

245.2 97FU

FUTURE APPROACHES TO TRACHOMA CONTROL

WHO/PBL/98.56
DISTR: GENERAL
ORIGINAL: ENGLISH

REPORT OF A
GLOBAL
SCIENTIFIC
MEETING



WORLD HEALTH ORGANIZATION

245.2-97Fu-16921

LIBRARY IRC
PO Box 93190, 2509 AD THE HAGUE
Tel.: +31 70 30 689 80
Fax: +31 70 35 899 64

BARCODE: 16921
LO:

245.2 97 FU

FUTURE APPROACHES TO TRACHOMA CONTROL

REPORT OF A GLOBAL SCIENTIFIC MEETING

GENEVA, 17-20 JUNE 1996

Library
IRC International Water
and Sanitation Centre
Tel: +31 70 30 899 80
Fax: +31 70 35 899 64



Programme for the Prevention of
Blindness and Deafness

WORLD HEALTH ORGANIZATION
GENEVA 1997

ACKNOWLEDGEMENT

The WHO Programme for the Prevention of Blindness wishes to acknowledge with gratitude the support provided by The Edna McConnell Clark Foundation and the Task Force of the Partnership Committee towards the holding of this scientific meeting.

© World Health Organization, 1997

This document is not a formal publication of the World Health Organization (WHO),
and all rights are reserved by the Organization.

The document may, however, be freely reviewed, abstracted, reproduced and translated,
in part or in whole, but not for sale nor for use in conjunction with commercial purposes.

The views expressed in documents by named authors
are solely the responsibility of those authors.

TABLE OF CONTENTS

INTRODUCTION	3
1. MAGNITUDE OF THE PROBLEM	4
1.1 General aspects	4
1.2 Geographical distribution	4
2. PAST PROGRESS AND CONSTRAINTS IN TRACHOMA CONTROL	7
3. PRIMARY HEALTH CARE APPROACH TO TRACHOMA CONTROL	10
4. ASSESSMENT OF TRACHOMA	11
4.1 Clinical assessment	11
4.2 Epidemiological assessment	13
4.3 Laboratory assessment	13
5. CHEMOTHERAPY OF TRACHOMA	13
5.1 Topical treatment	14
5.2 Systemic treatment	14
5.2.1 General experience	14
5.2.2 Azithromycin	15
6. PROVISION OF TRICHIASIS SURGERY	16
Definition	16
6.1 Strategies	16
6.1.1 Epilation	16
6.1.2 Electrolysis	16
6.1.3 Cryoablation	16
6.1.4 Trichiasis surgery	16
6.2 Compliance	16
6.3 Training requirements	17
6.4 Community-based trichiasis surgery	17
7. HYGIENE PROMOTION AND COMMUNITY SUPPORT	18
8. FUTURE OPENINGS TO GLOBAL TRACHOMA CONTROL	18
8.1 Priority research topics	18
8.1.1 Azithromycin	18
8.1.2 Rapid assessment	19
8.1.3 Community-based trichiasis surgery	19
8.1.4 SAFE strategy	19
8.2 Resource mobilization and coordination of work	19

CONCLUSIONS AND RECOMMENDATIONS	21
ANNEX 1: Agenda	25
ANNEX 2: List of participants	26
ANNEX 3: Azithromycin	29
ANNEX 4: Priority settings for national programme control activities	32
ANNEX 5: Approach to rapid assessment	36
ANNEX 6: Programme objective, approaches, strategies and evaluation of indicators	40

INTRODUCTION

A global scientific meeting on "Future approaches to trachoma control" was convened by the WHO Programme for the Prevention of Blindness and Deafness, from 17 to 20 June in Geneva, Switzerland. The meeting was supported by The Edna McConnell Clark Foundation and the Task Force of the Partnership Committee of Nongovernmental Organizations collaborating with the WHO Programme.

Dr R. H. Henderson, Assistant Director-General, opened the meeting, pointing out that WHO had initially addressed the problem of trachoma as early as the Third World Health Assembly in 1950. However, despite activities undertaken and progress made in several Member States, trachoma remains a public health problem in the economically weak areas of the world, being today a disease of the poorest of the poor.

Recent developments to improve trachoma control have included:

- ▶ a simplified grading scheme to assess disease prevalence and severity;
- ▶ a standardized surgical procedure for trichiasis;
- ▶ development of strategies for community involvement in trachoma control;
- ▶ information on risk factors for trachoma, facilitating targeted intervention in priority areas.

Furthermore, the recent finding that azithromycin appears particularly effective in treating inflammatory disease offers a real possibility for more effective control of the disease in the future. As trachoma is found today in many of the poorest countries, where there are limited resources and competing priorities for health care, Dr Henderson acknowledged the important role that NGOs can play in assisting Member States to develop trachoma control activities.

After introduction of the participants, Dr Hannah Faal was unanimously elected Chairperson, and Dr Tun Aung Kyaw, Vice-Chairperson. Mr Jeff Mecaskey and Dr Allen Foster agreed to act as Rapporteurs. The draft agenda was adopted with no modification (Annex 1) and the list of participants is given in Annex 2.

1. MAGNITUDE OF THE PROBLEM

1.1 General aspects

Sources of data on trachoma are unfortunately very limited. The epidemiology of the disease is such that only population-based assessments are relevant. Surveys of schoolchildren were carried out in many countries in the 1970s, but their limitations are the low rate of school attendance in many settings where trachoma is prevalent and the lack of data on potentially disabling lesions (trichiasis) in this specific population. Data from eye clinics are notoriously unreliable for trachoma, considering the "patchy" (clustered) distribution of the disease and its social profile, being most common in impoverished marginalized populations. Overall, existing trachoma studies tend to be naturally biased to focus on areas where trachoma is strongly suspected, or known to exist. Very few nationwide surveys have attempted to give a mapping of trachoma, which is obviously difficult given the focal distribution of the disease, in relation to socioeconomic, cultural and environmental circumstances. Thus the sampling of sound, reliable epidemiological studies poses problems in such situations, when in fact precise epidemiological mapping is a priority for planning purposes.

There have been few attempts in the past to measure the global burden of trachoma and the resulting visual loss. Community-based surveys have not been undertaken in many countries in recent years (13 studies were found to have looked at the prevalence of trachomatous blindness), although the assessment of trachoma is part of the WHO/PBL suggested procedure for an overall blindness survey.

A WHO Scientific Group on Trachoma Research in 1959 refers to an estimated 400 million cases of trachoma. In the 1960s, the results of most surveys on trachoma and the experience gained in several campaigns led to a global estimate of 500 million cases worldwide, with at least 2 million blind (*Dawson, Jones & Tarizzo. WHO, 1981*). Subsequently, in the light of better epidemiological data on blindness, the figure for the number of blind was adjusted to between 6 and 9 million (*WHO, 1985*).

In 1985 (*Dawson & Schachter*), it was estimated, by means of a simple model, that there could be some 360 million people with trachoma. A more comprehensive model was developed a few years later by the WHO Programme (*Thylefors, Négrel & Pararajasegaram*), partially based on the results of a global questionnaire on trachoma. Thus, it was estimated that approximately 146 million people had active inflammatory disease requiring treatment with antibiotics and 5.9 million people were blind or at immediate risk of blindness from corneal opacification due to trichiasis. Accordingly, trachoma was responsible for 15.5% of the global burden of blindness, estimated at 37.9 million in 1994 (*Thylefors, Négrel, Pararajasegaram & Dadzie, 1995*).

1.2 Geographical distribution

In the *African Region*, severe trachoma is observed in all the countries of the Sahel area of west and central Africa and in the dry arid areas of southern, central and east Africa, including Ethiopia.

In the *Region of the Americas*, trachoma is known to occur in foci in southern Mexico, Guatemala, north-east Brazil, Bolivia and Peru. There are, however, few prevalence data on inflammatory disease and no known information on trichiasis surgery.

