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Trachoma: Time to learn from what is known


We read with interest the recent editorial entitled “What more is there to learn about trachoma” by Melese et al. Trachoma is responsible for up to two million cases of blindness worldwide, yet to a large extent it is a forgotten disease which affects the poorest and most medically underserved people.

The World Health Organisation (WHO) together with the International Agency for Prevention of Blindness jointly launched “VISION 2020 – the right to sight” in 1999 which aims to eliminate avoidable blindness by the year 2020, including blindness from trachoma. WHO has endorsed “SAFE” (Surgery for trichiasis, Antibiotics to reduce the prevalence of chlamydial infection, and Facial cleanliness and Environmental change to reduce the disease transmission) as the strategy implemented by national programmes to achieve the elimination of blinding trachoma. We have recently undertaken a review of the evidence base of the SAFE strategy and judged it to be strong for the surgery and antibiotics components, but weaker for the other components. We therefore concur with the opinion of Melese et al that more research is required, not only to develop a protocol for the rational use of antibiotics, as they suggest, but also to strengthen the evidence relating to the ‘F’ and ‘E’ components.

The SAFE strategy has been implemented by the national trachoma control programmes of many endemic countries in Africa, Asia and Latin America with varying degrees of success. Melese et al make the observation that the experiences gained from research studies are not directly transferable to real life settings; the need, therefore, is for the publication of the experiences of countries that have successfully dealt with trachoma through implementation of the SAFE strategy to serve as a best practice model for other countries. Morocco is a good example. A decade ago trachoma was a public health problem in five provinces of Morocco, but with the efficient implementation of the SAFE strategy the prevalence of active trachoma and trichiasis have declined dramatically so that Morocco is now close to eliminating trachoma as a public health problem. Real life country examples such as Morocco documented as case studies allow policy makers and programme managers to learn from the mistakes and successes of public health programmes, because, as Melese et al point out, real life is messier and more complicated than research studies.

Ferriman A. Blinding trachoma almost eliminated from Morocco. BMJ 2001; 323; 1387.
**Effect of 3 years of SAFE (surgery, antibiotics, facial cleanliness, and environmental change) strategy for trachoma control in southern Sudan: a cross-sectional study**

Jeremiah Ngondi, Alice Onsarigo, Fiona Matthews, Mark Reacher, Carol Brayne, Samson Baba, Anthony W Solomon, James Zingeser, Paul M Emerson  *Lancet* 2006; 368: 589–95

**Background:** A trachoma control programme was started in southern Sudan in 2001. We did a 3-year evaluation to quantify uptake of SAFE (surgery, antibiotics, facial cleanliness, and environmental change) interventions, and to assess the prevalence of active trachoma and unclean faces.

**Methods:** Cross-sectional surveys, including clinical assessment of trachoma (WHO simplified system) and structured questionnaires, were done in four intervention areas at baseline and follow-up. Process indicators were uptake of SAFE components; primary outcome indicators included trachomatous inflammation-follicular (TF) and unclean face in children aged 1–9 years.

**Findings:** There was heterogeneous uptake of SAFE between intervention areas. Surgical coverage was low in all areas (range 0.5% of 428 individuals in Katigiri to 6% of 5002 in Kiech Kuon), antibiotic uptake ranged from 14% of 1257 individuals surveyed in Kiech Kuon to 75% of 954 in Katigiri, health education ranged from 49% of 190 households in Kiech Kuon to 90% of 182 in Padak, and latrine coverage from 3% of households in Tali to 16% in Katigiri. Substantial decreases in prevalence of TF and unclean faces were recorded in Katigiri and Tali, two of three sites where uptake of antibiotics and health education was high: TF decreased by 92% (95% CI 87–96) and 91% (86–95), respectively, and unclean face decreased by 87% (78–94) and 38% (22–52), respectively. Moderate effects were recorded in Padak, an area with high coverage, with a 28% (14–41) decrease in TF and a 16% (7–25) decrease in unclean face. No evidence of decline was seen in Kiech Kuon, where uptake of antibiotics and health education was low, with a 2% (−10 to 12) decrease in TF and a 10% (−3 to 23) decrease in unclean face.

**Interpretation:** Our results show that substantial falls in active trachoma can occur where SAFE is implemented, and that good results could be achieved with the SAFE strategy in other trachoma-endemic areas.

**Implications of this study:**

Importance of evaluations
Regular evaluations of trachoma control activities are essential and warranted for decision making, programme planning, and the rational use of programme resources.

The SAFE strategy works
The study shows that the SAFE strategy for trachoma control works with substantial declines in active trachoma where it is well implemented. If such dramatic results can be achieved in southern Sudan, then it should be possible to replicate similar or even better results in other settings that are stable and not affected by conflict.

Decline in active trachoma is of great public health importance
The declines in active trachoma observed are of great public health importance since reduction in active trachoma will result in fewer cases of blinding trachoma in future. This good news brings hope to the people of southern Sudan and will help in priority setting for the provision of the full SAFE strategy in the entire region.
Need for flexibility in targeting SAFE interventions
Rational implementation of the SAFE strategy ought to be based on the needs of the endemic population such that the strategy focuses on the needs of the community. For instance, access to water is needed before hygiene promotion, or hygiene promotion should emphasize that facial cleanliness can be achieved by use of just small quantities of water. Low uptake of surgery indicates a need for much greater focus on TT surgery as soon as possible.

Synergistic effects of A, F and E components of SAFE
The greatest decreases in TF were generally achieved where there was highest uptake of antibiotics, facial cleanliness, and environmental change activities. This observation is consistent with a synergistic effect of these three components of SAFE, which are designed to slow transmission.

Collateral benefits of SAFE
The SAFE strategy was designed for trachoma control, but will have collateral health benefits on communicable diseases such as diarrhoea, intestinal helminths, pneumonia and malaria.
Associations between active trachoma and community intervention with Antibiotics, Facial cleanliness, and Environmental improvement (A,F,E)


Abstract
Background: Surgery, Antibiotics, Facial cleanliness and Environmental improvement (SAFE) are advocated by the World Health Organization (WHO) for trachoma control. However, few studies have evaluated the complete SAFE strategy and of these, none have investigated the associations of Antibiotics, Facial cleanliness and Environmental improvement (A,F,E) interventions and active trachoma. We aimed to investigate associations between active trachoma and A,F,E interventions in communities in Southern Sudan.

Methods and findings: Surveys were undertaken in four districts after 3 years of implementation of the SAFE strategy. Children aged 1-9 years were examined for trachoma and uptake of SAFE assessed through interviews and observations. Using ordinal logistic regression, associations between signs of active trachoma and A,F,E interventions were explored. Trachomatous inflammation-intense (TI) was considered more severe than trachomatous inflammation-follicular (TF).

A total of 1,712 children from 25 clusters (villages) were included in the analysis. Overall uptake of A,F,E interventions was: 53.0% of the eligible children had received at least one treatment with azithromycin; 62.4% children had a clean face on examination; 72.5% households reported washing faces of children two or more times a day; 73.1% households had received health education; 44.4% of households had water accessible within 30 minutes; and 6.3% households had pit latrines. Adjusting for age, sex and district baseline prevalence of active trachoma, factors independently associated with reduced odds of a more severe active trachoma sign were: receiving three treatments with azithromycin [odds ratio (OR)=0.1; 95% confidence interval (CI) 0.0-0.4]; clean face (OR=0.3; 95% CI 0.2-0.4); washing faces of children three or more times daily (OR=0.4; 95% CI 0.3-0.7); and presence and use of a pit latrine in the household (OR=0.4; 95% CI 0.2-0.9).

Conclusion: Analysis of associations between the A,F,E components of the SAFE strategy and active trachoma showed independent protective effects against active trachoma of mass systemic azithromycin treatment, facial cleanliness, face washing, and use of pit latrines in the household. This strongly argues for continued use of all the components of the SAFE strategy together.

Implications of this study:
1. The Surgery, Antibiotics, Facial cleanliness and Environmental improvement (SAFE) strategy was designed as a four-pronged community-based approach that provides a comprehensive programme for trachoma control that is adaptable to many different situations and which can be implemented at the community level.
2. Antibiotic therapy in individuals and facial cleanliness in children, combined with environmental improvement (A,F,E components of SAFE), have been designed to treat ocular Chlamydia infection and reduce the risk of transmission of ocular Chlamydia.
3. Regular evaluations of trachoma control activities are advocated for by the WHO for decision making, programme planning, and the rational use of programme resources. At present the WHO recommends evaluation of SAFE after three years of interventions.
4. Our study revealed that prevalence of active trachoma was less in children who had received treatment with azithromycin, had clean faces, had faces washed more frequently, and used latrines compared to children who had not received these interventions.

5. This study of associations between the A,F,E components of SAFE and active trachoma showed independent protective effects against active trachoma of mass systemic azithromycin treatment, clean face on examination, reported face washing, and presence and use of pit latrines in the household.

6. The study provides important evidence for continued advocacy for implementation of the full SAFE strategy as an integrated approach to control blinding trachoma; especially implementation of the A, F and E components of SAFE concurrently.

The paper is available from the internet URL link:
http://www.plosntds.org/article/info%3Adoi%2F10.1371%2Fjournal.pntd.0000229
ALEMBER, Ethiopia — Mare Alehegn lay back nervously on the metal operating table, her heart visibly pounding beneath her sackcloth dress, and clenched her fists as the paramedic sliced into her eyelid. Repeated infections had scarred the undersides of her eyelids, causing them to contract and forcing her lashes in on her eyes. For years, each blink felt like thorns raking her eyeballs. She had plucked the hairs with crude tweezers, but the stubble grew back sharper still.

The scratching, for Mrs. Alehegn, 42, and millions worldwide, gradually clouds the eyeball, dimming vision and, if left untreated, eventually leads to a life shrouded in darkness. This is late-stage trachoma, a neglected disease of neglected people, and a preventable one, but for a lack of the modest resources that could defeat it.

This operation, which promised to lift the lashes off Mrs. Alehegn's lacerated eyes, is a 15-minute procedure so simple that a health worker with a few weeks of training can do it. The materials cost about $10.

The operation, performed last year, would not only deliver Mrs. Alehegn from disabling pain and stop the damage to her corneas, but it also would hold out hope of a new life for her daughter, Enatnesh, who waited vigilantly outside the operating room door at the free surgery camp here.

Mrs. Alehegn's husband left her years ago when the disease rendered her unable to do a wife's work. At 6, Enatnesh was forced to choose between a father who could support her, or a lifetime of hard labor to help a mother who had no one else to turn to.

"I chose my mother," said the frail, pigtailed slip of a girl, so ill fed that she looked closer to 10 than her current age, 16. "If I hadn't gone with her, she would have died. No one was there to even give her a glass of water."

Their tale is common among trachoma sufferers. Trachoma's blinding damage builds over decades of repeated infections that begin in babies. The infections are spread from person to person, or by hungry flies that feed from seeping eyes.

In large part because women look after the children, and children are the most heavily infected, women are three times more likely to get the blinding, late stage of the disease. For many women, the pain and eventual blindness ensure a life of deepening destitution and dependency. They become a burden on daughters and granddaughters, making trachoma a generational scourge among women and girls who are often already the most vulnerable of the poor.

Trachoma disappeared from the United States and Europe as living standards improved, but remains endemic in much of Africa and parts of Latin America and Asia, its last, stubborn redoubts. The World Health Organization estimates that 70 million people are infected with it. Five million suffer from its late stages. And two million are blind because of it.

A million people like Mrs. Alehegn need the eyelid surgery in Ethiopia alone. Yet last year only 60,000 got it, all paid for by nonprofit groups like the Carter Center, Orbis and Christian Blind Mission International.

As prevalent as trachoma remains, the W.H.O. has made the blinding late stage of the disease a target for eradication within a generation because, in theory at least, everything needed to vanquish it is available. Controlling trachoma depends on relatively simple advances in hygiene, antibiotics and the inexpensive operation that was performed on Mrs. Alehegn.
But the extent of the disease far exceeds the money and medical workers available. In poor countries like this one, faced with epidemics of AIDS, malaria and tuberculosis, a disease like trachoma, which disables and blinds, has difficulty competing with those big killers.

Dr. Abebe Eshetu, a health official here in Ethiopia's Amhara region, described the resources available for trachoma as "a cup of water in the ocean."

Nowhere is the need greater than across this harsh rural landscape.

As dawn broke one day last year, hundreds of people desperate for relief streamed into an eyelid surgery camp run by the government and paid for by the Carter Center. Some of the oldest had walked days on feet twisted by arthritis to get here.

