, and Aboriginal

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Australia. Its epidemiology has evolved over the years. While it used to be endemic in Europe, it virtually disappeared in that continent even before the introduction of antibiotics. This was probably associated with improved sanitary conditions and water supply. The map shows the current areas of endemicity of trachoma. (Fig 1).

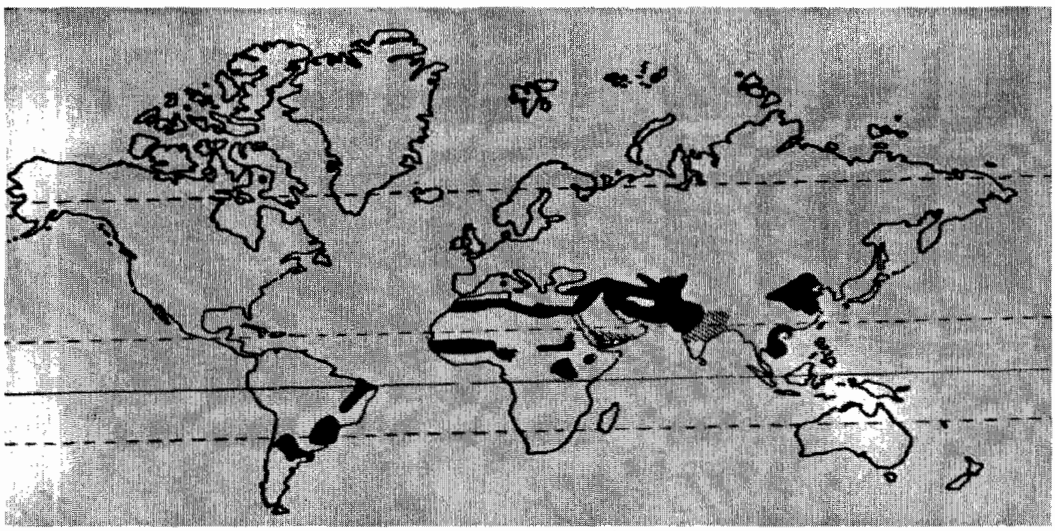


Fig. 1: Map showing areas of Trachoma endemity

Note that there is a trachoma belt in West Africa that embraces the savannah and sahel stretch. In Nigeria then, it is to be found more in the Northern fringes of the country. This is not to say that it cannot be found in all parts of the country. Wherever there are unsanitary conditions, and wherever the fly associated with its transmission , *Muscae Sorbens* , can thrive, it tends to be found. Even within the same town, village or city, there could be wide disparities in the prevalence from place to place. This is because other micro-ecological facts may come to play, such as overcrowding, localized difficulties with access to water, peculiar un-sanitary disposal of human waste etc.

Depending on the intensity of transmission, trachoma can be described as Endemic, Hyper-endemic, Meso-endemic and Hypo-endemic. Hyper-endemic trachoma is also often described as 'blinding' trachoma, largely because it tends to be associated with a high prevalence and incidence of blindness. In hyper-endemic situations, children below the age of 1year are often regarded as the reservoir of infection.

TRANSMISSION

The transmission of trachoma is from person to person through what is called the *three F's: Flies, Fomites and Fingers.* As indicated above, the fly species often associated with trachoma transmission is *Muscae Sorbens*, which feeds on the ocular discharge from the eyes of infected children. In an elegant experiment using fluorescence stained ocular discharge, Barry Jones *et al* were able to demonstrate that these flies indeed were capable of transmitting trachoma from person to person in a closed environment[4]. Fomites by definition will include things like handkerchiefs, items of clothing or other personal material that are held in close proximity by the source of infection.

The transmission of trachoma cannot be divorced from concepts concerning its staging. It has long since been recognized that trachoma expressed itself clinically in stages. Also, it needs to be noted that most of the pathology of trachoma is expressed on the inner lining of the eyelids, particularly the upper eyelid, what is otherwise known as the tarsal conjunctiva. These are in the form of follicles, and papillae in the early stages, and then as scarring in the later stages of the disease. Follicles are aggregates of lymphocytes and appear as pale yellow swellings. They are islands of intense B-cell proliferation surrounded by a sea of T-cells. Papillae are tufts of capillaries with a mucous membrane cover. To make a clinical diagnosis of

trachoma, it is mandatory to evert the eyelid in order to examine the tarsal conjunctiva, preferably with some element of magnification using an illuminated loupe. One of the first scientists to stage or classify trachoma was McCallan[5].

His staging was as follows:

Stage 1: **Incipient** stage. Here, follicles and papillae on the tarsal conjunctiva are 'immature', i.e. not fully developed.

Stage 2: **Established** stage: Here, the papillae and follicles are fully developed. In stage 2a, follicles predominate, in stage 2b, papillae predominate.