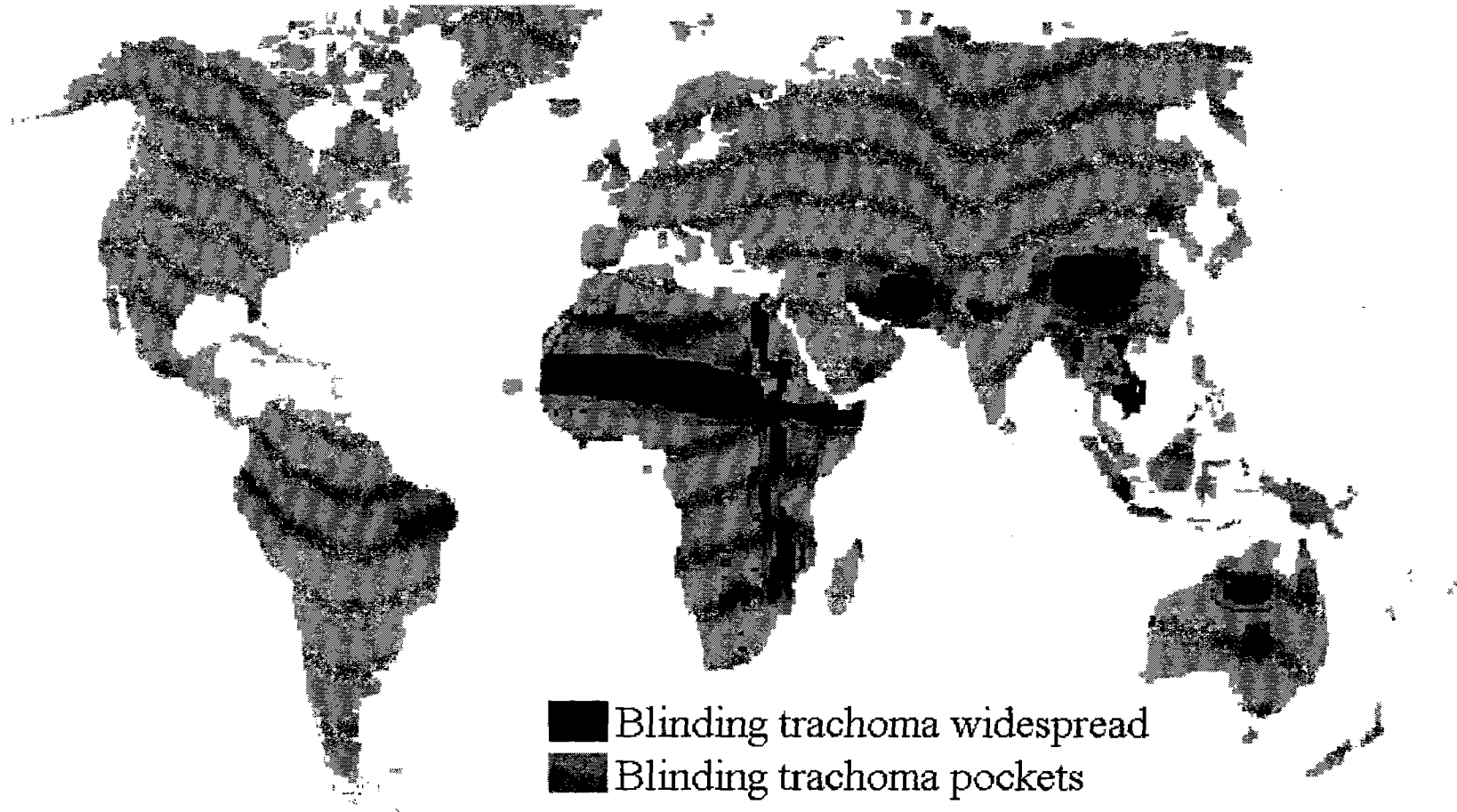
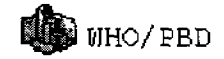
In the *Eastern Mediterranean Region*, trachoma occurs in pockets in south Morocco, Tunisia and Libya and is seen in Egypt, Sudan and Djibouti. Trachoma occurs in the eastern province of Saudi Arabia and in foci in the Gulf States, particularly Oman and Yemen. Iran, Afghanistan and parts of Pakistan, particularly Baluchistan and Sindh provinces, have blinding hyperendemic trachoma.

In the *South-East Asia Region*, trachoma still occurs in pockets in India and there is severe disease in south-west Nepal. In Myanmar there has been a well-developed and documented national programme for many years; available data have demonstrated a fall in the overall prevalence of trachoma from more than 40% in the early 1970s to around 6% in the early 1990s. Active disease is still seen, however, in children in some of the districts of Myanmar. There is little up-to-date information from Thailand or Indonesia. There is no evidence of disease in Sri Lanka, Mongolia and North Korea.

In the *Western Pacific Region*, trachoma occurs in parts of the Philippines, in foci of the Aboriginal population of Australia and in some of the Pacific islands. Trachoma has been documented in some provinces of China, but further up-to-date information is required in order to make more accurate estimates of disease prevalence and blindness. Trachoma is seen in Laos and Viet Nam, but data are not available for Cambodia.

There are no data on the present situation in the Central Asian States. (See further Fig. 1 for global distribution of trachoma.)

Fig. 1
TRACHOMA ACTIVE CASES (TF/TI)



During the **discussion**, it was noted that trachoma is particularly prevalent and severe in rural populations living in poor and arid areas of the world where personal hygiene is difficult. There are some survey data on trachoma in poor urban populations, but as yet this has not been documented to be a major problem.

The need for more population-based data was pointed out, as hospital-based data are unreliable, particularly for a disease which affects poor rural communities. Indicators are required to identify communities at risk so that the simplified grading scheme can be used to obtain baseline prevalence data. These data are needed in designing a global programme and also in deciding on the measurable objectives of such a programme. The GIS system may be useful in mapping the communities at risk.

Summary of global data on trachoma (year 1995, population in millions)		
World population	5900	UN Demographic Yearbook
Population at risk	590	WHO/PBL
Active cases (TF/TI)	146	WHO/PBL
Trachomatous trichiasis (all cases)	10.6*	
Trachoma blindness or disabling complications	5.9	WHO/PBL - Global Data on Blindness

* Calculated as 60% of population at risk having a trichiasis prevalence of 3%.

2. PAST PROGRESS AND CONSTRAINTS IN TRACHOMA CONTROL

Historically, there have been vertical control programmes in a great number of countries. These programmes have been resource-intensive and time-bound, often with good results in terms of reduction in disease but with long-term problems of sustainability, with a few exceptions, for example Myanmar, Saudi Arabia, Tunisia and Viet Nam.

Table 1. Results from vertical trachoma control programmes in 3 countries over the last 30 years

VERTICAL CONTROL PROGRAMMES				
<ul style="list-style-type: none"> ■ <i>Disease-specific</i> ■ <i>Non-integrated</i> ■ <i>Resource-intensive</i> ■ <i>Time-bound</i> ■ <i>Marked disease reduction</i> 				
Country	Indicator	Change	Period	Strategies
<i>Saudi Arabia</i> (Al Hasa)	Prevalence of active trachoma	100% 22%-1.5%	1965 1988-1990	Mass treatment with antibiotics (topical), hygiene promotion and eyelid surgery for trichiasis
<i>Myanmar</i>	Prevalence of active trachoma	43%-10%	1965-1993	Tetracycline eye ointment available at low price in commercial outlets
	Trachoma blindness	57%-7.5%	1962-1992	
<i>Tunisia</i>	Active trachoma	18.5%-3.7%	1980-1988	Mass treatment with antibiotics (topical), hygiene promotion and eyelid surgery for trichiasis
	Trachoma blindness	20%-4%		

More recently, trachoma control has often been integrated into a national eye care programme. The need for resources to be used is then less urgent and the programmes tend to be more long-term and sustainable. Documented examples have been Pakistan and The Gambia but, in fact, most countries with blinding trachoma do not have any specific or integrated programme to control trachoma.

In The Gambia, national population-based surveys of blindness conducted in 1986 and 1996 have shown an overall fall in the prevalence of inflammatory trachoma (TF/TI) from 8.8% to 2.9% and of trichiasis (TT) from 1.4% to 0.5%. These changes are in part due to an improvement in socioeconomic conditions, combined with an active eye care programme in which communities with trachoma are identified, and services for treatment of inflammatory disease and trichiasis are provided. However, it is acknowledged that patient compliance with treatment, both antibiotic eye ointment and trichiasis surgery, is a major problem.