The throng spread across the scrubby land around a small health clinic. They wrapped shawls around their heads to shield themselves from sun and dust, made all the more agonizing by their affliction. Their cheeks were etched with the salty tracks of tears.

' Hair in the Eye'

Typical of those was Mrs. Alehegn, led stumbling and barefoot through stony fields by Enatnesh, who worriedly shielded her mother under a faded black umbrella.

As they waited their turn, Mrs. Alehegn explained that her troubles began more than 15 years ago when she developed "hair in the eye," as trachoma is known here. The pain made it impossible for her to cook over smoky dung fires, hike to distant wells for water or work in dusty fields, the essential duties of a wife.

Gradually the affliction soured her relationship with her husband, Asmare Demissie, who divorced her a decade ago, so he could marry a healthy woman.

"When I stopped getting up in the morning to do the housecleaning, when I stopped helping with the farm work, we started fighting," Mrs. Alehegn said.

The operation she had come for is still exceedingly rare in Ethiopia. Only 76 ophthalmologists practice in this vast nation of 70 million people. Most work in the capital, Addis Ababa, not in the rural areas where trachoma reigns.

Because of the extreme doctor shortage, nonprofit groups have paid for the training of ordinary government health workers over two to four weeks to do the eyelid surgery. The Carter Center, which favors a month of training, estimates the cost at $600 per worker, plus $800 for two surgical instrument kits for each of them.

Those trained make an incision that runs the length of the eyelid's underside, through the cartilage-like plate, then lift the side of the lid fringed with the eyelashes outward. Then they stitch the two sides back together. The patient is given a local anesthetic.

The operation cannot undo the damage already done to corneas, which makes the abraded eyes vulnerable to infections. But it can stop further injury. And because the disease often takes decades to render its victims blind, the operation can save a woman's sight and halt disabling pain.

For Mrs. Alehegn, the surgery was her second. Her plight is typical, for trachoma is both a disease of poverty and a disease that causes poverty.

After separating from her husband, she, Enatnesh and another daughter, Adelogne, then just 4, moved to a small, poor piece of land belonging to Mrs. Alehegn's family. About a year later, Mrs. Alehegn scraped together enough money for her first eyelid surgery. But as she aged, the underside of her eyelids — scarred by past trachoma infections — continued to shrink, turning her lashes inward again.

In recent years, her poverty was so dire she could not afford to have the surgery again. Her only income was the dollar or so a week that Enatnesh collected when she went to market to sell the cotton fabric her mother wove. They were so poor they could not afford even 15 cents for soap.

"If I get my health back, it means everything," Mrs. Alehegn said. "I'll be able to work and support my family."
The others who journeyed to the camp told many such stories of hardship. In a land where early death is commonplace, some of those with the disease see their wounded eyes, ceaselessly leaking tears, as a kind of stigmata of sorrow. Banchiayehu Gonete, an elderly widow, said three of her eight children had died young. The bitterest loss was of her eldest daughter, carried off by malaria at 40 with a baby still inside her. It was this daughter who had plucked her in-turned lashes, cooked for her and kept her company. "God killed my children," said Mrs. Gonete, old and wrinkled, but unsure of her age. "I feel this pain as part of my mourning."

Nearby, Tsehainesh Beryihun, 10, sat with her grandmother, Yamrot Mekonen. Trachoma ended the girl's childhood years ago. When her parents divorced, her mother gave Tsehainesh, then just a baby, to her paternal grandmother. As the old woman's sight failed, Tsehainesh became her servant. Since she was 7, she has fetched water, cooked, cleaned, collected dung and wood for the fire and swept the dirt floors, her grandmother said. The girl sees her half brothers and sisters, the children of her father's second marriage, happily dashing to school, while she lives apart, her days filled with the grinding work of tending to a sickly, demanding old woman. Her grandmother explained that the girl owes her. "I've supported her this far," Mrs. Mekonen said impassively, "so now it's her turn to support me."

Tsehainesh wept bitterly as her grandmother spoke, refusing to utter a word.

**Ending Disability and Dependency**

To break this cycle of debilitation and dependency, the goal is not eradication of the eye infections themselves, which most agree is neither practical nor necessary, but rather to reduce their frequency and intensity, a more achievable goal. This would avoid development of the devastating late stage of trachoma, called trichiasis, that makes surgery the sufferers' only salvation.

Toward that end, the World Health Organization has approved a strategy known as SAFE, an acronym that stands for surgery, antibiotics, face washing and environmental change, notably improved access to latrines and water. Already, some researchers say, the growing use of antibiotics around the world to treat infections, even those unrelated to trachoma, has probably contributed to trachoma's decline. That is true even in very poor countries where there is no organized effort to tackle the disease, like Nepal and Malawi, they say. The use of Zithromax, an antibiotic manufactured by Pfizer, has proved a breakthrough. The most common alternative is a cheap, messy antibiotic ointment that has to be applied twice daily to the eyes for six weeks. Zithromax, in contrast, can be taken in a single dose — making compliance easier and distribution to millions simpler. By 2008, Pfizer, the world's largest drug maker, will have donated 145 million doses for trachoma control. Its contribution is administered by the International Trachoma Initiative, a nonprofit group. The drug has been provided in 11 of the 55 countries where trachoma remains a problem. But globally, the World Health Organization estimates that at least 350 million people need the antibiotics once a year for three years to bring infection rates under control. That equals more than a billion doses of azithromycin, the generic name for Zithromax. Trachoma is so rampant here in Ethiopia that an estimated 60 million people, or 86 percent of the country's population, need the drug. Pfizer has not officially announced any additional donations, but Dr. Joseph M. Feczko, a Pfizer vice president, says the company will provide whatever is needed. "There's no cap or limit on this," he said. "We're in it for the long haul."

But even free drugs cost money to distribute. No global estimates are available for carrying out the SAFE strategy for trachoma control, but the Ethiopian government, beset by
competing social problems, would have to come up with $30 million to reach even half the people who need the antibiotic, and $20 million more for public education on basic hygiene. For now, the aim here is a more modest effort at localized control, but even that will not be easy.

An Ancient Scourge

Chlamydia trachomatis, the microorganism that causes trachoma, has been a source of misery for millennia, thriving in poor, crowded and unsanitary conditions. In ancient Egypt, in-turned eyelashes were plucked, then treated with a mixture of frankincense, lizard dung and donkey blood. In Victorian England, infected children were isolated in separate schools. At the turn of the century, doctors at Ellis Island used a buttonhook to examine the undersides of immigrants' eyelids. Those with signs of trachoma were often shipped back to their home countries.

Swarming Musca sorbens flies play an ignominious role in spreading the disease. They crave eye discharge and pick up chlamydia as they burrow greedily, maddeningly into infected eyes.

"They cluster shoulder to shoulder around an infected eye," said Paul Emerson, the entomologist who did pioneering work on the role of the flies in spreading trachoma and who now runs the Carter Center's trachoma control program.

So inescapable, so persistent are they here in the Amhara region that children learn not to bother shooing them away. Even at the surgery camp, flies buzzed through the chicken wire that covered the windows of cramped operating rooms, harassing trachoma victims at the moment they sought relief.

Once the eggs of a female fly are ripe, she lays them in her preferred breeding medium, human feces, plentiful because most people here go to the bathroom outdoors.

But the flies cannot breed in simple, inexpensive pit latrines, Mr. Emerson said. He said he does not yet know why, but he thinks that a competing species that does thrive in latrines may eat the Musca sorbens maggots.

Ethiopia is now making a national effort to get people to build latrines, training thousands of village health workers to spread the word. It is also teaching children the importance of face washing in school.

But soap and water are scarce, too. Women often walk hours a day to wells to carry home precious pots of water balanced on their heads. And soap is a luxury for the poorest of the poor.

For those like Mrs. Alehegn, with late stage trachoma, surgery will continue to be necessary. When her operation was complete, the health worker who performed it, Mola Dessie, pressed white cotton pads on Mrs. Alehegn's eyes to soak up the blood and applied antibiotic ointment to prevent infection. Then he covered her eyes with bandages.

Enatnesh wrapped her mother's head in a dingy cloth and slipped her stick-thin arm around her mother's waist to lead her away.

Mrs. Alehegn, who is illiterate, says she hopes that once she heals she will be able to weave more cloth, earn more money and do the domestic chores, leaving Enatnesh freer to pursue an education. "I don't want her to live my life," she said.

Despite her dependence on her daughter, Mrs. Alehegn has allowed the girl to go to school. Enatnesh, though having fallen behind, is a diligent fifth grader at age 16, who proudly said she is ranked 5th out of 74 students in her class. She dreams of being a doctor.

Two days after her mother's surgery, Enatnesh led the way to her father's sturdily built hut a couple of hours walk away. There, as his second wife swept the compound and Enatnesh's 9-year-old half-brother sat in the shade, Mr. Demissie, 58, offered a regretful explanation for his decision to divorce his first wife.

He, too, had developed "hair in the eye," he said. And like his wife, he, too, had been forced to stop working. If they had not separated, he reckoned, they would both have died. Finally, Mr. Demissie decided to save himself.
His sick wife would never find anyone else to marry, he realized. But for him, a new, hardworking wife would provide a second chance. And after his marriage, he got the surgery to prevent his own blindness.
"If we had not been sick," he said sadly, "we would have raised our children together."
As he spoke, Enatnesh listened sorrowfully, her hand cupped over her mouth, her head bent low.
Surgery

*A randomised controlled trial of azithromycin following surgery for trachomatous trichiasis in The Gambia.*


Background/aim: Trachomatous trichiasis frequently returns following surgery. Several factors may promote recurrence: preoperative disease severity, surgeon ability, surgical procedure, healing responses, and infection. This study investigates whether enhanced control of infection, both of *Chlamydia trachomatis* and other bacteria, with azithromycin can improve surgical outcome in a trachoma control programme.

Methods: Individuals with trachomatous trichiasis were examined and operated. After surgery patients were randomised to the azithromycin or control group. The azithromycin group and children in their household were given a dose of azithromycin. Antibiotic treatment was repeated at 6 months. All patients were reassessed at 6 months and 12 months. Samples were collected for *C trachomatis* polymerase chain reaction and general microbiology at each examination.

Results: 451 patients were enrolled. 426 (94%) were reassessed at 1 year, of whom 176 (41.3%) had one or more lashes touching the eye and 84 (19.7%) had five or more lashes. There was no difference in trichiasis recurrence between the azithromycin and control group. Recurrent trichiasis was significantly associated with more severe preoperative trichiasis, bacterial infection, and severe conjunctival inflammation at 12 months. Significant variability in outcome was found between surgeons. Visual acuity and symptoms significantly improved following surgery.

Conclusion: In this setting, with a low prevalence of active trachoma, azithromycin did not improve the outcome of trichiasis surgery conducted by a trachoma control programme. Audit of trichiasis surgery should be routine.

Implications of this study:

1) Azithromycin does not reduce trichiasis recurrence

This study did not find any difference in the outcome of surgery between those who were given peri-operative azithromycin and those who were not. The Gambia is an area with low levels of *Chlamydia trachomatis* infection. It is possible that in areas with a high prevalence of endemic trachoma this intervention may be effective – a question that is currently being tested in a highly endemic country. Therefore, we currently do not advocate the additional use of azithromycin following surgery. All patients should continue to receive a topical antibiotic ointment for at least two weeks following the surgery.

2) High recurrence rate
There was a high trichiasis recurrence rate in this study, which is consistent with other studies. This is an important observation. At a national programme level it is important to remember when planning the provision of surgical services for a region that some of the trichiasis will return and need further surgery, may be as much as 20% by one year. On an individual level, patients should be warned before the operation that the trichiasis can come back. They should be clearly advised to seek help if there is a recurrence. Where possible, it is ideal for programmes to develop follow-up mechanisms to monitor patients for recurrence. For example, this follow-up could be done when a community is visited for an annual distribution of antibiotic for trachoma control.

3) Patients benefited from surgery

Despite the high recurrence rate, overall, patients really benefited from the surgery. There was a marked reduction in the pain experienced from trichiasis. There was a significant improvement in the visual acuity (objective and subjective), probably related to reduction in secretions and improvement in the health of the ocular surface. Even with recurrent trichiasis, the overall burden of trichiasis and associated bacterial infection was markedly reduced. Therefore, in counselling patients prior to surgery the surgeon can reasonably tell the patient that they will probably feel much more comfortable and that there may even be a modest improvement in vision in those who do not already have a lot of corneal scarring.