Stage 3: **Cicatrising** stage: here, the follicles and papillae begin to regress and scar tissue begins to form. These scar formations generally are disposed horizontally, and are referred to as Arlt's lines. The horizontal disposition is an important predisposition to development of entropion and trichiasis. This is a significant pathway to blindness

Stage 4: **Healed** stage: Here we find a regression of all active lesions.

There were two problems with the McCallan staging. First, it gave a false impression that there was only one linear cycle of disease. Second, it did not reflect the intensity of disease. Dawson and co workers in the 1980s came up with another intensity grading[4].

Thus it would have been possible to talk of trivial, mild, moderate and severe intensity of disease. This classification was useful but would have been too complicated to be used by the typical field worker. It was thus simplified by the World Health Organisation as follows:[7] (Fig. 2)

TF : Follicular trachoma: an active stage of the disease where you have follicles predominating. There must be at least five follicles and they must measure at least 0.5mm in size.

TI: Intense trachoma. Here you have papillary predominance, to the extent that at least half of the underlying deep tarsal vessels are obscured.

TS: Trachomatous scarring. Clear identifiable bands of cicatrisation on the tarsal conjunctiva.

TT: Trachoma with trichiasis. Here, there must be at least one 'offending' lash incident on the cornea.

CO: Here there are typical corneal opacities, but the opacity must obscure at least partially the undilated pupil, to be significant. CO in this context includes corneal vascularisation and pannus formation. This is known as the simplified grading and it has come into universal use in recent times.

The multi-cylclic nature of trachoma: It has been realized over the past decade or so, that trachoma tends to be a multi-cyclic disease. It has been possible to demonstrate persistent antigen in clinically quiescent trachoma and recrudescence of active lesions in 'healed' trachoma have been described [8, 9] Recently, Babalola proposed a three cycle theory of transmission,[10] which indicates that the transmission of trachoma is a little more complicated than had hitherto been assumed.

The clinical diagnosis of trachoma

There are some signs that are important in the diagnosis of trachoma. Obviously, the presence of some of the signs will depend on the stage of the disease. Also, the clinical diagnosis of trachoma is easier in endemic zones, but may be less straightforward when the cases are seen isolated.

- Tarsal conjunctival papillae or follicles. The differential diagnosis will be other causes of so called follicular conjunctivitis particularly the viral conjunctivitides (adenovirus and Acute Hemorrhagic conjunctivitis) and vernal conjunctivitis. Giant papillary conjunctivitis also needs to be considered in contact lens users
- Typical scarring of the tarsal conjunctiva and possible attendant entropion and trichiasis.
- Corneal Pannus formation. These are fibrovascular incursions into the upper half of the cornea.
- Herbert's pits. These are depressions on the limbus of the cornea that represent areas of regressed limbal follicles. These are pathognomonic of trachoma and they are a lifelong sign.

The laboratory diagnosis of trachoma.

- Demonstration of **antigen:** Inclusion Bodies were first demonstrated by Halberstaed-

Fig 2. The simplified WHO grading system illustrated.

Trachoma Follicular (TF) There must be at least 5 follicles measuring at least 0.5mm in diameter.	
Trachoma Intense (TI) At least half of the deep tarsal vessels must be obscured.	
Trachoma Scarring (TS) Note the Herbert's Pits. (Dark spots at the limbus).	
Trachoma Trichiasis (TT) (At least one 'offending' lash) And **Corneal Opacity (CO)** (The pupil must be at least partially obscured)	

ter and Prowazek [11] in 1907, hence they are called HP inclusions. These are demonstrable using Giemsa stains, Iodine, Fluorescent antibodies and Immunoperoxidase. They are generally of two types: the elementary body inclusions and the Initial body inclusions. Initial body inclusions for discrete masses subjacent to the nucleus while elementary body inclusions form so called 'nuclear caps'. (See Fig. 3.) Free elementary bodies can be targeted for detection using fluorescence conjugated species specific monoclonal antibody to *C. trachomatis*.

A more sensitive way to demonstrate antigens is to use Polymerase Chain Reaction techniques, in which case the DNA is detected [12].

- Demonstration of **antibodies**: ELISA (Enzyme linked Immunosorbent Assay) kits are available and antibodies can be demonstrated in tears or in blood. These tears can be adsorbed on sponges and transported to a laboratory for analysis.

Treatment of trachoma

Chlamydia trachomatis, the causative agent, is susceptible to a number of antibiotics including the tetracyclines, the sulfonamides and the erythromycins. The tetracyclines were traditionally used to treat trachoma, but the discovery of azithromycin has revolutionized the management of trachoma. This is because the single dose therapy makes possible Directly Observed Therapy and improves compliance, whereas the ordinary tetracyclines would need to be taken for six weeks inevitably at home. It is important to treat trachoma both topically and systemically because other mucous membranes particularly the nasopharynx, is usually involved in the infection, a fact that explains the nasal discharge often seen in children with the disease.

