The SAFE strategy for the elimination of trachoma by 2020: will it work?

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WHO has recently launched a programme (GET 2020) for the elimination of trachoma, the leading cause of preventable blindness. GET 2020 has adopted the SAFE strategy, a comprehensive set of control measures (Surgery for entropion/trichiasis; Antibiotics for infectious trachoma; Facial cleanliness to reduce transmission; Environmental improvements such as control of disease-spreading flies and access to clean water).

The present article reviews the strengths and weaknesses of each component of the strategy. Although significant hurdles remain to be overcome there is every reason to hope that GET 2020 will be successful.

Keywords: Trachoma/surgery/drug therapy/prevention and control; Meibomian glands/surgery; Azithromycin/therapeutic use; Hygiene; Environmental health (source: MeSH).

Mots clés : Trachome/chirurgie/chimiothérapie/prévention et contrôle; Glande meibomius/chirurgie; Azithromycine/usage thérapeutique; Hygiène; Hygiène environnement (source: INSERM).

Palabras clave: Tracoma/cirugía/quimioterapia/prevención y control; Glándulas meibomianas/cirugía; Azitromicina/uso terapéutico; Higiene; Salud ambiental (fuente: BIREME).


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Introduction

Trachoma is one of the leading causes of blindness worldwide and the leading cause of preventable blindness (1). It is endemic in Africa, the Eastern Mediterranean Region, Australia and parts of South-east Asia (2). Ocular serovars of Chlamydia trachomatis cause recurrent conjunctivitis in children. In older persons the disease progresses through a cascade of conjunctival scarring, inturned eyelids, trichiasis, and eventually, corneal ulcers and blindness (3). The treatment of children with antibiotics can eliminate chlamydia in a high percentage of cases but reinfection is almost inevitable unless there is a comprehensive programme to prevent transmission from the rest of the community (4).

WHO, in cooperation with various nongovernmental organizations and national health services, recently began implementing a programme to eliminate blinding trachoma — Global Elimination of Trachoma by 2020 (GET 2020) (5). This programme has adopted a strategy (SAFE), consisting of the following control measures: Surgery for entropion/trichiasis; Antibiotics for infectious trachoma; Facial cleanliness to reduce transmission; and Environmental improvements such as control of disease-spreading flies and access to clean water (6).

We review the strengths and weaknesses of the components of the SAFE strategy below and consider the opportunities and threats presented by its implementation.

Surgery

Surgery is the most direct and efficient way to prevent blindness from trachoma. Although blindness develops in only a small fraction of persons infected with chlamydial infection, a significant proportion of those with trichiasis become blind. Although a long time elapses between initial chlamydial infection and blindness, persons with trichiasis are at immediate risk of becoming blind (7). Bilamellar tarsal rotation can eliminate trichiasis over 1–2 years, and a randomized clinical trial showed that this technique was significantly more effective than several other methods (8).

While trichiasis is clearly the greatest risk factor for corneal ulcers and subsequent blindness, other important factors include decreased tear production and dry eye, decreased conjunctival goblet cells, and thus decreased mucin, conjunctival and lid margin keratinization, and poor lid closure. Numerous procedures have been proposed, including tarsal rotations, tarsal grooves, tarsal advances, cautery and cryotherapy, but no single procedure corrects all the risk factors for corneal ulcers and subsequent blindness. Some complications, such as dry eye and...
loss of mucin-producing goblet cells, cannot be
corrected by surgery. In addition there is a recurrence
of trichiasis after all forms of surgery to correct it, and
there is some indication that this continues to happen
even two years after surgery (9).

An excellent opportunity exists for improving
the implementation of bilateral tarsal rotation
surgery throughout those regions where trachoma
is endemic. Better access to and acceptance of
the surgery are necessary in many areas (10, 11). There
is interest in the development of procedures that
reduce recurrence rates and deal with the more
complicated entropion/trichiasis cases. Further-
more, it may be possible to reduce the progression
of cicatricial trachoma to trichiasis by reducing
reinfection with *Chlamydia*, and perhaps even the
recurrence rates of trichiasis after surgery can be
reduced also in this way (7).