4) Significant inter-surgeon variability in results – audit / training

An important observation in this study is the variation in results between the surgeons. There is very little published data on inter-observer variation. However, it is likely that such variations in results occur in other trachoma control programmes. This highlights the need to periodically audit the results of individual surgeons. It is vital that such an audit process is conducted in a supportive manner. If the results of a particular surgeon are less good, then steps will need to be taken to provide additional training and support to try to identify any technical problems and so improve the results.

5) Understanding recurrence

Recurrent trichiasis probably has a number of different causes. In addition to a significant effect from inter-surgeon ability, this study identified a number of other factors that contribute. Individuals with more severe entropion and trichiasis are more likely to get a recurrence. Therefore, where possible, such cases should be operated on by more experienced surgeons, to maximise the chance of a good outcome. Bacterial infection was commonly found in eyes with trichiasis, indicating the importance of cleaning the eyes with povidone iodine at the beginning of the surgery. Bacterial infection may be important in promoting conjunctival inflammation which can result in additional scarring.

6) Progression of corneal opacification

A worrying observation, which needs to be confirmed in other studies, is that corneal opacification may develop in eyes after trichiasis surgery even when there is no recurrence of the trichiasis. Bacterial infection may again be important in this process, but other factors such as ocular dryness and conjunctival inflammation may also have a role. An improved understanding of the development of corneal opacification is needed, in order to develop strategies to combat this.
**Uptake of trichiasis surgical services in Tanzania through two village-based approaches**


Aim: To determine the effectiveness of village-based strategies (using school and village leaders) to increase the use of surgical services.

Methods: A cohort study was conducted in Tanzanian using two village strategies (village leader and school teachers); trichiasis surgical uptake and the factors associated with uptake were measured after 1 year.

Results: The trichiasis surgical coverage at baseline was 16.9%: 200 patients who needed surgery were identified. One year later, we were able to re-examine and interview 163 of these patients. The surgical uptake among these patients was 44.8% (95% CI 37.2% to 52.4%). Patients in the school-teacher programme had a 36.5% uptake compared to with 52.1% for those in the village-leader programme. No difference was observed in uptake by age or sex. Uptake was highest among the coming from multiple-generation households and those with more household wealth. Of the 90 people who still had not surgery, 20 (22.2%) reported seeking surgery, but failing to receive it because of barriers at the provider side.

Conclusion: Improved surgical uptake for trachomatous trichiasis was achieved by using village-based promotion efforts and surgical services at existing health clinics. Even with free surgery at health clinics, indirect costs and social support barriers limit utilisation by the most vulnerable, the poorest and those living in single-generation households. Problem at the provider level also create barriers for patients who need surgery.

**Surgery for trachomatous trichiasis: findings from a survey of trichiasis surgeons in Tanzania**


Aims: To measure the productivity and factors associated with high productivity trichiasis surgeons.

Methods: A standardised, pretested questionnaire was posted to all trichiasis surgeons trained in Tanzania at the address listed at the time of training, and then followed up by post and telephone with those who did not return the form. Questions asked related to place of work, number of surgeries carried out, supplies and equipment available, and outreach activities. A random selection of high-productivity and low-productivity surgeons was invited to a focus group meeting to discuss factors that affected productivity.

Results: 28 of the trained surgeons had died, retired or could not be located. Forms were retrieved from 95 others. Productivity (averaged over the past 4 years) was low overall, but highly variable. The mean number of surgeries per year was 22.3 (SD 48.1) and the median was 7. The most important factor associated with higher productivity was conducting outreach activities. Conducting outreach was associated with having a complete set of instruments and consumables and with being able to identify a supervisor.

Conclusion: Redesigning the provision of trichiasis surgery (in particular, supervision, support and community programmes/outreach) is necessary to ensure that the investment from training is used adequately.
Synopsis:

These two companion papers look at the provision of trichiasis surgery and the surgeons themselves. The study on the uptake of trichiasis surgery was carried out first and led the research team to look at issues surrounding the training, deployment, and supervision of trichiasis surgeons.

The uptake study was based on the perception (which can be debated) that the cost of outreach to trachoma endemic communities to carry out surgery as a dedicated activity was not practical as a long-term solution to preventing blindness due to trichiasis. The study aim was to determine whether community-based activities to encourage utilization, when matched with surgical services as district hospitals or other facilities could lead to increased uptake. The study was population based and led to the establishment of a cohort of people with trichiasis in the community, which was followed up after one year. At the beginning of the study the trichiasis surgical coverage was only 17%. Both of the community-based methods (training of village leaders and training of schoolteachers) showed good uptake, achieving an increase of coverage among those who had not had surgery to 45% at the end of one year; the village leader programme being slightly higher than the schoolteacher programme. The study suggested that:

- Community-based approaches that did not require outreach to the specific communities can be effective in increasing utilization of trichiasis surgical services.
- These approaches, which focused on the needs of women, can lead to gender equity in use of trichiasis surgery.
- Factors which continue to thwart uptake by people in the community remain socio-economic in nature; even when surgery is provided free the most marginalized members of the community still do not have adequate access.
- Barriers are not simply at the community level; 22% of people sought surgery but because of surgeon related factors (being turned away by the surgeon, the surgeon not being at the health facility, or reported lack of instruments by the surgeon) they did not receive surgery. The dissatisfaction reported by this group is likely to lead to poor uptake by other members of the community.

Learning that almost one-quarter of the people with trichiasis sought surgery but did not receive such surgery led the team to investigate the productivity of surgeons and to try to determine some of the factors associated with high or low productivity. All trichiasis surgeons trained in Tanzania were sent a questionnaire to complete. This was followed by a meeting of selected surgeons to explore some of the quantitative findings through group discussion. Findings indicated a very high variability in productivity with the mean number of surgeries per surgeon per year at 22 but the median at 7; thus half of the surgeons trained were doing less than 7 surgeries per year. Productivity was associated with conducting outreach, having a full set of instruments, and supervision. The study suggested that:

- Training surgeons, although an essential component is insufficient to ensure that trichiasis patients actually get surgery.
- All surgeons were given instruments (by HKI or ITI) upon graduation but the lack of a system for replacement or obtaining consumables hindered the acquisition of new supplies.
- The lack of consistent, clearly understood supervision has been noted in many studies of human resource management in Africa. This is true for trichiasis surgeons as well. Management systems need to be well structured and well understood by all health providers for good job satisfaction as well as to meet the needs of the population.
During the time of the study the major national strategy for improving uptake of trichiasis surgery was outreach to communities, however less than half of the surgeons in the study did outreach. As reported in other settings, conducting outreach improves uptake; as noted in the uptake study, community based approaches can also improve uptake.

The continued low coverage of trichiasis surgery globally was noted at a number of recent trachoma review meetings including the recent GET 2020 meeting (Cairo), the Carter Center Trachoma Review Meeting (Atlanta), and the SightSavers International Trachoma Review Meeting (Mombasa). Findings from the work in Tanzania as well as important findings from research carried out in Ethiopia, Egypt, the Gambia, and Nigeria indicates that considerable work needs to be carried out to scale up surgery.
Trichiasis and disability in a trachoma-endemic area of Tanzania


Objective: To measure limitations in the daily activities of village life associated with having trichiasis for individuals with and without visual acuity loss.

Methods: Men and women 40 years and older in 6 randomly chosen rural villages in the Kongwa district of Tanzania had visual acuity measured and were examined by an ophthalmologist. Subjects indicated the degree of difficulty with daily activities of village life and whether the difficulty was related, in any way, to vision. Limitations were scored using an indicator of “any difficulty” and using a 4-point scale ranging from “no difficulty” to “unable to do”. Scores of individuals with and without trichiasis were compared separately for men and women.

Results: Among men, trichiasis was associated with excess functional limitation only for those with visual acuity loss (adjusted difference in proportion of tasks [AD] compared with men with neither trichiasis nor visual impairment, 0.35; 95% confidence interval [CI], 0.23-0.47). For women, trichiasis alone was limiting (AD, 0.15; 95% CI, 0.08-0.22) similarly to visual acuity loss alone (AD, 0.09; 95% CI 0.06-0.13), and the combination led to greater limitations (AD, 0.32; 95% CI 0.26-0.39).

Conclusion: The burden of trichiasis is likely greater than previously estimated, especially in women for whom trichiasis alone was disabling.

Synopsis

Using data from Tanzania, Frick and colleagues found that men with visual acuity impairments and trichiasis had greater functional limitation than men with visual acuity impairments only, although men with trichiasis and no visual acuity impairment were not functionally limited in comparison with men with neither visual acuity impairment nor trichiasis. In contrast, women with trichiasis and no visual acuity impairment were more functionally limited than women with neither condition. In addition, and similarly to men, women with trichiasis and visual acuity impairment were more functionally limited than women with visual acuity impairment only. This set of findings has two important implications.

First, for at least a portion of the population, trichiasis prior to visual acuity impairment can lead to a loss of functionality and possibly personal productivity. Even for individuals who do not work for pay this can be quite important as they will be less able to provide for themselves and may require greater assistance from others, thereby limiting the productivity of other individuals. When evaluating the benefits from expansion of the provision of trichiasis surgery, improvements in the productivity of those without visual acuity impairment should be considered a benefit in addition to the prevention of future visual acuity loss or greater visual acuity loss than the patient had already suffered.

Second, women appear to be more affected than men. While there would be little justification for exclusion of men from receiving a service, efforts to encourage the utilization of trichiasis surgery prior to visual acuity impairment might particularly focus on women as they seem to be affected more at this stage of the condition.
Surgery for trichiasis by ophthalmologists versus integrated eye care workers: A Randomized Trial


OBJECTIVE: To study the outcome of bilamellar tarsal rotation (BTR) trichiasis surgery performed by ophthalmologists versus that done by integrated eye care workers (IECWs).

DESIGN: Randomized prospective interventional trial. PARTICIPANTS: Nine hundred eighty-two patients with various degrees of trachomatous trichiasis in central Ethiopia. METHODS: Trachomatous trichiasis patients in 3 woredas (districts) in central Ethiopia were enrolled. Trichiasis severity was graded. Patients were randomly assigned to surgery by 2 ophthalmologists and 2 IECWs. On the seventh day postoperatively, patients were evaluated for undercorrection or other complications. If trichiasis was present, it was considered a failure of surgery (technical failure), and patients were excluded from the follow-up study, but repeat surgery was performed. Those patients with good correction at the seventh day were examined again on the third and sixth months. Further follow-up evaluation is planned for the first, second, and third years postoperatively. MAIN OUTCOME MEASURES: Recurrence rate, recurrence difference in the various grades, and difference between surgeries done by ophthalmic surgeons and those done by IECWs. RESULTS: In the third month of follow-up, it was possible to locate 713 (73.0%) of the operated patients. Eighty-one of 713 (11.4%) individuals and 94 of 1286 (5.4%) operated lids developed recurrent trichiasis in this period. There was a linear trend of recurrence with grading (severity) at baseline (chi(2) = 22.017, P<0.001), but there was no difference in recurrence by age (chi(2) =1.53, P = 0.9 at the third month; chi(2) = 1.43, P = 0.9 at the sixth month). There was also no difference with regard to gender (0.38 < odds ratio < 1.14, P = 0.1). The recurrence observed in the group of individuals operated on by ophthalmologists at the 3-month follow-up was 47 (12.1%) lids, and the recurrence observed in the group operated on by the IECWs was 34 (9.9%) lids, with no statistically significant difference (chi(2) =1.38, P = 0.24, 95% confidence interval [CI], -18% to 74%). At the 6-month follow-up, 43 (6.2%) persons had recurrence (95% CI, 4.4%-8%). There was no statistically significant difference between the 2 groups of surgeons at the 6-month point of follow-up examination (chi(2) = 4.46, P = 0.2). The overall recurrence was 124 (14.3%) lids within the first 6 months. CONCLUSION: Recurrent trichiasis is common, especially in cases where the degree of trichiasis is severe at baseline. This suggests that these patients may need surgical overcorrection to decrease the recurrence rate. The outcome of BTR surgery done by IECWs is similar to that of the ophthalmic surgeons. Because of these findings, we recommend that training of IECWs in trichiasis surgery may help to ameliorate the effects of the eye care worker shortage in developing countries.