Azithromycin is given in children in a dose of 20mg/kg in a single dose. In adults, 1 gram is given as a single dose. Second line treatment is topical tetracycline ointment which is given as a 0.5 inch ribbon to both eyes twice a day for 6 weeks. Where Azithromycin is not available, oral tetracyclines should not be given to children less than 7 years to obviate the danger of staining of the milk teeth.

The surgical management

This consists in the management of entropion/trichiasis in order to improve the quality of life of sufferers. Even if vision will not necessarily improve, although occasionally it does, at least further corneal damage is prevented.

Bi-lamellar rotation is the method of choice for managing trachomatous entropion, and can be taught to middle cadre health care manpower where ophthalmologists are not available[13, 14, 15].However there are often considerable barriers to the uptake of such surgery as was found by Rabiu *et al*[16], chief among which are the cost implications.

COMMUNITY ASPECTS

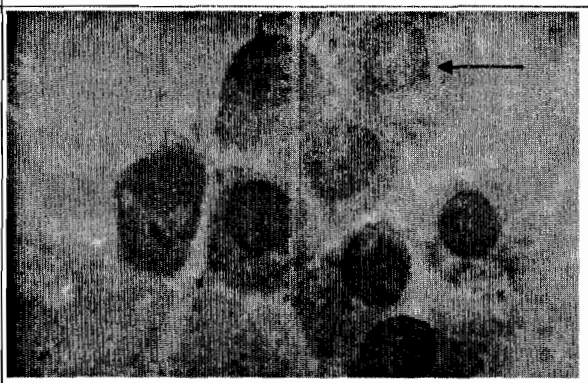
Trachoma is a quiet disease and a disease of the end of the road, affecting the poorest of the poor. It is the most important preventable cause of blindness, estimated to affect 84 million individuals and to cause blindness in 6 million[17].

It is one of the five target diseases of Vision 2020: the right to sight, which is a global initiative to eliminate avoidable causes of blindness by the year 2020. There are two main organizations working in tandem with the WHO on trachoma. These are the International Trachoma Initiative (ITI) , which anchors preventive measures on mass treatment with Azithromycin or Zithromax. This is in theory made freely available by Pfizer Inc. and the Clarke foundation in certain countries. The second body is the Global coalition for the Elimination of Trachoma by the year 2020 (GET 2020).

Rapid Assessment Methods are needed to identify areas of endemic trachoma so that intervention can be appropriately targeted. This generally involves the collection of anecdotal evidence from health workers, the assessment of environmental factors, the examination of a sample of the population under the age of 10 for signs of active trachoma and over the age of 40 for evidence of entropion trichiasis. Intervention would probably be indicated where the prevalence of active trachoma in the under ten was 10% or more, but all identified cases of entropion trichiasis need to have surgery. Relief from the constant irritation of trichiasis is important even where it appears vision may not be saved.

Figure 3:

Intra cytoplasmic inclusions in Giemsa stained conjunctival scrapings from patients with trachoma

Initial Body inclusion (1)	
Initial Body inclusions (2)	
Elementary body inclusions (nuclear caps) All cells are affected in this slide.	

The SAFE strategy has become the approach to the control of trachoma. This is an acronym for Surgical intervention, Antibiotics, Face washing and Environmental manipulation (fly control, provision of sanitary disposal of human waste, adequate water supply)[18, 19]. To impact blindness in Nigeria, the SAFE strategy will need to be implemented with greater commitment, particularly in the area of identification of communities in need of intervention by the more widespread application of the Rapid Assessment Methods.

The WHO recommendations for community treatment with azithromycin are as follows:

- The assessment is carried out at the district, community and family levels.
- Determine the district level prevalence of TF in 1-9yr olds
- Give mass treatment if > 10%. If < 10%, conduct assessment at suspect community level.
- If >10% at suspect community level, give mass treatment at community level.
- If 5-10%, identify suspect families in the community (using indices such as children with dirty faces, high fly concentration, poor sanitary disposal of human waste). Treat all members of the family in whom 1 or more have TF.
- If TF < 5% at community level, consider only targeted treatment. Treat index case and family in order to reduce risk of re-infection.

However the decision as to who to treat should still be carried out on a situational basis[9, 20].

In summary, while the scientific community appears to know what to do to control the scourge of trachoma, actually getting this done in practical terms is not as easy. However, a lot of progress has been made in some places, for instance in Morocco, where the possibility of eradication within a year is real. The challenges in trachoma research remain: to improve the accurate diagnosis of the active disease, to monitor emergence of antibiotic resistance and to improve understanding of transmission and reservoirs of *Chlamydia trachomatis.*

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