EYE CARE PROGRAMMES

- *Not disease-specific*
- *Trachoma control activities part of eye care services*
- *Resources not trachoma-targeted*
- *Moderate to minimal trachoma prevalence reduction*
- *Long term*

Pakistan

Socioeconomic development has led to overall reduction

Kenya

Active cases seen during outreach services have remained high (1989-1992)

East Africa

Emphasis on community-based strategies and sustainability has achieved some success

The Gambia

Overall reduction in disease prevalence with persistent pockets of severe disease

The major constraints to trachoma control which have been identified are:

- ▶ lack of socioeconomic development in some parts of the world;
- ▶ poor patient compliance with antibiotic eye ointment;
- ▶ lack of, and reluctance to access, services for trichiasis;
- ▶ the cost of providing services to isolated communities.

The situation today is more optimistic. Studies have demonstrated that improvement in personal hygiene with a consequent reduction in trachoma prevalence can be achieved in the absence of overall improvement in socioeconomic conditions. The advent of a systemic long-acting chemotherapeutic agent offers an opportunity for improved patient compliance, and studies have shown that a standardized surgical procedure for trichiasis (lid rotation) can be performed at the community level by trained paramedical personnel with good results.

Visual loss from trachoma often starts in middle life and is more common in women. It is therefore a major cause of disability in affected communities, attacking the economically important middle-aged female population. Furthermore, studies in Africa have indicated that blindness is associated with a 3-4 times age-specific excess mortality. A cost-benefit analysis of the trachoma control programme in Myanmar has indicated that trachoma is an important avoidable cause of disability, for which cost-effective control strategies are now available.

In summary, in societies where there has been socioeconomic development, trachoma is decreasing; however, it remains a major problem amongst the poorest of the poor, who often have little say in the priority-setting and policy-making of countries. Recent developments offer the possibility of overcoming previous constraints and developing new cost-effective trachoma control programmes which can have important social and economic benefit for individuals and society at large.

3. PRIMARY HEALTH CARE APPROACH TO TRACHOMA CONTROL

Several of the essential components of primary health care are relevant to trachoma control, particularly the provision of water and sanitation and the availability of essential drugs.

The primary health care (PHC) approach is based on the principles of equity and social justice and provides a realistic and practical basis for the development or strengthening of efforts to prevent and control blinding trachoma. It can be seen that the trachomatous infection, its transmission and its sequelae lend themselves admirably to prevention and control through a PHC approach which includes health protection and promotion, preventive activities (especially primary and secondary prevention), treatment and rehabilitation in one continuum.

The use of primary health care workers in health promotion and to treat families with inflammatory disease is an important potential resource in situations with a good primary health care infrastructure. Trachoma is a communicable disease of families, with repeated reinfection among family members. Trachoma control can therefore be included in the priority activities of Member countries in terms of control of communicable disease and improvement in family health, particularly of mothers and children.

It is clear that, in areas where blindness including blinding trachoma is still a public health problem, eye care needs to be integrated into the primary health care delivery system. This requires the need for task-oriented training based on the principles stated above. In this way, the need for unipurpose trachoma workers is obviated and a sustainable programme can be developed as part of PHC.

In addition to the essential elements of PHC, there are supportive activities which provide the health-related inputs to the delivery of primary health/eye care. These include:

intersectoral action - collaboration largely between sectors responsible for water supplies, sanitation, education, etc.;

community involvement and participation - communities empowered to be involved and participate in the health and health-related interventions as a part of community developmental efforts;

resource mobilization - from the community level upwards and including the nongovernmental and private sector, in addition to the traditional government health sector;

management - including data collection, analysis and utilization, monitoring and evaluation.

It was acknowledged, however, that at present in many of the most affected trachoma communities there is an inadequate primary health care infrastructure through which trachoma control strategies can be implemented.

4. ASSESSMENT OF TRACHOMA

Over the last 50 years the clinical and laboratory assessments of trachoma have gone through a major development.

4.1 Clinical assessment

The assessment of signs of active trachomatous inflammation and complications of trachoma has been the subject of discussions since the early part of the century, through MacCallan's classification, based on work in Egypt. The subject was further approached in the three expert committees convened by WHO during the 1950s, and a detailed classification system was proposed in 1966 by a WHO Study Group. This system was in use for about a decade in several countries, and WHO maintained a service for data compilation and analysis. In 1975, a

modification was proposed by Dawson et al.,¹ particularly for the grades of follicular involvement. This amendment was included in the 1981 WHO publication *Field Guide to Trachoma Control*.

Following the experience in some population-based surveys that the WHO classification system could give rise to a high degree of observer variation, the WHO Programme for the Prevention of Blindness commenced the elaboration of a simplified assessment scheme as from 1985. After two years of field work, this was published² in 1987. It has since become widely used and is included in the WHO documentation on trachoma control.

The simplified assessment of trachoma and its complications focuses on five "key signs" of inflammatory and complicated disease:

- TF:** Trachomatous inflammation, follicular
implies significant active disease, to be treated with topical antibiotics.
- TI:** Trachomatous inflammation, intense
implies intense active disease, in need of treatment and surveillance; this is the particular future "risk group" for trachomatous blindness.
- TS:** Trachomatous scarring
implies the presence of scarring, indicating present/previous inflammatory disease.
- TT:** Trachomatous trichiasis
implies trichiasis in need of surgery - a potentially disabling lesion.
- CO:** Trachomatous corneal opacity
implies corneal opacity due to trachoma - a disabling lesion.

Each of these signs has been qualified at a defined level, thus minimizing observer variation while maintaining relevant clinical and epidemiological information.

The application of the WHO simplified trachoma grading system can be used to give a picture of "active trachoma" (TF and/or TI), "intensity of disease" (e.g. prevalence of TI) and "potentially disabling lesions" (e.g. TT). These signs can be expressed as prevalences in specific age groups, such as the amount of "active disease" in children less than 10 years of age being $\geq 20\%$, or the prevalence of trichiasis in women aged 40+ being $>1\%$. Thus, these indices have

¹ Dawson, Chandler R. et al. Blinding and non-blinding trachoma: assessment of intensity of upper tarsal inflammatory disease and disabling lesions. *Bulletin of the World Health Organization*, **52**, 279-282, 1975.

² Thylefors, B. et al. A simple system for the assessment of trachoma and its complications. *Bulletin of the World Health Organization*, **65**(4), 477-483, 1987.

been used in the past for operational considerations of "blanket" treatment with topical antibiotics, or provision of additional surgical services for trichiasis.

The WHO simplified assessment scheme for trachoma is easily applicable by PHC-level health personnel and it can be used in a variety of settings, with little need for equipment. Once trained, the local health staff can apply the scheme and carry out treatment. The existing training material for the WHO simplified scheme, developed with the support of The Edna McConnell Clark Foundation,³ has proved its usefulness. It should therefore be possible to make use of the scheme globally in trachoma control efforts in all endemic countries.

4.2 Epidemiological assessment

There is a great need for a rapid field method for the epidemiological assessment of trachoma, i.e. in terms of blinding versus non-blinding disease, and to have a rough idea about the prevalence of active disease and its gravity/intensity. There is as yet no fully evaluated methodology for this kind of assessment but guidelines have been developed (see further Annex 5).

There is also a need to develop a rapid assessment methodology for the behavioural and environmental determinants for severe trachoma, with a view to identifying those easily amenable to intervention.

4.3 Laboratory assessment

There is increasing use of newer laboratory methods and techniques for assessment of the presence of *Chlamydia*. Apart from the classical direct microscopy, immunofluorescence, ELISA tests and, most recently, highly sensitive PCR tests are available.

The use of these laboratory tests should be clearly defined in relation to the clinical and epidemiological assessments. Laboratory assessment can play a very important role in studies of transmission dynamics, but is of less interest in clinical/operational studies on blinding trachoma unless elimination of disease is attempted.

5. CHEMOTHERAPY OF TRACHOMA

Since the early 1950s the mainstay of trachoma treatment has been the prolonged use of topical tetracycline. *Chlamydiae* are sensitive to a number of antimicrobials including sulfonamides, erythromycins and tetracyclines. In general, the infrequent but predictable occurrence of side-effects has prevented the widespread use of systemic antibiotics on a mass

³ Trichiasis surgery for trachoma: the bilamellar tarsal rotation procedure (Reacher, M. et al.) (document WHO/PBL/93.29); Primary health care level management of trachoma (document WHO/PBL/93.33); Achieving community support for trachoma control (Francis, V. & Turner, V.) (document WHO/PBL/93.36); Trachoma grading card.

scale. Low cost and convenience have led to the widespread use of topical tetracycline eye ointment, although it is often disliked by the populations concerned.