Synopsis

Trachoma is the second leading cause of blindness worldwide. Repeated inflammation of the conjunctivae results in scarring, which ultimately leads to trichiasis/entropion. Surgery is the recommended mode of treatment, but the recurrence is high. In developing countries there is a severe shortage of eye care workers to do the surgery, especially among the rural population. ORBIS with MoH of Ethiopia designed a one month programme to train nurses as Integrated Eye Care Workers (IECWs) on primary eye care including trichiasis surgery (Bilamellar Tarsal Rotation). Followed the training we sought to determine the quality of
surgery prior to expanding the training programme. The other question we sought to answer was who, among trichiasis patients, developed recurrence. In a separate study we developed a modified grading of trichiasis/entropion from simple to severe stages, which was important for recurrence and for patient management (Melese et al. Modified grading of trachomatous trichiasis. *Ophthalmic Epidemiology* 2003; 10:75-80). This study was designed to test the quality of surgery by IECWs and the recurrence level of trichiasis with the modified grading.

Nine hundred eighty trachomatous trichiasis patients in three woredas (districts) in central Ethiopia were enrolled. Trichiasis severity was graded. Patients were randomly assigned to surgery by 2 ophthalmologists and 2 integrated eye care workers. The recurrence rate at the 3 month follow-up was 11.4% and at the 6 months follow-up it was 6.2% of the persons. There was no statistical significant difference in recurrence between the ophthalmologist and IECWs groups. There was a linear trend of recurrence with grading (severity) at baseline ($\chi^2 = 22.017; P <0.001$). The overall recurrence was 14.3%.

**What is the take-home message :** The recurrence of trichiasis is high for baseline severe grades of trichiasis. The outcome of BTR surgery done by IECWs is similar to that of the ophthalmic surgeons. IECWs can fill the gap of trichiasis surgeons in developing countries.
Background/aim: Recurrence of trichiasis following surgery is a significant problem for national trachoma control programs. Reasons for high recurrence rates are not clear, although surgical factors likely play a role in immediate recurrence. Data also suggest that infection with *C. trachomatis* post-surgery may be a factor. The objectives of this clinical trial were to determine if treating trichiasis patients post-surgery with azithromycin compared to usual care (topical tetracycline) reduces recurrence of trichiasis, and if azithromycin treatment of other household members provides additional benefit, compared to treating only the surgical patient with azithromycin.

Methods: A randomized, single-masked, controlled clinical trial was conducted in a rural, trachoma hyperendemic district in Ethiopia. 1452 trichiasis patients ages 18 or older were randomized into three treatment arms: Azithromycin alone (single 1 gram dose), azithromycin for household members plus the patient (20mg/kg up to 1 gram single dose), and topical tetracycline (twice per day for six weeks). Recurrent trichiasis was assessed at 2 weeks, 1.5, 6, and 12 months post-surgery. Trichiasis surgery was provided by trained Integrated Eye Care Workers (IECW). All IECWs were certified for surgery by our study team, using WHO guidelines, to ensure quality (the effect of antibiotics cannot be adequately studied if surgical failures are high).

Results: Among the 1452 surgical patients, recurrence rates were low, overall 8/100 person-years. The azithromycin groups had significantly fewer recurrences, 6.9/100 person-years overall, compared to topical tetracycline, 10.3/100 person-years (p=0.047). There was no additional reduction with also treating the household members, 8.1/100 person-years, compared to treating the surgical patients alone, 5.8/100 person-years (p=.19).

Conclusion: Azithromycin was associated with a 33% reduction in post-surgical recurrence of trichiasis in this trachoma hyper-endemic setting, where overall recurrence rates were low.

Implications of this study:

1) Where early surgical failures are not high, Azithromycin reduces trichiasis recurrence compared to topical tetracycline

This randomised trial of large numbers of trichiasis patients in a trachoma hyper-endemic area of Ethiopia found a 33% reduction in one-year trichiasis recurrence in the group receiving azithromycin. There was no evidence for an additional benefit of treating the family members of surgical cases with azithromycin, so surgical programs can concentrate on post-operative treatment alone. The mechanism of action of azithromycin is unclear, but maybe due to its broad spectrum, long lasting intracellular levels, and anti-inflammatory properties. Where country programs have access to azithromycin, we recommend post surgical treatment to reduce recurrence.

2) Importance of training in good surgical technique, and certification using WHO Guidelines

This study was conducted in a trachoma endemic rural area of Ethiopia, using non-ophthalmologists. To ensure high quality for the trial, each surgeon was certified as
acceptable using the World Health Organization checklist. During the certification process, special attention was paid to understanding and practicing sterile techniques, and proper lid rotation. Surgeons who could not pass certification were offered more training, but did not perform surgery for this trial. National surgical programs should acknowledge that not all district eye care workers can be acceptable surgeons, and that training alone is insufficient to ensure quality. The extra step of certification by an expert other than the trainer should help reduce the unacceptably high recurrence rates observed in many other settings.

3) Overall low recurrence rates are possible

The recurrence rates observed in this trial were 8% at one year, a target that National Programs can achieve with proper training, certification, and post surgical treatment with azithromycin. Surgical audits of outcomes will also provide feedback to the surgeon, and should be an integral part of any surgical program. Follow up of surgical cases at one year by village health workers trained to recognize trichiasis may be an integral part of trachoma program. Any surgeon with a recurrence rate at one year that is greater than 15%, double our rate, should receive proper re-training and certification before resuming surgery. Recurrence rates will be higher in areas where recurrent trichiasis is re-operated, as previous surgery is a risk factor for further recurrence. Ideally, recurrent case should be operated by the most experienced surgeons, as they will be more difficult in any case.

4) Rates of Adverse Events with use of Azithromycin, in surgical patients and in families, were similar to groups with no treatment or treatment with topical tetracycline.

Use of azithromycin post surgery, and use in the surgical case’s families was safe, a finding previously reported. Morbidity and mortality rates were similar in all groups, so use of azithromycin, single dose of 20mg/kg up to 1 gm, can be recommended safely.
Background: The World Health Organization recommends trichiasis surgery to prevent blindness from trachoma; however, recurrence is common. Risk factors for recurrence have not been widely studied, particularly in trachoma hyper-endemic areas.

Methods: 394 trichiasis cases in Tanzania were examined. Participants had undergone surgery >18 months prior to the study. Trichiasis recurrence and active trachoma at study visit were assessed. Ocular swabs were collected and tested for *C. trachomatis*. Household members were examined for active trachoma.

Results: 28% of operated eyes had recurrence; 40% of patients had recurrence in one or both eyes. Rates did not vary by time since surgery. Eye-level recurrence rates varied significantly across districts, ranging from 16% - 38%. Current chlamydial infection among surgical cases was low (6%) and was not associated with trichiasis recurrence. Recurrence was associated with tarsal conjunctival inflammation (OR: 2.4; 95% CI: 1.6-3.8) and residence in Kongwa district (OR: 2.3; 95% CI: 1.2-4.6).

Conclusions: Recurrence after trichiasis surgery is high, suggesting vigilant follow up of surgical cases is needed to reduce blindness. Recurrence is associated with evidence of inflammation in the tarsal conjunctiva, although it is not clear if the inflammation contributed to recurrence, or is a result of the recurrence. Longitudinal studies of trichiasis cases following surgery are needed.

Synopsis

Many trachoma-endemic countries are currently establishing surgical programs to reduce the burden of trichiasis in the community. It is important that the initial results of these programs are very successful in order to develop long-term sustainability and high participation rates. Several studies have shown that trichiasis recurs in approximately 20% of cases within one year following surgery, and in some regions the long-term trichiasis recurrence rate is over 50%. In order to develop successful surgical programs with high participation rates, recurrence rates need to be much lower. Risk factors for trichiasis recurrence have just recently begun to be examined.

In this study, we estimated the long-term trichiasis recurrence rate in central Tanzania and examined risk factors for trichiasis recurrence in this region. Trichiasis recurrence was statistically significantly associated with having TI in the surgical eye and having two or more household members with TI. Given the cross-sectional nature of the data collection, we were unable to definitely conclude whether inflammation causes continuation of scarring and thus promotes trichiasis recurrence, or whether the inflammation is a result of recurrence itself. However, the association with TI among family members suggests that active trachoma in a household is a risk factor for trichiasis recurrence. Furthermore, although our infection rate was very low, there was a statistically significant association between TI and *C. trachomatis* infection. 10% of eyes with TI were infected while only 2% of eyes without TI were infected.
We also found an association between district of residence and trichiasis recurrence. Our study included participants from five districts. Participants living in Kongwa district were more than twice as likely to have recurrence as individuals living in Singida district (adjusted OR: 2.3, 95% CI: 1.2-4.6). District may serve as a proxy for a variety of factors such as trachoma markers and surgical factors. The rate of trachoma within these districts varied significantly. Kongwa had the highest rate of trachoma among family members. Therefore, even after adjustment for household trachoma, the increased rate of recurrence in this population may be a marker for community-level exposure to trachoma. Alternatively, district may be a marker for differences in surgical factors. In each of these districts, with the exception of Kongwa, 1 or 2 individuals complete nearly all of the trichiasis surgeries. The use of district as a covariate serves as a proxy for the individual performing the surgeries. Kongwa district is a training area for trichiasis surgeons; hence, many newly trained individuals perform surgeries in this region and the higher rate of recurrence may be an indicator of the skill level of the surgeon.

While the cross-sectional nature of this study prevents drawing firm conclusions regarding the importance of community trachoma levels and skill level of the surgeon, these data suggest that thorough training and certification of health care workers prior to performing surgery are important components of a successful surgical program. Longitudinal studies involving trachoma treatment are needed in order to evaluate the importance of TI in surgical cases and the community burden of trachoma on trichiasis recurrence. These studies will shed light on the importance of individual or community mass treatment on reducing the rate of trichiasis recurrence.
Antibiotics

*Height as a proxy for weight in determining Azithromycin treatment for paediatric trachoma.*


Azithromycin (Zithromax, Pfizer In., New York, NY, USA) is effective in the control of blinding trachoma. Community based Azithromycin treatment is recommended by the World Health Organization as part of a multipronged strategy aimed at the global elimination of blinding trachoma by the year 2020. Paediatric trachoma is treated with azithromycin according to weight at a target dosage of 20 mg/kg. However, conventional weight-based treatment may be problematic in the field due to the logistical difficulties associated with weight scales. We assessed the accuracy of using height as a proxy for weight to determine Azithromycin treatment in 4 countries—Viet Nam, Tanzania, Ghana, and Mali—where mass treatment programmes are underway. Population-based data collected from 1988 to 200 were analysed using least squares regression. Height treatment schedules were developed for each data set. The accuracy of each schedule was evaluated according to the percentage of children receiving treatment within a dosage range of 20-30 mg/kg, a conservative estimate of the safe and effective treatment range for paediatric trachoma. Using height to determine dose, 89-95% of children would receive a dosage of 20-30 mg/kg. In these population, height-based treatment is a reliable alternative to conventional weight-based treatment. Methods for developing height schedules presented in this analysis could be applied to other regions and therapeutics.

Synopsis

Pediatric trachoma is treated according to weight at a target dosage of 20 mg/kg. However, weight-based treatment can be problematic in the field. Weight scales are easily damaged, difficult to calibrate and read, and costly when considering the large numbers of scales required during mass treatment.

Experience suggests that height can be used as a proxy for weight to provide a more efficient system of dose determination. Height scales, made of wooden boards inscribed with drug doses, are sturdy, cheap, and easy to construct and use. Measurement is direct and frequent calibration unnecessary.

We assessed the accuracy of using height as a proxy for weight to determine azithromycin treatment for 20,829 children in four countries -- Vietnam, Tanzania, Ghana, and Mali -- where mass treatment programs are underway. A height treatment schedule that maximized the number of children receiving treatment of 20-30 mg/kg, a conservative estimate of the safe and effective treatment range for pediatric trachoma, was developed for each age group in each country. Treatment was delivered in 2 mL increments of suspension (40 mg/mL) to children 1-4 years of age and in half tablet increments (250 mg/tablet) to children 5-15 years of age.
In each age group within each country, between 89 and 95 percent of children would have received a dosage of 20-30 mg/kg, if height had been used to determine dose. The highest dosage that would have been received was 48 mg/kg and the lowest, 12 mg/kg. Because even the highest dosage was well within the range of safety, the risk of overdosing was considered to be minimal.

The results of this study suggest that height-based treatment is a reliable alternative to weight-based treatment in the four countries examined. However, new data showing that azithromycin is safe at higher dosages than previously thought presents an opportunity to improve height-based treatment in several ways.

First, a higher safety limit would allow us to minimize, if not virtually eliminate, the number of children receiving dosages less than the target dosage of 20 mg/kg. By reducing the number of sub-clinical dosages administered, program effectiveness is likely to be improved. A wider treatment range would also provide the flexibility for a single standardized schedule that could be applied to any country. A single schedule would eliminate the need to collect country-specific data, a time-consuming and expensive exercise.