In 1995 WHO estimated that there were 10.6
million people worldwide attributable to trachoma (12). Such people are at high risk for
bacterial or fungal corneal ulcer. If trichiasis cases are
left untreated, a significant fraction of them develop
corneal scarring and blindness. Even if programmes
succeeded in reducing or eliminating chlamydial
infections there would still be individuals at risk for
trichiasis and blindness from cicatrical trachoma,
much in urgent need of surgery. Because of the
recurrence of trichiasis, there is bound to be a
continuing need for reoperation. It is important for
surgical trachoma programmes not to lose momen-
tum, even if new incident cases of cicatrical trachoma
can be eliminated by reducing chlamydial infection.

**Antibiotics**

The feasibility of this component of the SAFE
strategy has been greatly enhanced by the advent of
azithromycin (a macrolide-like antibiotic) for the
treatment of active trachoma in one or a few doses,
together with Pfizer’s Zithromax® donation pro-
gramme. Several trials have confirmed that azithro-
mycin treatment is at least as good as, if not better
than, topical tetracycline for the clinical and micro-
biological cure of active trachoma (13–16). Most of
these trials have striven to maintain compliance
with topical tetracycline treatment. The relative advantage
of azithromycin is greatest under practical opera-
tional conditions (17). Community volunteers can
administer azithromycin treatments and can effec-
tively use height-based dosing. A million doses of
azithromycin have been administered without ap-
parent serious side-effects and with favourable
effects on other common diseases (18).

It is assumed that a reduction in active disease
by antibiotic treatment will prevent future blindness.
However, this may never be rigorously tested
because of the long time lapse between initiation
of active disease and the development of blindness.
Antibiotic treatment alone does not give lasting
control because: disease re-emerges in the absence of
other control measures; not everyone with infection
receives treatment; or migration from untreated areas
takes place. The rate and sources of disease re-
emergence are poorly understood but knowledge of
them is vital when decisions are being taken on whom
and how often to treat.

There is an unparalleled opportunity to obtain
new knowledge through research within the frame-
work of the donation programme and the implemen-
tation of the SAFE strategy. Studies using quantitative
molecular diagnostic and typing methods could lead to
a better understanding of the relationship between
infection and clinical signs and to the identification of
likely sources of infectious shedding in affected
communities. The public health significance of
extraocular reservoirs of infection and subclinical
infections in different groups can be evaluated by
comparing different treatment strategies. Azithromy-
cin apparently suppresses infection for prolonged peri-
ods even in the context of re-emergent disease, perhaps
by enhancing functional immunity to chlamydial
infection (16). This requires further study.

The development of serious resistance of *C.
trachomatis* to azithromycin or tetracyclines would
seriously compromise the antibiotic component of the
SAFE strategy. There are, however, few indications
that this is likely to occur. Tetracyclines, for example,
have remained effective for many years. The emer-
gence of resistance to common dangerous pathogens
such as *Streptococcus pneumoniae* and *Plasmodium falciparum*
needs to be monitored, although macrolide
antibiotics are not widely used against these pathogens
in areas where trachoma is endemic. The risk of
Stevens–Johnson syndrome stopped mass treatments
of trachoma with sulfonamides among native Amer-
icans in the south-west of the USA (19), but there are
no reports of such rare serious side-effects associated
with azithromycin. Nevertheless, appropriate mon-
toring should be in place (18).

**Facial cleanliness**

There is considerable evidence that persons with
clean faces are less likely than others to have active
trachoma. Consequently, there is an assumption that
promoting hygiene may reduce trachoma (20, 21). A
controlled trial suggested that a vigorous campaign
promoting facial cleanliness may reduce the like-
lihood of persons developing intense trachoma (22).
Educational activities in the form of skits, school
programmes and national radio announcements have
been implemented in a variety of cultural conditions,
and many groups have long included the distribution
of soap and the availability of fresh water as
important aspects of trachoma programmes.

Unfortunately, it has been difficult to show that
facial cleanliness programmes substantially reduce
the prevalence of trachoma in communities. Several
studies have attributed changes in the prevalence
of active trachoma to such programmes without
adequately accounting for chance variation, seasonal
effects, or secular trends (23). When villages with intense facial cleanliness campaigns were compared to control villages it was found that face-washing had a minimal effect on the prevalence of active trachoma after a year (24). It is hoped that programmes lasting more than a year will have a greater effect.