5.1 Topical treatment

Early studies, particularly those in Morocco and Tunisia, showed that topical tetracycline was effective in reducing the prevalence and severity of inflammatory trachoma, at least in the short term. However, the effect was relatively small and was enhanced by the prolonged use of the antibiotic. This treatment was recognized to be substantially suppressive rather than curative, and treatment was given either continuously for six weeks or intermittently for six months. This became the recommended treatment for children with endemic trachoma and many millions of applications of tetracycline ointment have been given throughout the world over the last five decades.

The treatment of an individual with topical tetracycline will cause the short-term elimination of ocular chlamydial infection and reduction of secondary bacterial infection. This will result in a short-term reduction of the presence and severity of ocular inflammation. However, extraocular sites of chlamydial infection will not be affected, so auto-reinfection of the eye can occur. In addition, if not all infected people are treated effectively transmission of *Chlamydia* can restart in the community at the conclusion of antibiotic treatment.

The current recommended treatment for inflammatory trachoma is tetracycline eye ointment 1% twice per day for six weeks. When used correctly it has a short-term effect in suppressing signs of clinical inflammatory disease for up to six months, but there are problems with patient compliance particularly in pre-school children, and when used in mass programmes there is a certain cost (estimated at approximately US\$ 0.25 per person and year treated).

While tetracycline eye ointment therefore remains the recommended treatment at present there are major programmatic constraints regarding its role in a trachoma elimination programme.

5.2 Systemic treatment

5.2.1 General experience

Systemic antibiotics have been recommended for those with severe inflammatory trachoma. Initially sulfonamides were used but they have been replaced by tetracyclines, either oxytetracycline used four times a day, or doxycycline used once a day. Erythromycin used four times a day has been recommended for use in children and pregnant or lactating women because of the possible side-effects of tetracyclines in these groups.

The systemic treatment of an individual with severe inflammatory trachoma will almost always result in the short-term elimination of chlamydial infection and usually in the reduction or the resolution of active disease. However, without other measures, children living in endemic areas will almost always be reinfected by others within a short period of time.

Some large-scale treatment programmes, notably in Australia, have used systemic antimicrobials for mass treatment. Sulfamethoxazole, trimethoprim was used with little severe

toxicity, and a significant treatment effect was noticeable at one year. Systemic doxycycline caused marked gastrointestinal symptoms when used for mass treatment and had to be discontinued.

5.2.2 *Azithromycin*

Recently azithromycin, an azalide, has been shown to be efficacious in treating chlamydial diseases when given as a one-time oral medication of 1 gram in adults. The drug is absorbed in 2-3 hours, concentrated in the tissues, including conjunctiva, where tissue levels are maintained for up to 8 days. The drug is relatively free of serious adverse effects. It can be used in children aged 6 months and over. It is not registered for use in pregnancy although animal studies have shown no adverse effects. (See further Annex 3.)

Recent studies in The Gambia, Egypt and Saudi Arabia have shown that generally one dose of oral azithromycin 20 mg/kg body weight was as effective as 6-7 weeks of topical tetracycline in treating inflammatory disease in children, as measured over a period of 6 months. There was good compliance and there were no serious adverse effects.

Preliminary reports were received on the recent azithromycin trials in Egypt, Tanzania and The Gambia. These studies have compared treatment of all people in matched villages with either 6 weeks of topical tetracycline eye ointment or a weekly dose of oral azithromycin for 3 consecutive weeks; erythromycin was used in women of child-bearing age. Preliminary results based on clinical grading have shown that:

- (i) in two countries the azithromycin villages showed a 35-50% decrease in prevalence of inflammatory disease at 1 year;
- (ii) the clinical cure rate with azithromycin in individuals with inflammatory disease (TF, TI) at 2 months after start of treatment was more than 80%, which was at least as good as with tetracycline eye ointment and better in two countries;
- (iii) azithromycin is well tolerated with good patient compliance;
- (iv) azithromycin was seen to have other positive clinical benefits, e.g. decrease in other common infections.

In the subsequent **discussion**, the excellent treatment results of azithromycin against trachoma were noted, and it was agreed that this drug can be recommended for treatment of inflammatory trachomatous disease. However, the cost of azithromycin, and thus the access to this treatment by the target populations, is a matter of concern. The participants therefore urged the manufacturer, Pfizer Inc., to consider all possible means of making azithromycin available on a sustainable basis to all those in need, to prevent blindness from trachoma.

6. PROVISION OF TRICHIASIS SURGERY

Definition

Trichiasis is defined as “*at least one eyelash rubbing on the eyeball, or evidence of recent removal of inturned eyelashes*”. It is reasonable to consider 1-2 inturned eyelashes which rub on the globe but do not rub on the cornea as “minor” trichiasis, and all other cases as “major” trichiasis.

6.1 Strategies

There are a variety of possible strategies, which are briefly summarized as follows:

6.1.1 Epilation.

This is simple and inexpensive. Patients can remove their own inturned eyelashes at their convenience when necessary. There have been no community trials to evaluate the effectiveness of self-epilation. It seems likely that self-epilation could work for minor trichiasis, particularly if the patient is instructed how to perform the procedure. It may be an appropriate strategy if for some reason trichiasis surgery is not available.

6.1.2 Electrolysis

This is relatively simple to perform but does require the appropriate equipment. A success rate of only 25% for minor trichiasis at two-year follow-up has been reported.

6.1.3 Cryoablation

As with electrolysis, the appropriate equipment is required and the technique of cryo-application has to be learnt. Depigmentation of the eyelid skin is a problem, and the success rate is only similar to electrolysis.

6.1.4 Trichiasis surgery

There are many different described surgical procedures to correct trichiasis. Five different procedures were evaluated in a clinical trial in Oman. The results showed that **tarsal rotation** gave a better success rate than (i) tarsal splinting, (ii) tarsal advance with or without rotation or (iii) tarsal grooving.

Given the above information, it would appear that the best treatment for trichiasis is surgical correction with tarsal rotation, although epilation may be sufficient for some individuals. Other surgical procedures, electrolysis and cryoablation do **not** seem to offer any advantages.

6.2 Compliance

In the United Republic of Tanzania, a study of more than 200 women with trichiasis (West et al., 1994) showed a mean age of 45 years; 25% had corneal opacity and 40% performed

self-epilation. Over a two-year period less than 1 in 5 came to a health centre where trichiasis surgery was provided. The major reasons for non-compliance were lack of escort, cost of journey and need to look after their children. A similar observation has also been documented from Malawi.

Patients with trichiasis are often women aged 20-60 years from poor families and villages, who are likely to have many children and who may consider the development of trichiasis as a normal part of life (because their mother and/or grandmother had trichiasis). It is therefore not surprising that relatively few of the women will make the effort to attend a health centre or hospital even if trichiasis surgery is provided free of charge.

In another study in the United Republic of Tanzania (Bog, Yorston & Foster, 1993), performing tarsal rotation surgery on 94 patients in the villages of the patients, an 80% success rate was reported at a two-year follow-up. There are anecdotal reports of similar results for **community-based trichiasis surgery** by trained eye nurses or assistants in other countries of Africa.

6.3 Training requirements

A manual⁴ for training eye workers in community-based tarsal rotation has been produced by WHO/The Edna McConnell Clark Foundation and a video on trichiasis surgery is also available from the International Centre for Eye Health in London.⁵

Eye nurses or assistants with reasonable dexterity can be taught to perform successful trichiasis surgery under local anaesthetic. The training takes 1-4 weeks and requires at least 10 patients for trichiasis operation. The training should be conducted by an ophthalmologist or ophthalmic assistant well experienced in trichiasis surgery.

6.4 Community-based trichiasis surgery

Having trained the trichiasis surgeon (using the yellow manual) and identified communities with trichiasis (using the blue manual), it is necessary to provide trichiasis surgery in the community. The trichiasis surgeon will require transport, instruments, medicines and sutures (details are given in the yellow manual). The cost of instruments and consumables for 1000 cases is less than US\$ 1000.

Data presented from the Institute of Tropical Ophthalmology in West Africa confirmed that the Trabut tarsal rotation has a success rate of at least 80% with long-term follow-up. More than 500 ophthalmic nurses have been trained in West Africa to perform that surgical technique.

⁴ Reacher M, Foster A & Huber J. *Trichiasis surgery for trachoma - The bilamellar tarsal rotation procedure* (WHO/PBL/93.29) available on request.

⁵ Yorston D. Video on "Eye surgery for the prevention of blindness".