A final potentially important improvement involves the unit of delivery. Until now, practice has been to administer treatment in half tablet units because a smaller increment of delivery supports more accurate achievement of target dosage. However, the process of dividing tablets is imprecise and can be time-consuming, due in part to the absence of tablet scoring. In addition, by altering the surface area of the tablet, the process of division may affect absorption and compromise the therapeutic effect of the drug. A wider range of acceptable dosages would make the half tablet unnecessary, contributing to improved program efficiency and perhaps improved program effectiveness.

Studies incorporating the new safety information on azithromycin have been conducted using data from Morocco, Egypt, Nepal, Viet Nam, Ethiopia, Tanzania, Niger, Mali, and Ghana. Preliminary results, presented in January 2003 at the WHO, are promising. A final height schedule reflecting the improvements outlined above may soon be available to countries where weight-based treatment is problematic.
Trachoma causes blindness; the prevention strategy includes mass antibiotic treatment. In a community in Northern Tanzania offered mass treatment with azithromycin for the control of trachoma, we used focus group discussions, individual interviews, questionnaires and direct observation to quantify, explore and contextualize reasons for acceptance or refusal of the drug. In the village studied, 76% of the population eligible to receive azithromycin were treated. Uptake was significantly higher among women (79% treated) than men (72%). Factors affecting acceptability included: local prevention norms (such as the belief that injections, rather than oral medicine, should be used for prevention); perceptions of drugs in general and azithromycin in particular; perceptions of the distribution team's expertise; witnessing adverse effects in others; and the timing, quality and quantity of information about azithromycin and its availability. Familiarity with trachoma as a blinding disease was significantly associated with uptake. Individuals who refused treatment seemed to be less altruistic than other respondents. Neither socio-economic status nor use of traditional healers was related to uptake. Pre-distribution community assessment and community education, advance notice of the distribution, standardized distribution guidelines and improved distributor training are recommended to maximize acceptance of azithromycin in future campaigns.

**Synopsis**

The World Health Organization recommends application of the ‘SAFE’ strategy in the control of trachoma, the world’s leading infectious cause of blindness. Specifically ‘SAFE’ involves surgery to correct advanced disease, antibiotics to clear *C. trachomatis* infection, facial cleanliness and environmental improvement to reduce transmission. Antibiotic azithromycin to clear infection has been shown to be at least as effective for trachoma control as 6 weeks of tetracycline eye ointment but the success of any treatment campaign depends on coverage achieved which in turn depends on community acceptability of the drug as prophylaxis. The paper ‘Acceptability of azithromycin for the control of trachoma in Northern Tanzania’ investigates acceptability in terms of uptake of, and attitudes towards azithromycin in a trachoma-endemic community in Rombo District, Tanzania.

In order to measure uptake and to investigate reasons for acceptance or non-acceptance of offered antibiotic under representative, rather than research, conditions, the study was carried out alongside the government’s trachoma control initiative in collaboration with the Christoffel Blinden Mission and the International Trachoma Initiative. At the time of the distribution (2001) the programme’s community-level target for antibiotic coverage was 75% or greater. A single does of azithromycin was targeted to all non-pregnant residents over the age of 12 months and uptake coverage of 76% was achieved in a population of 2786 individuals eligible for treatment. Uptake was higher amongst women (79%) than men (72%, P<0.0001) and in both sexes uptake was higher among 1-10 year olds and lowest among 16-40 year olds; a finding that is encouraging since in a nearby village children under 10 have been shown to harbour 90% of the total ocular *C. trachomatis*.

Since the overall figure narrowly exceeded the programme’s community-level coverage target of 75%, the study investigated the reasons for non-uptake of antibiotic. Factors were
multifarious and included both socio-cultural norms and practices and those related to the
distribution procedures themselves. Whilst the former are likely to be culturally
heterogenous, and may differ according to social context, the latter are crucial in influencing
future uptake in other regions. An understanding of both, however, may have salience in
increasing community-level coverage and improving future trachoma control.

Socio-cultural factors found to affect uptake included prevention norms and the belief that
injections are more effective than oral medicines in preventing disease. Individual
perceptions of drugs in perceived relation to an individual’s body and beliefs in the efficacy
of oral versus systemic prevention of trachoma also contributed to treatment decisions.
Further, heightened awareness and perceptions of severity of the problem in the village,
(77.2% of those who accepted treatment were able to relate trachoma to blindness, odds ratio
for treatment if had heard of trachoma was 1.8, 95% CI 1.1-3.1 Fisher’s exact P=0.02)
positively influenced uptake. In contrast, the lack of phenomenological connection made
between childhood ocular discharge and trichiasis in old age, combined with the minimal
disruption of social life caused by active trachoma in children, encouraged perceptions of the
disease as a normal part of childhood, recognised but not prioritised for treatment. Finally,
prevailing social conditions in the village promote community-level reliance on peer
knowledge and experience, thus rumours of benefits or problems following uptake spread
rapidly throughout community social networks and awareness of adverse effects was often
cause for refusal but conversely provided others with evidence of the drug’s effectiveness.

In operational terms, distribution procedures also affected decisions regarding uptake. Both
the timeliness of information dissemination and the timing of the distribution over a weekend
adversely affected residents’ attendance, generally due to alternative social commitments.
Perceived levels of providers’ biomedical knowledge were related to their position as either
co-residents or outsiders. Team members from elsewhere were regarded as ‘doctors’, whilst
village health workers were often not trusted. Trust in external ‘others’ was also linked to
treatment decisions; some residents simply followed instructions because the distribution was
associated with the government. Finally, uncertainties and dissimilarities in distribution
protocols regarding contra-indications with alcohol meant that treatment decisions were not
always consistent between teams and some of those who were eligible and willing were
refused treatment.

The results suggest that there is need for improvement in the design of community-based
distribution programmes and that a greater understanding of the socio-cultural context prior
to distribution would likely improve antibiotic coverage. Specifically, pre-distribution
community assessment and education, advance notice of distribution, standardized
distribution guidelines and improved distributor training may help to maximise acceptance of
azithromycin in future trachoma control programmes.
Eliminating trachoma in areas with limited disease.


The common wisdom is that a trachoma program cannot eliminate ocular Chlamydia from a community, just reduce infection to a level where blindness would be minimal. We describe the success of multiple mass antibiotic treatments, demonstrating that complete elimination of infection may be an attainable goal in an area with modest disease.

Synopsis

Many healthcare workers feel that attempting to eliminate the ocular strains of chlamydia that cause trachoma is unrealistic and perhaps even unnecessary, and that a more attainable goal would be to reduce clinically active trachoma to some threshold, below which scarring and blindness would become rare. The WHO has tentatively defined *Elimination of trachoma as a public health concern* as <5% clinical activity in children (true *Elimination* would require the reduction of infection to zero, at least locally).

We monitored trachoma prevalence in a village in Western Nepal for three years, using both clinical grading system and nucleic acid amplification tests. Three annual oral azithromycin treatments were distributed to all children in the village aged 1-10 years (Figure below). Before the first treatment, 39% were clinically active by the clinical exam and an estimated 26% were infected with chlamydia. At the final, May 2001 visit, 7 of 187 children (4%) were clinically active. Only a single child of the 187 (0.5%) had evidence of chlamydia by PCR.

This study suggests that it may be possible to reduce the prevalence of ocular chlamydia to zero, at least in a village with moderate baseline disease. After three annual treatments, only a single infected child could be identified, and children are by far the most likely to harbor ocular chlamydia. Whether success in this village was due solely to our treatment program or due in part to a favorable secular trend in the area, the results are encouraging (Jha, H., et al., *Disappearance of trachoma in western Nepal*. *CID* 35, 765-8, 2002 implies that there is a significant secular trend in the area).

Is true *Elimination* (reduction of infection to zero locally) necessary? It may not be for at least 3 reasons: First, it almost certainly takes repeat infections to get severe conjunctival scarring, occasional sporadic infections probably do not lead to blindness. Second, some investigators hope that if ocular chlamydia is reduced to a low enough level, it will have difficulty repopulating the community (population biologists call such a rare prevalence threshold an *Allee effect*, and there is little evidence that it exists with trachoma). Finally, bacterial, viral, and allergic conjunctivitides can occasionally mimic ocular chlamydia, so eradication of “clinically active” trachoma will never be possible.

The prevalence of clinically active trachoma (gray curve) and ocular chlamydial infection as determined by DNA amplification tests (black curve,
with 95% CI due to stratified sampling) in children aged 1-10 years in a village in Western Nepal over time. All children were examined at each visit, so no sampling confidence interval is indicated. Likewise, all children were swabbed for evidence of infection at the May 2001 visit.
The effect of antibiotic treatment on active trachoma and ocular Chlamydia trachomatis infection


Antibiotics are one of four arms of the SAFE strategy for the control of trachoma, an eye infection that is responsible for more cases of blindness than any condition other than cataract. The evidence for the use of topical tetracycline and oral tetracycline, doxycycline, erythromycin, cotrimoxazole and azithromycin in trachoma are reviewed here and a number of issues are nominated as research and policy priorities.

Synopsis

Active trachoma has been treated with antibiotics since the late 1930s. Many different topical and systemic antibiotics have been used. The two regimens recommended by the World Health Organization are (a) 1% topical tetracycline ointment placed in both eyes twice daily for six weeks, or (b) one oral dose of 20mg/kg azithromycin (maximum dose 1g). The effect of antibiotic treatment on active trachoma and ocular Chlamydia trachomatis infection was the subject of a review by Denise Mabey and Anthony Solomon published in Expert Review of Anti-infective Therapy in 2003 (1(2): 209-16).

On pages 212-3 of that paper, a number of priority issues for research and policy for the next five years were identified. This synopsis revisits those priority issues and considers them in the light of new guidelines for antibiotic use in trachoma control and research findings that have become available since the paper’s publication.

1) The World Health Organization now recommends mass antibiotic treatment (treatment of all residents of a community) in places where the prevalence of TF in 1-9 year-old children is 10% or more. If the prevalence of TF in 1-9 year-old children is 5% or more, but less than 10%, targeted treatment (identification and treatment of families in which there are one or more members with TF or TI) is recommended. In communities in which the prevalence of TF in 1-9 year-old children is less than 5%, antibiotic distribution is not recommended. The problem is that in low prevalence areas, and following one or more antibiotic distribution rounds, the presence or absence of TF is known to be a poor indicator for the presence or absence of ocular C. trachomatis infection. Giving communities with very few C. trachomatis infections mass treatment with anti-chlamydial antibiotics wastes drugs and other resources that are needed elsewhere. A cheap, rapid, accurate test of infection that could be used in the field to estimate the community prevalence of C. trachomatis conjunctival infection is required. Such tests are currently in development.

2) Children have the highest prevalence of active trachoma, and harbour the bulk of the ocular C. trachomatis load. However, suggestions that antibiotic treatment only be given to, for example, children under 10 years old, do not yet have any support from controlled studies. Community-randomised trials comparing the effect of treatment only of children to the effect of mass community treatment should be undertaken before such strategies are implemented at programme level. The cost-effectiveness and community acceptance of each strategy should be considered as part of those studies.

3) Mathematical models suggest that mass antibiotic treatment is needed every 6-12 months in populations where >50% of children have clinical evidence of active trachoma, and
every 12-24 months where <35% of children have active trachoma. The prediction that hyperendemic communities will need biannual treatment has recently received support from a study in Ethiopia, in which the rate of return of ocular C. trachomatis infection after mass azithromycin treatment was determined. The prediction that mesoendemic communities may need treatment less frequently than once yearly has recently received support from a study in Tanzania, in which high coverage mass treatment with azithromycin, perhaps aided by periodic re-treatment of active cases with tetracycline eye ointment, appeared to have interrupted transmission of ocular C. trachomatis and reduced the prevalence of infection to virtually zero two years after treatment. However, the comparative effect of different dosing intervals still needs to be tested by controlled trials.

4) Where azithromycin is available, for logistical reasons, it should be given by height rather than weight. Azithromycin doses given by height are likely to be both safe and effective. Height-based dosing is now used by a number of national trachoma control programmes.

5) Strategies to improve uptake of antibiotics should be sought: the proportion of the community given antibiotics may be critical in determining the impact of the antibiotic component of SAFE.

6) Despite decades of use of tetracycline eye ointment in trachoma control programmes, tetracycline-resistant ocular strains of C. trachomatis have not yet been identified. There is some concern that mass treatment of trachoma-endemic communities with azithromycin may lead to the emergence of resistant strains of C. trachomatis or other human pathogens. Further studies are warranted.

