The Mentor Initiative

Devoted to reducing malaria deaths & suffering in humanitarian crises
Trachoma: Diagnosis, Treatment, & Prevention

Melina Lopez
February 24th, 2012
The conjunctiva is a thin, transparent tissue that covers the outer surface of the eye. It consists of two continuous parts, one on the inner surface of the eyelid (the tarsal conjunctiva), and the other over the sclera (the bulbar conjunctiva). These are outlined in the drawing as a thin pink line.
DIAGNOSIS OF TRACHOMA

- Active Trachoma—mostly seen in young children

- Cicatricial (scarring) complications and blindness—seen in late childhood and adulthood

UpToDate 2012
## DIAGNOSIS OF TRACHOMA

### Simplified WHO trachoma grading system

<table>
<thead>
<tr>
<th>Grade</th>
<th>Clinical signs</th>
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<tbody>
<tr>
<td>Trachomatous inflammation follicular (TF)</td>
<td>Five or more follicles of &gt;0.5 mm on upper tarsal conjunctiva.</td>
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<td>Trachomatous inflammation intense (TI)</td>
<td>Inflammatory thickening obscuring more than half the normal deep tarsal vessels.</td>
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<td>Trachomatous conjunctival scarring (TS)</td>
<td>The presence of easily visible scars in the tarsal conjunctiva.</td>
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<tr>
<td>Trachomatous trichiasis (TT)</td>
<td>At least one eyelash rubbing on the eyeball or evidence of recent removal of in-turned eyelashes.</td>
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<tr>
<td>Corneal opacity (CO)</td>
<td>Corneal opacity blurring part of pupil margin.</td>
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DIAGNOSIS OF TRACHOMA

Active trachoma: follicles and their sequelae

The Centre for Eye Research, Australia and UpToDate 2012

The MENTOR initiative
DEVOTED TO REDUCING MALARIA DEATHS & SUFFERING IN HUMANITARIAN CRISES
Trachomatous Inflammation Intense (T)

The Centre for Eye Research, Australia
Progression of Trachoma and Cicatricial Disease: Conjunctival Scarring
Eyelid scar tissue can lead to inward rolling of the eye (entropion) and subsequent ingrown eyelashes (Trichiasis). Diagnosis of trichiasis is crucial as this should prompt surgical intervention to prevent scratching of the cornea and subsequent blindness.
DIAGNOSIS OF TRACHOMA

◆ The picture to the right depicts progression of Pannus, the growth of vascular tissue over the cornea due to edema and ulceration as a result of eyelash abrasion of the cornea.

◆ The bottom picture shows evidence of corneal opacification and loss of vision.

UpToDate2012
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CLINICAL DIAGNOSIS DISADVANTAGES

- Over- or under-diagnosing
  - Overlooking asymptomatic cases

- Recovery phase of infection can result in misdiagnoses
  - Clinical diagnosis before and after treatment

- Misallocation of treatment following misdiagnoses
LABORATORY DIAGNOSTICS

◆ Laboratory assays used for research studies and areas with low prevalence

◆ Nucleic Acid Amplification Test (NAAT)
  ◆ Highly specific
  ◆ Used in areas with low prevalence
  ◆ Not necessary in areas with higher prevalence because of higher correlation between disease and infection

UCSF.org
Call for Point-of-Care Tests

- Resources required for laboratory tests are expensive.
- Clinical grading has remained the most common form of diagnosis because of this.
- Many physicians and officials call for the development of a point-of-care test.
- 2006 Tanzania: point-of-care test
  - Further development needed.

University of Cambridge, 2011
TREATMENT

◆ Mass treatment of antibiotics

◆ Azithromycin—single dose, preferred treatment

◆ Tetracycline—1 percent eye ointment twice a day for six weeks
  → lower compliance because of daily administration and many doses

http://labspace.open.ac.uk/mod/oucontent/view.php?id=452781&section=1.3.5
TREATMENT

- Mass treatment of azithromycin specifically has brought up questions of antibiotic resistance.

- Chlamydial resistance to azithromycin has not been documented thus far.

- At the same time, while azithromycin may not cause bacterial resistance for Trachoma, resistance has developed due to other bacterial infections including S. Streptococcus.

- Overall, however, Azithromycin has proven to reduce mortality in children due to its protection against other pressing infections.
◆ Surgical intervention for trichiasis, followed by topical ointment for seven days after surgery

◆ Bilamellar tarsal rotation to direct the lashes away from the globe
  → Early intervention for both major and minor trichiasis

◆ Epilation (eyelash removal)