It was emphasized that the delivery of trichiasis surgery at the community level is essential in increasing patient compliance. The "yellow" trichiasis manual⁴ is an important tool for training mid-level workers in trichiasis surgery.

Resource centres for training mid-level workers (ophthalmic assistants and nurses) are now functional in East and West Africa; there is still a need to have a similar facility in Central Africa.

7. HYGIENE PROMOTION AND COMMUNITY SUPPORT

A manual ("green") has been developed by WHO and The Edna McConnell Clark Foundation for district and community workers to explain how to work with communities and achieve community support for trachoma control.

The manual promotes the SAFE strategy:

S - surgery for trichiasis, TT (in the community)

A - antibiotics to treat inflammatory disease, TF and TI

F - face washing, to encourage clean faces in children

E - environmental activities, to improve water supply and household sanitation

It was emphasized that the SAFE strategy requires an ongoing dialogue, partnership and full participation of the communities with the eye care workers.

A number of studies have shown a relationship between trachoma and access to water; however, the pattern and decision-making for use of water for hygiene is equally important. Very effective and water-saving measures for promoting facial cleanliness amongst children have been designed in African settings, but there is still a need to field test these strategies in other cultures.

Further operational research work at the community level is also needed in order better to define how to achieve community support and involvement in each of the four components of SAFE.

8. FUTURE OPENINGS TO GLOBAL TRACHOMA CONTROL

8.1 Priority research topics

The participants discussed areas for future operational research which needs to be undertaken to facilitate global action against trachoma.

8.1.1 *Azithromycin*

- (i) Dosage - should azithromycin be used on an annual or twice-annual basis?

- (ii) Dosage - is the recommended 20 mg/kg body weight dosage for trachoma adequate for respiratory tract infections?
- (iii) Target group - should azithromycin be used to treat everyone, or all children and mothers, or only children with clinical trachoma?
- (iv) The effect of azithromycin when inadvertently given in pregnancy.

8.1.2 Rapid assessment

There is a need to validate the rapid assessment methodology, as soon as possible, to allow interested countries to start their own mapping and updating of trachoma endemicity information.

8.1.3 Community-based trichiasis surgery

There is a need to investigate compliance to community-based trichiasis surgery and the barriers to uptake.

The outcome of trichiasis surgery in terms of quality of life, particularly for middle-aged women, should be evaluated.

8.1.4 SAFE strategy

Further field research is needed to identify optimal ways of achieving community support and sustainability for the various components of the SAFE strategy, including the important hygiene/behavioural aspects of trachoma prevention.

8.2 Resource mobilization and coordination of work

Some countries have experience of mobilizing resources for trachoma control from multilateral agencies, including the World Bank and UNICEF. Several NGDO partners have also been involved in assisting in the development of trachoma control activities. It was therefore suggested that a global coordinating body of interested parties for trachoma elimination be established, under the auspices of WHO. Such a group could include interested nongovernmental development organizations, bilateral and multilateral agencies, as well as scientific and research institutions. The first meeting of such a group should preferably take place in the autumn of 1996 in Geneva. The group should, in the first instance, focus its work and resources on building up elimination programmes in the 16 tentative countries suggested (see Table 2 and Annex 4) and support the operations research agenda. It was felt that it would be of particular importance to have Pfizer Inc. represented in the global coordination group, to facilitate and coordinate the future application of azithromycin against trachoma.

It was agreed that the new initiative be called

GLOBAL ELIMINATION OF TRACHOMA

as a disease of **public health importance** and that the target date for completion be 2020, given the long natural history for development of trichiasis.

Table 2. Trachoma elimination in 16 suggested countries*

Pilot countries	Phase I	Phase II
The Gambia Morocco Myanmar United Republic of Tanzania	Algeria Ghana Mali Nepal Niger Viet Nam	Chad Ethiopia Guinea Bissau Oman Pakistan Yemen

Pilot countries: This refers mainly to countries with an existing programme and data base for trachoma control, and thus in a position to implement elimination of the disease rapidly.

Phase I: This refers to countries where there may still be a need to obtain, or update, information on trachoma and its severity in certain population groups, and where there may be a need to strengthen the local PHC system for the elimination of the disease.

Phase II: This refers to countries where an overall assessment of trachoma is needed, together with the integration of trachoma control into PHC for ultimate elimination of the disease.

* This list is only tentative and is subject to countries' specific requests and agreements.

CONCLUSIONS AND RECOMMENDATIONS

OVERVIEW

Trachoma is still the main global cause of preventable blindness despite long-standing control efforts; the disease has gradually disappeared in many areas, as a result of socioeconomic progress and medical intervention, but it remains a serious public health problem amongst many poor population groups in developing countries. The present estimates point to a total of 146 million cases of active disease, of whom more than 10 million have trichiasis and close to 6 million are blind.

The large-scale application of community-based interventions against trachoma could lead to its global elimination. In order to review possible elimination options and to facilitate needed developments, a global scientific meeting on "Future Approaches to Trachoma Control" was convened in Geneva from 17 to 20 June 1996; the participants of the meeting made the following specific conclusions and recommendations.

1. **Priorities in trachoma control**

A review of available data on trachoma identified 46 countries as having known areas of blinding trachoma. Sixteen countries, according to severity of disease and feasibility of programme development, were tentatively identified for priority action over the next five years.

It is recommended that the WHO/PBD Programme with its collaborating organizations focus its efforts in the first instance on supporting trachoma elimination activities in the 16 identified priority countries. Other endemic countries should be encouraged to undertake assessment and put in place national elimination efforts.

2. **"SAFE" strategy**

Blinding trachoma can be eliminated through a combination of interventions: **S**urgery for trichiasis, **A**ntibiotics, **F**acial cleanliness and **E**nvironmental improvement (known as SAFE).

It is recommended that these interventions be community-targeted and to seek community involvement through the primary health care approach.

3. **Trichiasis surgery**

Recent studies have shown that a tarsal rotation procedure is the operation of choice for trachomatous trichiasis. However, there is often a problem of access and acceptance of surgery.

It is therefore recommended that the tarsal rotation procedure be provided at the community level by trained personnel to communities with trichiasis.

4. Antibiotic treatment

The mainstay of trachoma treatment has been, and still is, the suppressive treatment with topical administration of tetracycline, although unsatisfactory patient acceptance and compliance are often encountered in long-term treatment. The application of large-scale systemic antibiotic treatment has so far been limited, due to adverse side-effects of the available drugs and their cost.

It is therefore recommended to develop and apply alternative trachoma treatment schemes which are acceptable, largely accessible and affordable to the populations concerned.

5. Azithromycin

Recent community trials using azithromycin as a single dose against trachoma have demonstrated a very good therapeutic effect for 6-12 months in reducing inflammatory disease.

It is therefore recommended that azithromycin be used for treatment of trachoma, both at the individual and at the community level.⁶ There is, however, an urgent need to consider how azithromycin can be made accessible to those in need, to prevent blindness from trachoma.

6. Face washing and environmental improvement

It is recognized that although measures to improve hygiene - such as promoting facial cleanliness and better disposal of human and animal waste - will be culture- and setting-specific, they are critical to reducing the transmission of *Chlamydia* infection. It is acknowledged that these changes in behaviour are difficult to achieve and sustain and must therefore be promoted with full community participation; it is therefore recommended that activities to promote facial cleanliness and improve environmental hygiene be considered an essential component of the SAFE strategy for trachoma control.

7. Rapid assessment

Financial and manpower constraints in many trachoma-endemic countries demand that elimination programmes focus on areas of blinding disease. It is recommended that appropriate qualitative and epidemiological data through a rapid assessment methodology be used to target elimination activities to the regions and communities at greatest need.

⁶ Reference Annex 6.

8. Global elimination of trachoma

The global elimination of trachoma as a blinding disease by the year 2020 is now seen as an achievable goal. Although inflammatory trachoma may be controlled quite quickly, those cohorts with more severe cicatricial trachoma will need surveillance and trichiasis surgery over this period.

It is therefore recommended that:

- (i) countries where the disease is still a public health problem strengthen their resolve to address elimination of trachoma through the SAFE strategy as a priority; technical cooperation among developing countries (TCDC) at different stages of elimination progress be encouraged;
- (ii) WHO take a lead in developing and coordinating international efforts towards assisting Member States in achieving the goal of global elimination of trachoma as a blinding disease by 2020.