7) It seems likely that implementation of the ‘F’ and ‘E’ components of the SAFE strategy will enhance or prolong antibiotic-driven reductions in the prevalence of active trachoma and ocular C. trachomatis infection. However, ‘F’ and ‘E’ are expensive and difficult to implement, and good evidence of their effectiveness (which is presently lacking) would be of great benefit in advocating their use. The cost effectiveness of various strategies should be considered as part of any studies of the impact of ‘F’ and ‘E’ interventions.
Mass treatment with single-dose azithromycin for trachoma.


BACKGROUND: Trachoma, caused by repeated ocular infection with Chlamydia trachomatis, is an important cause of blindness. Current recommended dosing intervals for mass azithromycin treatment for trachoma are based on a mathematical model. METHODS: We collected conjunctival swabs for quantitative polymerase-chain-reaction assay of C. trachomatis before and 2, 6, 12, 18, and 24 months after mass treatment with azithromycin in a Tanzanian community in which trachoma was endemic. For ethical reasons, at 6, 12, and 18 months, we gave tetracycline eye ointment to residents who had clinically active trachoma. RESULTS: At baseline, 956 of 978 residents (97.8 percent) received either one oral dose of azithromycin or (if azithromycin was contraindicated) a course of tetracycline eye ointment. The prevalence of infection fell from 9.5 percent before mass treatment to 2.1 percent at 2 months and 0.1 percent at 24 months. The quantitative burden of ocular C. trachomatis infection in the community was 13.9 percent of the pretreatment level at 2 months and 0.8 percent at 24 months. At each time point after baseline, over 90 percent of the total community burden of C. trachomatis infection was found among subjects who had been positive the previous time they were tested. CONCLUSIONS: The prevalence and intensity of infection fell dramatically and remained low for two years after treatment. One round of very-high-coverage mass treatment with azithromycin, perhaps aided by subsequent periodic use of tetracycline eye ointment for persons with active disease, can interrupt the transmission of ocular C. trachomatis infection.

Synopsis

The World Health Organization now recommends annual mass antibiotic treatment in any area in which the prevalence of TF in 1-9 year-old children is 10% or greater. The paper “Mass treatment with single-dose azithromycin for trachoma” evaluates the impact of one very high coverage round of mass azithromycin treatment in a meso-endemic community in Rombo District, Tanzania.

In the study, the principal outcome measures are the prevalence and intensity of ocular Chlamydia trachomatis infection, as measured by quantitative PCR: a very sensitive and specific laboratory technique that can determine not just whether or not chlamydial infection is present, but how much Chlamydia is present in a standard swab taken from the eye.

At baseline, there were 978 residents in Kahe Mpya, the sub-village involved in the study. 956 were examined, and 195 of them (20.4%) had active trachoma (TF and/or TI in either eye); the prevalence of TF in 1-9 year-old children was 36.0%. The prevalence of ocular C. trachomatis infection (all ages) was 9.5%. Treatment immediately followed swabbing. Of the 978 residents, 916 (93.7%) received azithromycin, and another 39 (4.0%) received two tubes of tetracycline eye ointment for self-application at home. In total, therefore, 955 people (97.6% of residents) were treated.
No further azithromycin was given over two years of post-treatment follow-up. At 6, 12 and 18 months after treatment, however, people who had clinical evidence of active disease were given tetracycline eye ointment. This was done to satisfy the requirements of our ethics committees.

Prevalence of infection fell from 9.5% before treatment to 2.1% at two months after treatment, 1.5% at 6 months, 0.9% at 12 months, 0.6% at 18 months, and 0.1% at 24 months. A measure of the average intensity of infection, called the “Community ocular C. trachomatis load” (COCTL), fell from 0.423 before treatment to 0.059 at 2 months (13.9% of its baseline value), then continued to fall, reaching 0.003 (0.8% of baseline) at 24 months. There were few new infections after treatment: at each time point after baseline, over 90% of the total community burden of ocular C. trachomatis was found among subjects who had been positive the previous time they were swabbed. Population turnover over the course of the two year study totalled nearly 20%, but only 2 of 195 new residents brought C. trachomatis infection with them, and they did not appear to infect their household contacts. In the paper, analyses are presented which suggest that post-mass-treatment use of tetracycline eye ointment did not itself have much impact on the community’s burden of infection; however, a possible effect of this intervention can not be ruled out.

The results suggest that a single round of mass azithromycin treatment was successful in interrupting transmission of ocular C. trachomatis infection in this sub-village. The most likely explanation for this effect is the extremely high antibiotic coverage that was achieved. Though this finding is extremely encouraging, ensuring that over 95% of residents take offered antibiotic is much more difficult at district- or national-level. Operational research is required to further investigate the reasons for incomplete acceptance of offered antibiotic in trachoma control programmes.
Objectives: To investigate the relationship between distance to water source, altitude and active trachoma in children in Rombo district, Tanzania.

Methods: In each of Rombo’s 64 villages, 10 balozis (groups of 8-40 households) were selected at random and all resident children aged 1-9 years were examined for clinical signs of active trachoma. The households of these children and village water sources were mapped using differentially corrected global positioning system data to determine each household’s altitude and distance to the nearest water supply.

Results: We examined 12 415 children and diagnosed 1171 cases of active trachoma (weighted prevalence = 9.1%, 95% CI: 8.0, 10.2%). Active trachoma prevalence ranged from 0% to 33.7% across villages. Increasing distance to the nearest water source was significantly associated with rising trachoma prevalence (age-adjusted odds ratio for infection (OR) for highest quartile compared to lowest = 3.56, 95% CI 2.47, 5.14, P for trend <0.0001). Altitude was significantly inversely associated with trachoma prevalence (age-adjusted OR for highest quartile compared to lowest = 0.55, 95% CI 0.41, 0.75, P for trend <0.0001). These associations remained significant after adjustment in multivariate analysis.

Conclusion: Trachoma is endemic in Rombo district, although the prevalence varies considerably between villages. Spatial mapping is a useful method for analysing risk factors for active trachoma.

Implications of this study:

- Increasing distance to nearest water source is associated with increased trachoma prevalence

This association supports the findings of other studies. Lack of water is thought to be a risk factor for trachoma because hygiene practices such as face washing protect against disease. When water access is poor, frequency of face and hand washing declines.

- Higher altitude is associated with decreased trachoma prevalence

The relationship between trachoma and altitude has not previously been investigated. There are a number of plausible explanations for the association, including differences in socioeconomic status, water availability and fly density with altitude. Since flies are mechanical vectors of ocular Chlamydia trachomatis, the effect of altitude on trachoma transmission may be related to fly density. It may also be due to decreasing population density with increasing altitude (crowding is a risk factor for trachoma), or because of higher rainfall and improved reliability of water sources higher up the slopes. It could also be due to differences in socioeconomic status.

- Trachoma prevalence, socio-economic status and stability of communities
According to local anecdote, households of higher socio-economic status tend to reside higher up the slopes of Mt. Kilimanjaro. Many ‘down-slope’ communities are relatively new, comprising people who have moved from up-mountain because of lack of land, and therefore do not have the cohesiveness of more established villages. Such communities may have poorer access to healthcare and education.

- Children with a fly on their eye (‘fly-eye’) were significantly more likely to have active trachoma (age-adjusted OR 3.98 95% CI 2.98-5.31). Prevalence of ‘fly-eye’ was inversely correlated with altitude.

This provides more support to the role of flies in the association between active trachoma and altitude, as well as supporting the use of fly control in order to fight trachoma transmission.

- Trachoma prevalence varies considerably between villages

Prevalence in individual villages in Rombo varied between 0% and 34%. While this variation may primarily be due to the large differences in access to water sources and altitude that were found to be associated with trachoma prevalence, it highlights that small pockets of high prevalence areas could remain within a region with a typically low trachoma prevalence.

- Prevalence of active trachoma decreased strongly with increasing age, but there was no relationship with gender. Prevalence was substantially higher in Masai than other ethnic groups (predominantly Chagga).

The relationship between active trachoma prevalence and age is well established and the results of this study are consistent with other studies. Trachoma prevalence was lowest amongst children of Chagga ethnicity (weighted prevalence 8.9%, n=11 296). Masai children had the highest weighted prevalence (42.9%, n=32). For Kamba, Mpare and Msambaa children, weighted prevalences were 14.7% (n=54), 14.1% (n=497) and 9.1% (n=294), respectively.
“Implementing the SAFE Strategy for Trachoma Control: A Toolbox of Interventions,” is a manual designed to assist program managers and planners in the implementation of the F and E components of the SAFE strategy. The manual offers a “toolbox” of interventions, along with case studies that illustrate specific examples of their successful implementation. The toolbox helps program managers to identify patterns in trachoma transmission and prevalence according to their own country-specific contexts; encourage the participation of community leaders and representatives in developing behavior change activities; design and implement social marketing activities; and monitor and evaluate program interventions. The manual outlines all F and E interventions that are currently in use worldwide, discusses their strengths and weaknesses, highlighted by case studies.

The toolbox is the result of three years of collaboration with the International Trachoma Initiative. The Conrad N. Hilton Foundation generously supported the publication of the toolbox available in both English and French, the toolbox has been field tested extensively in both languages. Electronic versions are available at The Carter Center website (www.cartercenter.org). Requests for paper copies should be sent to ecromwe@emory.edu. Anyone interested in using the toolbox is encouraged to copy and share the electronic or paper version without any copyright hindrance.
Human and other faeces as breeding media of the trachoma vector
Musca sorbens

Emerson PM, Bailey RL, Walraven GEL, & Lindsay SW. Medical & Veterinary Entomology; 2001;15:314-320

The fly *Musca sorbens* Wiedemann (Diptera: Muscidae) apparently transmits *Chlamydia trachomatis*, causing human trachoma. The literature indicates that *M. sorbens* breeds predominantly in isolated human faeces on the soil surface, but not in covered pit latrines. We sought to identify breeding media of *M. sorbens* in a rural Gambian village endemic for trachoma. Test breeding media were presented for oviposition on soil-filled buckets and monitored for adult emergence. *Musca sorbens* emerged from human (6/9 trials), calf (3/9), cow (3/9), dog (2/9) and goat (1/9) faeces, but not from horse faeces, composting kitchen scraps or a soil control (0/9 of each). After adjusting for mass of medium, the greatest number of flies emerged from human faeces (1426 flies/kg). Median time for emergence was 9 (inter quartile range = 9-9.75) days post-oviposition. Of all flies emerging from faeces 81% were *M. sorbens*. Male and female flies emerging from human faeces were significantly larger than those from other media, suggesting that they would be more fecund and live longer than smaller flies from other sources. Female flies caught from children's eyes were of a similar size to those from human faeces, but significantly larger than those from other media. We consider that human faeces are the best larval medium for *M. sorbens*, although some breeding also occurs in animal faeces. Removal of human faeces from the environment, through the provision of basic sanitation, is likely to greatly reduce fly density, eye contact and hence trachoma transmission, but if faeces of other animals are present *M. sorbens* will persist.

Synopsis

This journal is not held in many libraries, reprints are available on request from the author
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Background:
*Musca sorbens* is a domestic fly commonly found in and around homes in trachoma-endemic areas. It feeds avidly from human eyes and on nasal discharge and moves purposely from eye to eye. Through this behaviour it has been identified as a trachoma vector and is, in part, responsible for transmission of the disease. Historical literature suggests that it breeds in isolated human faeces lying on the surface of the soil, but not in pit latrines. If this is true then controlling this fly, and thereby reducing trachoma transmission, may be possible by removing human faeces from the environment and providing latrines. This research aimed to identify the preferred breeding media of *Musca sorbens* in a Gambian village.

Methods:
Human, calf (milk-fed), cow, dog, horse and goat faeces, kitchen scraps or a soil control were presented on soil-filled buckets in a trachoma-endemic Gambian village for flies to lay eggs on. The faeces were as fresh as possible and weighed before placing on the surface of the buckets filled with earth. The buckets were placed about 1.5m apart in random order in a circle. After three days in the village the buckets were taken to the laboratory, covered with a trap to catch emerging flies and left in the shade. Flies were removed from the traps every morning and evening until they stopped emerging. The trial was repeated 9 times.
Findings:
*Musca sorbens* emerged from human faeces in 6 of the 9 trials, calf faeces (3/9), cow faeces (3/9), dog faeces (2/9) and goat faeces (1/9) but not from horse faeces, kitchen scraps or the control. The greatest productivity of *Musca sorbens* flies was from human faeces (1426 flies/Kg). Flies from human faeces were significantly larger than those from other faeces, and the same size as those caught from the faces of children.