Any effect of hygiene on trachoma would be extremely important. Antibiotics may well reduce the prevalence of trachoma, but unless mass antibiotic administration is to be continued indefinitely the reintroduction of even a few chlamydial infections may eventually lead to pretreatment levels of infection (25). Infection may be delayed or even prevented if a facial cleanliness campaign can reduce transmission.

There is some concern that excessive faith in mass antibiotic distribution could result in diminished enthusiasm for the improvement of hygiene. It should be emphasized, however, that measures to reduce transmission are crucially important unless antibiotics alone can eradicate chlamydial infection locally.

Environmental improvements

There are compelling grounds for believing that trachoma is a disease of poverty and under-development. Much circumstantial evidence suggests that environmental improvement reduces the incidence of trachoma. Evidence from a small intervention trial indicated that the transmission of trachoma could be reduced by fly control and that members of a subpopulation of the fly species Musca sorbens were probably mechanical vectors (23, 26). This may be why the use of pit latrines, which reduces the numbers of breeding sites available to M. sorbens, has a protective function (27).

No single environmental intervention can be recommended for trachoma control since the environmental risk factors are not the same in all settings. Few studies have been free of methodological difficulties, and observational studies typically find that a number of attributes indicative of poverty are correlated (23).

The evidence base for the environmental component of the SAFE strategy needs to be strengthened by creative and opportunistic studies. Many of the same issues have been rehearsed in diarrhoeal disease research where considerable experience has been gained in attempts to modify environmental and hygiene factors through participatory health education. Studies of hygiene interventions aimed at diarrhoeal disease should include evaluations of trachoma, which is present in many of the same settings (28). Opportunities exist for evaluating sustainable interventions such as the use of latrines and fly traps.

The main threat to the environmental component is that it will be ignored. In many countries there is a separation of education, community development, and water and sanitation from the health ministries, where disease control activities are usually based. Establishing links between agencies and departments in order to underpin action on the environmental component of trachoma control is a formidable challenge on which the ultimate success of SAFE may depend.

Conclusion

We have attempted to review the strengths, weaknesses, opportunities and threats of the SAFE strategy for trachoma control. Pfizer has generously donated over a million doses of oral azithromycin, and is committed to donating millions more. Public health care workers around the world have already begun the difficult task of eliminating blinding trachoma. The early results of GET 2020 have been encouraging but many hazards clearly have to be avoided. There is still severe trachoma in areas where the disease was known to be endemic over 3500 years ago (29). Facilitated by WHO and the International Trachoma Initiative, GET 2020 needs to maintain its early success over a very wide area. With adequate support, however, there is every reason to hope that it will achieve results comparable to those of previous mass drug administrations for eye diseases, including Credé’s prophylaxis for ophthalmia neonatorum, ivermectin for onchocerciasis, and vitamin A for xerophthalmia.

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Résumé

La stratégie CHANCE permettra-t-elle d’éliminer le trachome d’ici 2020 ?

L’OMS a lancé récemment un programme (EMT 2020) visant à éliminer le trachome, cause première de la cécité évitable. EMT 2020 a adopté la stratégie CHANCE intégrant une série complète de mesures de lutte, à savoir : chirurgie de l’entropion/trichiasis ; antibiothérapie de l’infection trachomateuse ; nettoyage du visage pour réduire la transmission de la maladie ; changements de l’environnement (lutte contre les mouches qui favorisent la propagation de la maladie et accès à l’eau propre).

Dans le présent article, les auteurs passent en revue les avantages et les faiblesses de chaque composante de la stratégie. Même s’il reste bon nombre d’obstacles à surmonter, tout porte à croire que le programme EMT 2020 sera un succès.
Resumen

Eliminación del tracoma para 2020: ¿funcionará la estrategia SAFE?

La OMS ha iniciado recientemente un programa (GET 2020) para eliminar el tracoma, causa principal de ceguera prevenible. GET 2020 ha adoptado la estrategia SAFE, un conjunto integrado de medidas de control (cirugía para el entropión/triquiasis; antibióticos para el tracoma infeccioso; higiene facial para reducir la transmisión; y mejoras ambientales como la lucha contra las moscas transmisoras de enfermedades y el acceso a agua salubre).

En el presente artículo se analizan los puntos fuertes y débiles de cada componente de la estrategia. Aunque quedan importantes obstáculos por salvar, todo hace confiar en el éxito del programa GET 2020.

Referencias