9. Training

The training of health workers, including volunteers, is necessary to deliver promotive, preventive and curative services efficiently for elimination of trachoma, as part of the SAFE approach.

It is recommended that endemic countries establish or strengthen appropriate training facilities and programmes, within the primary health care system, to achieve these objectives.

10. Global coordination

In order to promote and coordinate support for trachoma elimination activities, it is recommended that WHO/PBD convene a Group for the Global Elimination of Trachoma by 2020, consisting of nongovernmental development organizations and other interested partners.

11. Monitoring and evaluation

The intensified global initiative for elimination of trachoma as a blinding disease requires a monitoring and evaluation system to track and measure progress.

It is recommended that existing systems be reviewed and strengthened to meet the needs of the new objectives of national and global elimination of trachoma.

12. Operational research

Identification of areas of blinding trachoma and adoption of the recommended combined interventions need to be implemented in the most cost-effective manner.

It is recommended that operational research be applied to identify and adopt optimal methods of programme planning, implementation, monitoring and evaluation.

ANNEX 1**AGENDA**

Opening of Meeting
Introduction of Participants
Election of Officers
Adoption of Agenda

1. The magnitude of the problem

Review of present estimates on prevalence and geographical distribution of trachoma and related blindness
2. Overview of past progress and constraints in trachoma control
3. The primary health care approach to trachoma control and strategies for intervention
4. Assessment of trachoma and its complications
5. Chemotherapy of trachoma
 - (i) Topical schemes
 - (ii) Systemic treatment
6. The provision of trichiasis surgery
7. Hygiene promotion and community support
8. Future openings to global trachoma control

Conclusions and recommendations

Closure of Meeting

ANNEX 2

LIST OF PARTICIPANTS

Professor Gabriel Coscas*

President, International Organization against Trachoma, Chef de Service, Clinique Ophthalmologique Universitaire, Centre Hospitalier Intercommunal, Université de Paris - Val de Marne, 40 Avenue de Verdun, 94010 Créteil, France

Dr Chandler R. Dawson

Director, Francis I. Proctor Foundation for Research in Ophthalmology, University of California, San Francisco, California 94143-0412, USA

Dr Hannah Faal

Consultant Ophthalmologist, Coordinator, Gambia National Eye Plan, Eye Unit, Royal Victoria Hospital, Independence Drive, Banjul, The Gambia [*Chairman*]

Professor Mohammad Daud Khan

Department of Ophthalmology, Lady Reading Hospital, Post Graduate Medical Institute, Peshawar, Pakistan

Dr Tun Aung Kyaw

Assistant Director/Project Manager, Trachoma Control and Prevention of Blindness Programme, Department of Health, Ministry of Health, Hsaywa Setyon Road, West Gyogone, Insein, Yangon, Union of Myanmar [*Vice-Chairman*]

Dr David Mabey

Professor of Communicable Diseases, Clinical Sciences, London School of Hygiene and Tropical Medicine, University of London, Keppel Street, London WC1E 7HT, UK

Professor Hugh R. Taylor

Department of Ophthalmology, The University of Melbourne, The Royal Victorian Eye and Ear Hospital, 32 Gisborne Street, East Melbourne, Victoria 3002, Australia

Dr Sheila West

Associate Professor, Dana Center for Preventive Ophthalmology, Wilmer Eye Institute 129, Johns Hopkins University, 600 North Wolfe Street, Baltimore, Maryland 21287-9019, USA

* Unable to attend.

NONGOVERNMENTAL ORGANIZATIONS AND INTERESTED PARTIES

Mr J. Bruggemann

International Pharmaceuticals Group, Pfizer Inc., 235 East 42nd Street, New York, N.Y. 10017-5755, USA

Dr Y. Chami Khazraji

Chef du Service Central des Maladies Oculaires, Direction de l'Epidémiologie et des Programmes Sanitaires, Ministère de la Santé Publique, Rabat, Morocco

Dr Marcel Chovet

Médecin Général Inspecteur, Organisation pour la Prévention de la Cécité, 9 rue Mathurin Régnier, 75015 Paris, France

Dr Hannah Faal

Consultant Ophthalmologist, Coordinator, Gambia National Eye Plan, Eye Unit, Royal Victoria Hospital, Independence Drive, Banjul, The Gambia (*Representative of Sight Savers International, UK*)

Dr Allen Foster

Medical Consultant to Christoffel Blindenmission, International Centre for Eye Health, Institute of Ophthalmology, Bath Street, London EC1V 9EL, UK [*Rapporteur*]

Professor D. Hartani

Chef de Service Ophtalmologie, CHU Alger Centre, Hôpital Mustapha, Alger, Algérie

Ms Paula Luff

International Pharmaceuticals Group, Pfizer Inc., 235 East 42nd Street, New York, N.Y. 10017-5755, USA

Mr Jeffrey W. Mecaskey

Associate, Program in Tropical Disease Research, The Edna McConnell Clark Foundation, 250 Park Avenue, New York, New York 10177-0026, USA [*Rapporteur*]

Dr Glenda Treadway

Senior Associate Medical Director - Antibiotics, Product Planning & Development Division, International Pharmaceuticals Group, Pfizer Inc., 235 East 42nd Street, New York, N.Y. 10017-5755, USA

Dr Virginia Turner

Trachoma Task Force, Helen Keller International, 14 Churchill Terrace, Newtonville, MA 02160, USA

SECRETARIAT

Dr M. R. Couper

Division of Drug Management and Policies, World Health Organization, 1211 Geneva 27, Switzerland

Dr R. H. Henderson

Assistant Director-General, World Health Organization, 1211 Geneva 27, Switzerland

Dr A.-D. Négrel

Prevention of Blindness, Programme for the Prevention of Blindness and Deafness, World Health Organization, 1211 Geneva 27, Switzerland

Dr T. A. Ogada

Regional Adviser, Noncommunicable Diseases, World Health Organization, Regional Office for Africa, P.O. Box N° 6, Brazzaville, Congo

Dr R. Pararajasegaram

Programme for the Prevention of Blindness and Deafness, World Health Organization, 1211 Geneva 27, Switzerland

Dr S. Resnikoff

Prevention of Blindness, Programme for the Prevention of Blindness and Deafness, World Health Organization, 1211 Geneva 27, Switzerland

Dr M. Simpson-Hebert

Rural Environmental Health, Division of Operational Support in Environmental Health, World Health Organization, 1211 Geneva 27, Switzerland

Dr B. Thylefors

Director, Programme for the Prevention of Blindness and Deafness, World Health Organization, 1211 Geneva 27, Switzerland *[Secretary]*

Dr Anna Verster

Regional Adviser, Nutrition, Food Security & Safety, World Health Organization, Regional Office for the Eastern Mediterranean, P.O. Box 1517, Alexandria 21511, Egypt

ANNEX 3**AZITHROMYCIN****1. Chemistry of azithromycin**

Azithromycin is the first of a new class of antibiotic compounds, the azalides. It is derived from erythromycin, a 14-membered macrolide, with the carbonyl at position 9a of the lactone ring being replaced by a methyl-substituted nitrogen and the addition of a further carbon atom to the ring. This chemical modification renders azithromycin more acid-stable than erythromycin, improving its resistance to the gastric environment.

2. Microbiology of azithromycin

In vitro, azithromycin is more potent against Gram-negative organisms than erythromycin or other macrolide antibiotics, including roxithromycin and clarithromycin; particularly notable is its activity against *Haemophilus influenzae* and *Neisseria gonorrhoeae*. In addition, azithromycin possesses good *in vitro* activity against Gram-positive organisms, including *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Staphylococcus aureus*. Azithromycin's spectrum of activity extends to anaerobic bacteria, with activity that is comparable to or greater than that of the macrolides. Intracellular organisms, including *Mycoplasma* species, *Legionella pneumophila* and *Listeria monocytogenes*, are highly susceptible to azithromycin *in vitro* when grown in tissue culture. The broad spectrum of activity of azithromycin also includes chlamydial species, including *Chlamydia trachomatis*.

In vitro studies have shown that the activity of azithromycin is comparable to that of erythromycin, tetracycline and doxycycline against *C. trachomatis* isolated from patients with sexually transmitted diseases and to that of tetracycline against isolates from trachoma patients. In addition, azithromycin's ability to penetrate and remain within cells infected with intracellular pathogens contributes to its activity against these organisms.