Interpretation:
Human faeces was the best larval medium for *Musca sorbens*. It produced flies most often and the flies were more numerous and of better quality than those from other breeding media. (Larger flies are more likely to live longer and have more offspring than smaller flies). Reducing environmental contamination with human faeces, for example by promoting latrines, would be likely to reduce the population of *Musca sorbens*, and hence trachoma transmission. However the flies would not disappear altogether as they would continue to breed in the faeces of other animals (particularly calves, cattle and dogs).
Objectives: To verify reported construction of 22,385 household latrines in 2004, after community mobilization, as part of a trachoma control programme in one district of Amhara, Ethiopia, and to explore characteristics of early latrine adopters and non-adopters.

Methods: We used a two-stage cluster sample survey design to randomly select eight sub-districts and 160 households listed as having built a latrine, and visited them to verify presence and use. Household heads were interviewed to determine latrine cost and knowledge, attitude and practice regarding latrines. Non-latrine adopting neighbours were interviewed for comparison. We estimated district latrine ownership and calculated adjusted odds ratios for factors associated with latrine use.

Results: Latrines were present in 87% (95% CI 77–97) of listed households; 90% (81–99) were in use. Among all district residents we estimated ownership as 50.2% (44–56) and use as 45.2% (36–55). Of latrine owners who had built in 2004, 69% (53/77) had spent nothing on their latrine, those who paid spent an average of US$4.0 (standard deviation (SD) US$3.6); overall the median cost was US$0 and the mean US$0.80 (SD US$1.7). Household heads adopting latrines were 1.9 times (95% CI 1.3–2.8) more likely to have any education and 1.5 times (95% CI 1.1–2.0) more likely to have a larger family than non-adopting neighbours. Cleanliness (48%, 56/116) and health benefits (42%, 49/116) were the most frequently reported advantages of latrines.

Conclusion: The latrine promotion programme dramatically increased latrine access and use at very low cost. The method of community mobilization used could be an effective way of reaching millennium development sanitation targets.

Implications of this study

1) Community mobilization for latrines worked well in this setting
This study demonstrates how a community mobilization programme promoting latrines led to a dramatic increase in the number of latrines in a community in rural Ethiopia. The mobilization took the form of education of community leaders and health workers, setting targets for the district and dissemination of the education to the community by those who attended the training. The community leaders set an example by building latrines at their own homes and building demonstration community latrines. The process of community mobilization for this programme has been documented in the local language and disseminated to other districts to share experiences.

2) Administrative data reflected the actual situation
We found that the proportion of households with latrines (50.2%) was close to the estimate of 57.7% based on administrative data. Community leaders kept detailed lists of householders with latrines and these were used to verify the reported figures. We recommend that programmes maintain lists of latrine owners to provide estimates of the impact of mobilization and to facilitate verification.
3) Latrines are not expensive
An important finding of this study is that it is possible to establish widespread latrine use at low cost. Most latrine owners did not have any material costs for their latrine and for those who paid anything (31%) the mean unit cost was US$4. However, ‘opportunity costs’ to the household were not calculated and would consist of several person days of labour. The Carter Center and UNICEF provided set up costs, such as the community leader’s training and local government released employees to attend training, and mobilize the community.

4) Urban dwellers are more likely to have a latrine
A comparison of characteristics of households with a latrine with households without a latrine showed some differences for example in education of head of household and some economic indicators. All of these characteristics were also associated with urban residence, which suggests that in this study the principal characteristic of the early adopter was urban living. Community mobilization may also be easier in towns as more people can be reached and there may be some peer pressure. More effort is required to mobilize people living in more rural areas to build latrines.

5) Sustainability
This study was carried out approximately 9 months after the main community mobilization efforts, which makes assessment of the durability of the latrines and the behavioural sustainability impossible. We observed that while the majority of latrines were in use, many were poorly constructed indicating that further education is required and we recommend latrine construction guidelines for this community. We also recommend continued education of the community and continued supervision of building and maintenance in the early years of this project to promote sustained behavioural change. Future follow-up studies will be required to assess sustainability by determining use, maintenance and replacement.
Environmental sanitary interventions for preventing active trachoma


Background
Trachoma is the second or third major cause of blindness. It is responsible for about six million blind people worldwide, mostly in the poor communities of developing countries. One of the major strategies advocated for the control of the disease is the application of various environmental sanitary measures to such communities.

Objectives
To assess the evidence for the effectiveness of environmental sanitary measures on the prevalence of active trachoma in endemic areas.

Search strategy
We searched the Cochrane Central Register of Controlled Trials - CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) on The Cochrane Library (Issue 4, 2004), MEDLINE (1966 to January 2005), EMBASE (1980 to January 2005), LILACS (April 2004), the reference list of trials and the Science Citation Index. We also contacted agencies, experts and researchers in trachoma control.

Selection criteria
This review included randomised and quasi-randomised controlled trials comparing any form of environmental hygiene measures with no measure. These hygienic measures included fly control, provision of water and health education. Participants in the trials were people normally resident in the trachoma endemic areas.

Data collection & analysis
Two authors independently extracted data and assessed the quality of trials. Study authors were contacted for additional information. Three trials met the inclusion criteria but meta-analysis was not conducted due to heterogeneity of the studies.

Main results
Two studies that assessed insecticide spray as a fly control measure found that trachoma is reduced by at least 55% to 61% with this measure compared to no intervention. One study found that another fly control measure, latrine provision, reduced trachoma by 29.5% compared to no intervention; this was, however, not statistically significantly different. Another study revealed that health education on personal and household hygiene reduced the incidence of trachoma such that the odds of reducing trachoma in the health education village was about twice that of the no intervention village. However, all the studies have some methodological concerns relating to concealment of allocation and non-consideration of clustering effect in data analysis.

Reviewers’ conclusions
There is evidence that insecticide spray as a fly control measure reduces trachoma significantly. Latrine provision as a fly control measure has not demonstrated significant trachoma reduction. Health education may be effective in reducing trachoma. There is a dearth of data to determine the effectiveness of all aspects of environmental sanitation in the control of trachoma.

Synopsis
Trachoma is the second or third major cause of blindness. It is responsible for about six million blind people worldwide, mostly in the poor communities of developing countries. One of the major strategies advocated for the control of the disease is the application of
various environmental sanitary measures to such communities. These measures are believed to be more sustainable in the control of the disease.

A systematic review of available literature was conducted to assess the evidence for the effectiveness of these environmental sanitary measures in reducing active trachoma.

The review searched MEDLINE, EMBASE, LILACS, Cochrane library to identify randomized and quasi-randomized controlled trials on this topic. Also the reference list of trials and the Science Citation Index were screened. Agencies, experts and researchers in trachoma control were also contacted.

Three studies were identified for inclusion into the review, but the studies were not combined in meta-analysis because of their heterogeneity. Two studies that assessed insecticide spray as a fly control measure found that trachoma is reduced by at least 55% to 61% with this measure compared to no intervention. One study found that another fly control measure, latrine provision, reduced trachoma by 29.5% compared to no intervention; this was, however, not statistically significantly different. Another study revealed that health education on personal and household hygiene reduced the incidence of trachoma such that the odds of reducing trachoma in the health education village was about twice that of the no intervention village. However, all the studies have some methodological concerns relating to their quality.

We concluded that evidence from two studies suggests insecticide spray can reduce transmission of active trachoma, however, sustainability of such an intervention and the possible untoward effects of prolonged usage of such chemicals are uncertain. One other trial suggests that health education may reduce transmission of active trachoma.

Non-Cochrane reviews, which included mostly observational studies, also suggest a potential benefit for environmental interventions for reducing trachoma in communities. However, it is difficult to rely on this evidence because of validity issues.

As we await more studies that assess the individual contribution of each component of environmental sanitation to the control of trachoma it is difficult to be certain which component of environmental sanitation is more effective. Therefore, all available interventions need to be applied in communities with trachoma, within the context of the SAFE strategy. These interventions include health education on personal and environmental hygiene; water supply and education on water use for hygiene; and fly control measures such as provision of latrines, refuse dumps and insecticide spray.
Sustainability and acceptability of latrine provision in The Gambia

Simms, VM, Makalo M, Bailey RL, & Emerson PM. Transactions of the Royal Society of Tropical Medicine and Hygiene; 2005;99:631-637

As part of a trachoma control programme in a rural part of The Gambia all households in 32 villages were provided with improved pit latrines. Latrine provision was externally driven and was not in response to a request from the communities involved. Materials were provided for free, and labour was paid for. To assess durability and acceptability we conducted a follow-up 25-47 months after construction. Before the intervention only 32% of households in these villages had access to any type of latrine, at follow-up this had risen to 95%. On visual inspection 585/666 latrines (87.3%) were usable and 510 (87.2% of those usable) were currently used. During interviews 566/637 latrine owners (89%) said they were either happy or very happy with their latrines, and 620 (97.3%) reported that they would make a new latrine of some kind when the current one was full or unusable. We interpret these data to suggest that externally driven latrine provision, without additional health education, to an area with poor latrine coverage can result in high, sustainable levels of uptake and generate future demand for sanitation.

Synopsis

As part of a randomised controlled trial of pit latrines to reduce trachoma, Emerson and colleagues supplied pit latrines to all households in 32 villages, achieving 100% coverage of targeted households. Prior to the study only a third of households had access to a latrine. 25-47 months after construction of the latrines we conducted a follow-up survey to establish physical durability of the latrines, continued usage, and their acceptability to the households.

There were 666 latrines, in 639 households. The survey consisted of a visual inspection of each latrine to establish whether it was usable and in use, and a short, structured questionnaire with the household head. This included questions on whether anyone was excluded from using the latrine, what was done with young children’s faeces, and whether the latrine would be replaced when it filled up.

Results

585 latrines were usable and 510 in use. The main reasons for a latrine being unusable were collapse or damage due to heavy rains. Some latrines were temporarily not in use, the commonest reasons being because owners had moved away, the fence needed replacing, or they were being kept as a spare. 95% of households had access to a latrine at the time of the survey, since if their own was unusable they usually shared the neighbours’ one. In almost all cases everyone except young children was allowed to use the latrine. Children under about six years who did not use the latrines reportedly defecated either on the ground, on the rubbish heap, or in a potty. 97.3% of household heads said they intended to use a latrine of some kind when this one was filled up.

Interpretation

The latrines were provided externally, not in response to demand, and no health education was given apart from trachoma information. Nonetheless, a median of 3 years after construction, a high proportion of the latrines were still in use and the programme had generated demand for improved sanitation. These results suggest that a blanket approach to latrine provision could be successful as a sustainable way of reducing trachoma.
Epidemiology

Spatial clustering of ocular chlamydial infection over time following treatment, among households in a village in Tanzania


PURPOSE: To observe the spatial distribution of households with high loads of ocular chlamydia infection in children, before and after mass treatment with azithromycin to determine whether there exists spatial clustering of households with high loads of infection and the spatial scale of the clustering. METHODS: All residents of a village in Tanzania were invited to participate in the study. A global positioning system unit recorded the location of each house. Mass treatment with azithromycin was offered, with participation above 80%. Active trachoma and swab samples of the conjunctiva were assessed at baseline and at 2, 6, 12, and 18 months after treatment. A k-function analysis was performed to detect clustering of households with high loads of ocular chlamydia in children younger than 8 years.

RESULTS: A total of 1055 villagers were examined during the study; of these, 374 (35.4%) were children younger than 8 years. The total number of households was 215, with 182 (84.6%) households having at least one child. K-function analysis showed clustering of households with high loads of ocular chlamydia at distances up to 2 kilometers (km) at baseline; at 6 months, slight clustering existed within 0.5 km. At 12 and 18 months, high load households clustered at distances up to 1.3 km. CONCLUSIONS: This analysis suggests that infection spreads between households with children or that nearby households share the same risk factors for infection. Mass treatment has value in lowering infection prevalence within the community, and clustering of households with infection takes up to 1 year to reemerge at the same level as baseline. Re-treatment at yearly intervals may interrupt spread of infection.

Synopsis

1) Children with high loads of *C. trachomatis* infection are likely transmitting this infection to children of nearby households.

In endemic conditions, households with high levels of infection in children clustered together at distances less than 2 km. Our analysis showed that households with high levels of infection were more densely situated than households with low or no levels of infection in children. The clustering of households with high infection loads suggests transmission of infection between children of different households, but we cannot rule out that households close together may share the same risk factors for infection.

2) Re-infection after treatment will radiate out from households with infection, but it takes at least six months.