3. Pharmacokinetics of azithromycin

The greater stability of azithromycin at low pH results in increased oral bioavailability compared with erythromycin; after a single 500-mg oral dose of azithromycin, the bioavailability is 37%. Azithromycin is rapidly absorbed from the stomach, a peak serum azithromycin concentration of 0.4 mg/l being reached 2-3 hours after the ingestion of a 500-mg oral dose. The patient's age does not affect the absorption of azithromycin, and dose adjustment is not required in the elderly. After reaching the peak serum concentration, azithromycin levels decline slowly in a biphasic manner; the terminal half-life is 68 hours. The high serum clearance of azithromycin, together with the high steady-state volume of distribution, indicates that the low terminal elimination rate is due to extensive uptake and subsequent release of the drug by the tissues.

Significantly higher concentrations of azithromycin are found in tissues than are concurrently detected in serum. Concentrations in mucosal and epithelial tissues exceed 2.0 mg/kg, which is above the minimum inhibitory concentrations of many important pathogens responsible for respiratory tract, skin, soft tissue and genital tract infections.

Mean concentrations of azithromycin in conjunctival tissue are greater than those in concurrently obtained serum samples and exceed the minimum inhibitory concentration for *Chlamydia trachomatis* (0.06-1.0 µg/ml) up to 14 days after the oral administration of 1 g to patients undergoing surgery for cataracts. Levels in tear fluid are also greater than concurrent serum values, whereas concentrations in aqueous humour are usually lower than those in serum.

The redistribution of azithromycin into tissue compartments from the circulation following absorption is rapid, the drug being concentrated intracellularly in lysosomes. In common with other basic drugs, azithromycin becomes ionized in the low pH conditions within the lysosomes and is localized there. Subsequent fusion of the lysosomes with the phagosomes enables azithromycin to act on pathogenic organisms that have been ingested by phagocytes. The excellent activity of azithromycin against intracellular pathogens results from its concentration within cells. Phagocytic uptake of azithromycin does not require high serum concentrations of the drug, and phagocyte-associated azithromycin levels are high at sites of acute infection, as a result of the migration of phagocytes in response to inflammation.

4. Toxicology of azithromycin

Acute toxicity of azithromycin is very low in rats and mice; oral LD₅₀ is >2000 mg/kg. The pregnancy rate is reduced when both male and female rats are chronically treated with 30 mg/kg/day (males for 64-66 days and females for 14 days before mating). Azithromycin has no effect on fetotoxicity or teratogenicity when doses as high as 40 mg/kg/day are administered to pregnant mice or rats. No azithromycin-related changes in perinatal and postnatal development have been reported in rats treated with up to 200 mg/kg/day from day 15 of pregnancy. Treatment of neonatal rats with doses of up to 40 mg/kg/day for 17 days is well tolerated with no effect on body weight gain.

5. Azithromycin in the treatment of other diseases

Clinical studies have established that a single 1-g dose of azithromycin is as clinically effective as doxycycline 100 mg twice daily for 7 days in the treatment of nongonococcal urethritis and cervicitis, with comparable microbiological cure rates.

Studies reveal that a 3-day, once-daily course of azithromycin is comparable to clarithromycin, cefaclor, or roxithromycin given for a minimum of 7 days in the treatment of otitis media, pharyngitis/tonsillitis, and sinusitis in adults and children. Other studies have shown that 3-day, once-daily azithromycin is as clinically and bacteriologically effective as 10-day courses of clarithromycin, amoxicillin/clavulanic acid, or roxithromycin against lower respiratory tract infections in both adults and children.

Among the other potential uses of azithromycin is the prevention and treatment of malaria.

6. Safety profile of azithromycin

Azithromycin has a good safety profile. In adults in comparative clinical trials treated with either a single 1-g dose of azithromycin or 1.5 g given over 3 or 5 days, adverse events were reported in 15%. The most common side-effects were gastrointestinal symptoms, and in more than 90% of patients the effects were classed as mild or moderate. Laboratory abnormalities were rare with transient increases in liver enzyme activities in a small proportion of patients treated with azithromycin (2%) or comparators (2.7%). No pharmacokinetic or clinical interactions were observed with theophylline, warfarin, cimetidine, carbamazepine, methylprednisolone, oral contraceptives, terfenadine or zidovudine.

When the tolerability of therapy was assessed in children monitored over 35 days included in 45 comparative studies, the incidence of adverse events among those treated with azithromycin was 8.7%, and in children treated with other comparator agents events were reported in 9.8%. The events, which were mainly gastrointestinal, were predominantly of only mild or moderate severity. Only 1.3% of azithromycin- and 1.7% of comparator-treated children were withdrawn from treatment because of an adverse event. Treatment was not discontinued in any child due to abnormal laboratory test.

ANNEX 4

Table 1

Priority settings for national programme control activities				
Region: Sub-Saharan Africa				
Disease status	Trachoma control activities existing		Potential for trachoma control activities	
Blinding trachoma known	Botswana Burkina Faso Ethiopia Gambia Ghana Kenya	Mali Niger South Africa Sudan United Republic of Tanzania Zimbabwe	Benin Cameroon Central African Republic Chad Côte d'Ivoire Djibouti Eritrea	Guinea Bissau Mauritania Mozambique Nigeria (North) Senegal Togo Uganda Zambia
Blinding trachoma suspected	Guinea Malawi		Namibia Sierra Leone Zaire	
Non-blinding trachoma suspected			Angola Burundi Rwanda Somalia	
Bold print indicates "first priority" countries for intervention				

The other countries of Sub-Saharan Africa are not known to have endemic trachoma.

Table 2

Priority settings for national programme control activities		
Region: Middle-Eastern Crescent		
Disease status	Trachoma control activities existing	Potential for trachoma control activities
Blinding trachoma known	Algeria Morocco Saudi Arabia	Afghanistan Egypt Iran Libya Oman Pakistan (some areas) Yemen
Blinding trachoma suspected		Iraq Kazakhstan (TT) Kyrgyzstan (TT) Tajikistan (TT) Turkmenistan (TT) Uzbekistan (TT) United Arab Emirates
Non-blinding trachoma suspected	Tunisia	Armenia Azerbaijan Palestine Turkey
	Bold print indicates "first priority" countries for intervention	

The other countries of the Middle-Eastern Crescent are not known to have endemic trachoma.

Table 3

Priority settings for national programme control activities		
Region: Latin America and Caribbean		
Disease status	Trachoma control activities existing	Potential for trachoma control activities
Blinding trachoma known	Mexico	Brazil (North-East)
Blinding trachoma suspected	Guatemala	
Non-blinding trachoma suspected		Bolivia Peru
Bold print indicates "first priority" countries for intervention		

The other countries of Latin America and Caribbean are not known to have endemic trachoma.

Table 4

Priority settings for national programme control activities		
Region: Asia and Islands (including China and India)		
Disease status	Trachoma control activities existing	Potential for trachoma control activities
Blinding trachoma known	Australia Cambodia India: Andaman & Nicobar Islands Chandigarh Haryana Punjab Rajasthan	China: Hubei Hunan Jilin Sichuan Yunnan Anhui (?) Henan (?)
Blinding trachoma suspected		
Non-blinding trachoma suspected		Bangladesh Indonesia Papua New Guinea Philippines Thailand Some Pacific Islands
Bold print indicates "first priority" countries for intervention		

The other countries of Asia are not known to have endemic trachoma.

ANNEX 5**APPROACH TO RAPID ASSESSMENT****GOAL**

For programmatic purposes, there is a need for a method to identify rapidly areas within countries that are liable to have a significant problem of blinding trachoma. If so identified by this rapid assessment method, the area could then be characterized in more depth using the WHO simplified grading scheme and some assessment of environmental and community resources.

METHOD

The following approach can be used for the quick determination of high-risk regions within countries and high-risk districts within regions (see Fig. 2). The rapid assessment does not take the place of proper surveys to assess the magnitude of the trachoma problem or provide a baseline for programme evaluation.

The goal is to divide the regions and districts into those with a high, moderate and low trachoma problem. At the national level, the use of key informants and reports of which regions have trichiasis, reports of trichiasis surgery and other anecdotal evidence can provide information on the regions with severe trachoma and trichiasis. Key informants include national ophthalmic personnel, directors of health, representatives of NGOs, UN agencies and others with knowledge of which regions have serious problems with trachoma, based on experience, hospital reports, etc. Where there is insufficient knowledge to categorize the regions, a rapid survey should be undertaken as described below.

To determine high-risk districts within the regions, the same approach can be used, i.e. information from regional key informants such as regional directors of health and regional ophthalmic personnel and from any regional records. Where there is insufficient knowledge to categorize the district, a rapid survey should again be undertaken.

The goal of a rapid survey at the regional or district level is to measure the prevalence of TF/TI in children and of TS in adult women for the purposes of categorizing regions or districts. **Two to three rural villages** should be selected which are among the most socioeconomically disadvantaged in the **district**. The conjunctiva of the upper lid of 50 children aged 5-7 years should be examined using the WHO simplified grading scheme, noting especially TF and TI, and of 30 women (aged 30+), noting especially TS. Children and women should be selected from at least **20 households**, which should include some of the most socioeconomically deprived and representing different geographical areas in the village. If at least 90% of children aged 5-7 years are believed to attend school, children may be sampled at school.

In assessing a region, **two to three villages** should be selected in **at least two districts**.

A prevalence of TF/TI of >20% in children, and/or a prevalence of TS of >30% in women aged 30 and older, indicates that trachoma is a serious public health problem. If the prevalence of TF/TI is less than 10% (fewer than 5 out of 50) and scarring is less than 5% (fewer than 2 out of 30), then trachoma is not a serious public health problem.

Applying these criteria, further ranking of villages by priority for **intervention** can then be made, depending on the local setting.

Initial assessment at the district level

The district is the administrative unit which will be in charge of administering the SAFE strategy. Depending on the size and resources of the district, the strategy may be implemented throughout. The availability of surgical services is likely to be at the district level. However, where district health may cover large populations, it may well become important to prioritize communities or population groups for the implementation of the rest of the SAFE strategy. At this level, a survey approach is essential as part of planning services. A district health person

would, as part of an assessment of needs for surgical services, visit the village. At this time, a small survey (as described above) could be undertaken. The results of all the surveys can be used by district personnel to prioritize communities for initiation of the entire SAFE strategy.

ANNEX 6

**PROGRAMME OBJECTIVE, APPROACHES, STRATEGIES
AND EVALUATION INDICATORS****I. Objective**

The overall **goal** of a trachoma intervention programme should be the elimination of trachoma as a blinding disease.

II. Approaches

1. Assess the magnitude and distribution of trachoma as a blinding disease and prioritize areas for intervention.
2. Provide the combined intervention of surgical correction of trichiasis, the prevention and treatment of active inflammatory trachoma and measures for improvement of personal and environmental hygiene.
3. Develop surveillance systems for monitoring/evaluation of changes in trachoma as a blinding disease.

III. Strategies

The elimination of trachoma as a blinding disease has four components that form a **combined intervention**, as part of primary health care. The components are summarized in the acronym SAFE.

1. The provision of **S**urgery to correct trachomatous trichiasis.
2. The use of appropriate **A**ntibiotics to reduce the reservoir of chlamydial infection within the community.
3. The promotion of personal hygiene with a particular emphasis on **F**acial cleanliness in pre-school children.
4. The initiation of **E**nvironmental changes to reduce the transmission of trachoma.

Surgery (1)

1. The surgical correction of trichiasis
 - Identify those in need of surgery (those with TT)
 - Motive and mobilize people to undergo trichiasis surgery
 - Provide accessible trichiasis surgery, which may need to be community-based
 - Train and equip appropriate personnel to undertake this surgery
 - Establish appropriate programme management
 - Establish ongoing programme evaluation of success of case-finding, proportion of patients having surgery and surgical outcome

The use of appropriate Antibiotics (2)

The use of antibiotics must be seen as being complementary to the improvement of personal and community hygiene. The objectives of antibiotic treatment are:

- ▶ to reduce the intensity of infection and inflammation in individuals;
- ▶ to reduce the transmission of infection within the family living unit.

In order to achieve sustained trachoma elimination it is desirable to reduce the community pool of infection, including both ocular and extraocular sites; this can only be achieved with the large-scale application of systemic antibiotic treatment.

For communities with active inflammatory trachoma (TF and TI) in more than 20% of children aged 1 to 10 years, **community-based** mass distribution of azithromycin is recommended. For children aged 1 year or older, a single dose of 20 mg/kg is recommended. In adults a single 1-g dose can be considered. Azithromycin should only be used by pregnant or lactating women where adequate alternatives are not available.

Operational research is required to determine whether this dosage should be repeated on an annual basis and, if so, for how long.

For communities with a prevalence of active inflammatory trachoma of less than 20% but greater than 5% in children 1 to 10 years of age, azithromycin treatment should be **household-based**, aiming to treat all members of the households that contain children with active disease.

For communities with a prevalence of active inflammatory trachoma (TF) of less than 5% and no TI in children aged 1 to 10 years, azithromycin treatment may **not** be required.

In areas in which azithromycin is not available, the currently recommended suppressive treatment with topical tetracycline may be used.

The utility of other antibiotics, particularly newer macrolides, is not known but may be evaluated.

To promote personal hygiene, in particular Facial cleanliness (3)

Facial cleanliness in children has been identified as a significant risk factor for trachoma in a number of diverse regions, and interventions to improve facial cleanliness are associated with a reduction of the amount of trachoma.

Programmes aimed at ensuring that children have consistently clean faces must mobilize community resources and support. They must address issues of water availability, water utilization and current face-washing practices.

The combined intervention (SAFE) must be tied to a social contract with the community, indicating their willingness to work together on the long-term improvement in facial cleanliness and community hygiene.

To initiate Environmental changes

Activities in this area must be targeted to the particular situation and requirements of a given region.

In general, measures that reduce the fly density will reduce the likelihood of transmission of trachoma. Activities may include the safe and proper disposal of domestic, human and animal waste and the provision of adequate water supplies.

Such activities are dependent on full community involvement. They often will need intersectoral action.

Operational priorities include the following:

- ▶ To identify and prioritize communities for intervention.
- ▶ To mobilize community support for the intervention programme.
- ▶ To foster the close integration of trachoma intervention activities with primary health care or community-based activities where these exist. In areas where these structures do not yet exist, consideration should be given to their establishment.
- ▶ To arrange for the community-based distribution of azithromycin or topical tetracycline.
- ▶ To devise and implement appropriate managerial and supervisory systems to safeguard the distribution of antibiotics.

- ▶ To undertake operations research to refine dosage, target and schedule of azithromycin treatment and the size of an intervention area.
- ▶ To establish mechanisms for ongoing evaluation and surveillance.

Evaluation methods and indicators will include the following:

- ▶ Change in prevalence rates of trachoma, with regard to active disease and its intensity
- ▶ Coverage levels achieved with antibiotic distribution
- ▶ Changes in measurable personal and community hygiene parameters such as the percentage of children with clean faces or the number of houses with easy access to safe water compared to baseline levels.

Goal indicators for the reduction in active trachoma are the elimination of TI and the reduction of the prevalence of TF to less than 5% in children aged 1 to 10 years in any community.

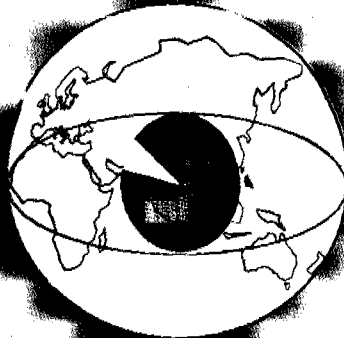
Global Elimination of Trachoma Coordinating Body

There clearly is a need for an international body to supervise and coordinate the anticipated national and regional trachoma elimination programmes, especially those utilizing azithromycin.

This body should include representatives of WHO, NGOs, national organizations, Pfizer, academia and other interested parties.

Terms of Reference to include the following:

- ▶ To identify areas of blinding endemic trachoma and prioritize these for intervention
- ▶ To recommend and monitor intervention programmes, especially those utilizing azithromycin
- ▶ To assess the capacity of proposed programmes to achieve their objectives
- ▶ To advise and provide technical assistance to those seeking to establish or strengthen intervention programmes
- ▶ To establish guidelines to ensure that azithromycin is delivered to the target population
- ▶ To review on a global level the success of the programme to eliminate trachoma as a cause of blindness
- ▶ To foster the integration of trachoma elimination within primary health care



Programme for the Prevention of Blindness and Deafness
World Health Organization
1211 Geneva 27 – Switzerland

Tel: +41 22 791 2111
Fax: +41 22 791 0746
E-mail: pbd@who.ch