Prevalence of infection in children dropped following mass treatment, but while prevalence remained low, clustering of high infection households reappeared after 6 months, at distances less than 0.5 km, and at 12 months clustering occurred at distances less than 1.3 km. This increasing cluster size of high infection households suggests that residual infection in
children is passed to nearby households and stresses the importance of mass treatment to protect all households in endemic communities.
How reliable is the clinical exam in detecting ocular chlamydial infection?


Purpose: To describe the relationship between the clinical exam for trachoma and the polymerase chain reaction (PCR) for ocular chlamydia.

Methods: One hundred children in a trachoma-endemic area of Ethiopia were examined three times and swabbed twice for PCR analysis. The assays were compared, and an analysis of the variance between exam and PCR was performed.

Results: Inter-examiner agreement was 0.57 (Cohen’s k), inter PCR agreement 0.98, and agreement between examiner and PCR, 0.26-0.34. The positive predictive value of the exam in identifying infection was 66%. Inter-examiner variance accounted for 30% of the total variance between the exam and PCR, with the remainder presumably due to an underlying difference in what the exam and PCR measure.

Conclusions: Despite modest inter-grader reliability and correlation with evidence of infection, the clinical exam is widely used due to its convenience and low cost. Efforts to make laboratory tests for Chlamydia trachomatis more affordable would be useful.

Synopsis

With the millions of doses of oral antibiotic being distributed for trachoma, it is becoming increasingly important to monitor the prevalence of trachoma in the community. Due to low cost and ease of use, clinical examination is a key tool in the campaign to eliminate trachoma. Although more detailed systems are available, the WHO's simplified trachoma grading scale is by far the most widely used. In the last few years, investigators have been discouraged at how well clinical activity as measured by the WHO simplified scale correlates with PCR testing, the de facto standard for chlamydial infection. Some point out that there are marked differences between examiners, while others note that the inter-test variability of PCR in the eye has never really been tested. Everyone agrees that the two approaches measure two different things; conjunctival inflammation is not always present when there is ocular chlamydia and vice versa. In this study, we assessed the correlation between the clinical exam and PCR tests (before antibiotic treatment), as well as the inter-examiner variability between 3 examiners and the inter-PCR test variability between 2 swabs taken back to back.

One hundred children aged 1-6 years from Gurage Zone in Ethiopia were examined. Results demonstrate that there was moderate agreement between the 3 examiners, which was slightly less than other studies (although not statistically different from other studies). The 100 pairs of PCR swabs were nearly completely concordant. Analyzing the variance between the PCR and clinical exam, almost one third of the difference between these two methods can be explained by the variability in grading of the clinical exam itself, rather than due to the fundamental difference in what each method is measuring.
Field trial of applicability of lot quality assurance sampling survey method for rapid assessment of prevalence of active trachoma.

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OBJECTIVE: To test the applicability of lot quality assurance sampling (LQAS) for the rapid assessment of the prevalence of active trachoma.

METHODS: Prevalence of active trachoma in six communities was found by examining all children aged 2-5 years. Trial surveys were conducted in these communities. A sampling plan appropriate for classifying communities with prevalences < or =20% and > or =40% was applied to the survey data. Operating characteristic and average sample number curves were plotted, and screening test indices were calculated. The ability of LQAS to provide a three-class classification system was investigated.

FINDINGS: Ninety-six trial surveys were conducted. All communities with prevalences < or =20% and > or =40% were identified correctly. The method discriminated between communities with prevalences < or =30% and >30%, with sensitivity of 98% (95% confidence interval (CI)=88.2-99.9%), specificity of 84.4% (CI=69.9-93.0%), positive predictive value of 87.7% (CI=75.7-94.5%), negative predictive value of 97.4% (CI=84.9-99.9%), and accuracy of 91.7% (CI=83.8-96.1%). Agreement between the three prevalence classes and survey classifications was 84.4% (CI=75.2-90.7%). The time needed to complete the surveys was consistent with the need to complete a survey in one day.

CONCLUSION: Lot quality assurance sampling provides a method of classifying communities according to the prevalence of active trachoma. It merits serious consideration as a replacement for the assessment of the prevalence of active trachoma with the currently used trachoma rapid assessment method. It may be extended to provide a multi-class classification method.

Full text of article available:

http://www.scielosp.org/pdf/bwho/v81n12/v81n12a06.pdf

Synopsis

Resource constraints in trachoma-endemic countries demand that interventions should be as cost-effective as possible. A method of identifying areas of high trachoma prevalence in order for resources to be used where they are most needed is a necessary component of trachoma control programs. The WHO/TRA method was developed for this purpose. This method has, however, been found to be unreliable under field conditions. ASTRA is a replacement for the WHO/TRA method. ASTRA classifies communities by prevalence just like the WHO/TRA method but it improves upon the reliability of the original method by employing more rigorous sampling and analysis methods while remaining both rapid and easy to use.

ASTRA is an application of the lot quality assurance sampling (LQAS) method which is widely used in manufacturing to judge the quality of a lot (batch) of items. In the manufacturing context, LQAS is used to identify lots that are likely to contain an unacceptably large number of defective items. In the public health context, LQAS may be used to identify communities with (e.g.) high prevalences of disease. Data analysis is performed as the data is collected and consists of counting the number of defects (e.g. children with active trachoma) in the sample and checking whether a pre-determined number has been exceeded.
This combination of data collection and analysis is called a sampling plan. Using a sampling plan in the field is straightforward. Sampling stops when either the maximum sample size is met or the number of defects allowed in the sample is exceeded. If the maximum sample size is met without the number of defects allowed in the sample being exceeded, the community is classified as low prevalence. If the number of defects allowed in the sample is exceeded, sampling stops and the community is classified as high prevalence. Finer classifications may be achieved by applying more than one sampling plan.

The LQAS method requires that representative samples are taken from surveyed communities. This can be very difficult to do in many trachoma-endemic countries and has held back the widespread adoption of LQAS for use in rural settings in the developing world. A recently developed sampling method known as map, segment, and sample has now removed this hurdle. The combination of LQAS sampling plans and sampling methods suitable for use in urban and rural locations means that this important survey tool may now be used for public health problems almost anywhere in the world. ASTRA is the first application of this combination of LQAS and universally applicable sampling methods.

In 2002, the International Trachoma Initiative in collaboration with SightSavers International, The Institute of Ophthalmology at University College London, and the Malawi Ministry of Health undertook computer-based simulations (in the UK) and field trials (in Malawi) aimed at evaluating the applicability of LQAS using the map, segment, and sample sampling method to the problem of classifying communities by the prevalence of active trachoma. A sampling plan appropriate for classifying communities with prevalences $\leq 20\%$ and $\geq 40\%$ was applied to data collected in ninety-six surveys of communities in which the true prevalence was already known from door-to-door surveys. The ability of LQAS to provide a three-tier classification system ($\leq 20\%$, $> 20\%$ and $\leq 30\%$, and $> 30\%$) was also investigated using the same data. The results of the field trials were:

1. All communities with prevalences $\leq 20\%$ and $\geq 40\%$ were identified correctly.
2. The method discriminated between communities with prevalences $\leq 30\%$ and $>30\%$ with a sensitivity of 98.0%, a specificity of 84.4%, a positive predictive value of 87.7%, a negative predictive value of 97.4%, and an accuracy of 91.7%.
3. The agreement between the three prevalence classes and survey classifications was 84.4%.
4. The time required to complete the a single ASTRA surveys was one day or less.

More details can be found at:

http://www.who.int/entity/bulletin/volumes/81/12/en/877-885.pdf

ASTRA is a rapid and reliable tool for classifying communities according to the prevalence of active trachoma. If coupled with spatial sampling techniques the method may be used to map trachoma prevalence over wide areas at reasonable cost. Operational research into using ASTRA to map the wide-area prevalence of trachoma is currently ongoing in Vietnam.

A CD-ROM describing the ASTRA method is available. This CD-ROM provides training material (video, slides, and manuals), background documents, and data-collections forms for the ASTRA method as well as easy to use software for developing LQAS sampling plans. The CD-ROM is available free of charge. If you would like a copy of the CD-ROM then you should contact: mark@brixtonhealth.com
Strategies for control of trachoma: observational study with quantitative PCR


Antibiotics are an important part of WHO’s strategy to eliminate trachoma as a blinding disease by 2020. At present, who needs to be treated is unclear. We aimed to establish the burden of ocular Chlamydia trachomatis in three trachoma-endemic communities in Tanzania and the Gambia with real-time quantitative PCR.

Conjunctival swabs were obtained at examination from 3146 individuals. Swabs were first tested by the qualitative Amplicor PCR, which is known to be highly sensitive. In positive samples, the number of copies of omp1 (a single-copy C trachomatis gene) was measured by quantitative PCR.

Children had the highest ocular loads of C trachomatis, although the amount of pooling in young age groups was less striking at the site with the lowest trachoma frequency. Individuals with intense inflammatory trachoma had higher loads than did those with other conjunctival signs. At the site with the highest prevalence of trachoma, 48 of 93 (52%) individuals with conjunctival scarring but no sign of active disease were positive for ocular chlamydiae.

Children younger than 10 years old, and those with intense inflammatory trachoma probably represent the major source of ocular C trachomatis infection in endemic communities. Success of antibiotic distribution programmes could depend on these groups receiving effective treatment.

Synopsis

Trachoma is caused by repeated re-infection of the conjunctivae by the bacterium Chlamydia trachomatis. It is the second commonest cause of blindness worldwide. Trachoma is usually diagnosed on clinical grounds. Active disease for example, is the presence of TF (five or more follicles in the central part of the conjunctiva of the upper lid) and/or TI (pronounced inflammatory thickening of the conjunctiva of the upper lid that obscures more than half the normal deep tarsal vessels). However, other conjunctival infections sometimes cause these signs, and not everyone who has an ocular C. trachomatis infection will have them.

In spite of this, clinical diagnosis of active disease is appropriate for individual patients in the field, because (1) laboratory tests for C. trachomatis infection are expensive and are rarely available in endemic areas; and (2) antibiotic treatment, which is designed to clear ocular C. trachomatis infection, has few serious adverse effects (regardless of whether topical tetracycline or oral azithromycin is used), so it does not matter if a few people who don’t actually have the infection are given antibiotics.
In this study, we wanted to determine which population subsets are most important as reservoirs of ocular *C. trachomatis*, in order to help inform antibiotic distribution guidelines. For this purpose, clinical signs alone would have been inadequate. We therefore used a new quantitative PCR (Q-PCR) assay (which measures the number of copies of a *C. trachomatis* gene collected in a standardised conjunctival swab), and tested every consenting individual in entire communities in Rombo, Tanzania; Kongwa, Tanzania; and Jareng, The Gambia. At the time that swabs were taken for Q-PCR, the all-ages point prevalences of active disease were 18%, 36% and 8% at these three locations, respectively. About 1000 individuals were seen at each site.

Children under ten years of age had the highest loads of ocular *C. trachomatis*. They therefore probably constitute the major source of organism for transmission to others, and should be the main target group for antibiotic distribution programmes. Individuals with TI had higher loads than those in other clinical categories. However, some people who only had conjunctival scarring (TS) but no active disease, and some adults, also had *C. trachomatis* positive swabs.

What is the take-home message for people working in trachoma control? Achieving high antibiotic coverage levels in children and people with TI will probably be critical to the success of the ‘A’ component of SAFE, but other demographic or clinical groups should not be ignored.
Health education

Trachoma Health Education (Web-based) Library

Over the past few years, trachoma control program managers and international partners have requested assistance from The Carter Center Trachoma Control Program to develop new health education and IEC materials. For most trachoma control program staff, the development of health education materials is often limited by what they can find in country—we needed to be able to share the wealth of our collection, although limited by the few print copies of these materials stored in Atlanta. In response to this demand, an online library of trachoma health education materials has been created to share this resource worldwide. The Carter Center has compiled an extensive collection of these materials, developed by both The Carter Center and partner organizations. These resources are now available online at: www.cartercenter.org/trachoma/education.html.

The electronic collection contains over 100 different items, including flip charts, posters, t-shirts and hats, manuals, leaflets, storybooks and school-based materials. In addition, the website offers a tutorial page with guidance on the steps to developing health education materials, from formative research to pre-testing to production. Each page is categorized by type of material; each section contains thumbnail images of each item available.

This collection features materials available from trachoma control programs worldwide. It encompasses the range of materials produced—black and white, color images, from expensively produced materials to basic documents. The purpose of the online health education materials library is to inspire programs to develop their own materials having seen what others have done. Each program will probably want to develop unique materials appropriate for their specific local context and the financial resources available to them.

The library is a work in progress. Partner organizations and country program managers who have additional items who would like them included should send either print or electronic copies to:

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