◆ Short-term eyelid taping

◆ No vaccine is currently available, however, research is underway

http://www.ntd-ngdonetwork.org/diseases.php
IDENTIFY NEED FOR INTERVENTION

- Gold Standard PBPS: Population Based Prevalence Surveys
- Collect previous surveys, written reports, hospital eye surgery records and interview people with local experience
- Identify water access and latrines in community
- Random sample representative cluster
- Alternate methods: trachoma rapid assessment (TRA) and acceptance sampling TRA (ASTRA).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PBPS, e.g. CRS</th>
<th>ASTRA</th>
<th>TRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sampling design</td>
<td>One or multistage cluster sample</td>
<td>Stratified random sample from population list; modified LOAS</td>
<td>Convenience sample of communities with greatest perceived trachoma burden</td>
</tr>
<tr>
<td>Sub-populations</td>
<td>Clusters based on geographical or political boundaries; supposed to be heterogeneous</td>
<td>Lots based on geographical or political boundaries; supposed to be homogenous</td>
<td>Villages or communities</td>
</tr>
<tr>
<td>Sample size</td>
<td>Estimate based on a population proportion</td>
<td>Estimate based on hypothesis test (desired proportion and level of Type I and Type II errors)</td>
<td>Fixed sample of 50 children aged 1–9 years</td>
</tr>
<tr>
<td>Lists of units</td>
<td>List of primary sampling units needed; complete census not needed, but useful</td>
<td>Population census is essential</td>
<td>No census needed</td>
</tr>
<tr>
<td>Basis for inference</td>
<td>Confidence interval for estimate</td>
<td>Hypothesis test</td>
<td>Ranking of communities</td>
</tr>
<tr>
<td>Outcome</td>
<td>Overall population estimate (e.g. prevalence); estimate from individual clusters should not be calculated</td>
<td>Individual lots judged as acceptable or not acceptable; overall estimates if stopping rule is not used</td>
<td>Proportions in each village or community</td>
</tr>
<tr>
<td>Weighting of sample</td>
<td>Self-weighting if PPS</td>
<td>Weights calculated for each lot if overall estimate is required</td>
<td>Weighting not required</td>
</tr>
<tr>
<td>Cost</td>
<td>Decreased travel time and preparation; reduced cost since census not required</td>
<td>Low cost due to small sample sizes claimed; however, the need to sample each lot may yield higher cost for population census</td>
<td>Cheap since sample is convenient</td>
</tr>
<tr>
<td>Reasons for potential bias</td>
<td>Geographical clustering of sample</td>
<td>Small samples in each lot</td>
<td>Selection bias</td>
</tr>
<tr>
<td>Advantages</td>
<td>Simple and efficient to conduct; population census not required; multiple indicators may be assessed in one survey; periodic surveys allow changes in prevalence to be known over time; multiple indicator surveys enhance interpretation of prevalence change</td>
<td>Small sample sizes for deciding acceptability of a lot; suitable for small study units; suitable for monitoring programme coverage; periodic surveys allow a “snap decision” on whether to continue or stop intervention</td>
<td>Simple and cheap to conduct.</td>
</tr>
<tr>
<td>Disadvantages</td>
<td>Does not derive estimate for individual clusters; error estimates require adjustment for sample design</td>
<td>Population census list essential; expertise required deciding acceptable proportions and risks; small samples in each lot may result in imprecise estimates; large sample sizes if overall estimate is required; cannot be used for multiple indicators</td>
<td>Inaccurate and inconsistent estimates; does not produce prevalence estimates; not based on accurate epidemiological methods; not suitable for monitoring or surveillance</td>
</tr>
<tr>
<td>When to use</td>
<td>Interest in overall population estimate; population-based prevalence surveys are the “gold standard”</td>
<td>Interest in information for each lot; suitable for monitoring or surveillance</td>
<td>May identify where prevalence surveys are required; limited use due to inadequate statistical rigour</td>
</tr>
</tbody>
</table>

ASTRA, acceptance sampling trachoma rapid assessment; CRS, cluster random sampling; LOAS, lot quality-assurance sampling; PBPS, population-based prevalence surveys; PPS, probability proportional to size; TRA, trachoma rapid assessment.
IDENTIFY NEED FOR INTERVENTION

**Table 2** WHO criteria for mass antibiotic treatment distribution (WHO-ITI 2004)

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<thead>
<tr>
<th>Prevalence of TF in children</th>
<th>Recommendation</th>
</tr>
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<tbody>
<tr>
<td>1–9 years</td>
<td></td>
</tr>
<tr>
<td>District level</td>
<td></td>
</tr>
<tr>
<td>≥10%</td>
<td>Mass treat whole district annually for 3 years, then re-assess the prevalence in the district</td>
</tr>
<tr>
<td>&lt;10%</td>
<td>Do community-level assessment</td>
</tr>
<tr>
<td>Community level</td>
<td></td>
</tr>
<tr>
<td>≥10%</td>
<td>Mass treat whole community annually for 3 years, then re-assess the prevalence in the community</td>
</tr>
<tr>
<td>≥5% but &lt;10%</td>
<td>Target treatment to affected children and the household they live in</td>
</tr>
<tr>
<td>&lt;5%</td>
<td>Antibiotic treatment not recommended</td>
</tr>
</tbody>
</table>

WHO 2006 Report
◆ Remember high risk population is children <10 years old

◆ “Herd immunity” gained by administering azithromycin to children

◆ Even though, remember at least 80% population needs to be treated

With large waves of immigration in the 20th century, the US prohibited immigrants from entering the US if they were infected with Trachoma.

Early 20th century US Anti-Trachoma legislation to control infection, especially in Indian reservations.

As a result of this legislation, subsequent improved housing and living standards, Trachoma is no longer is a major public health threat in the US.

http://www.ellisisland.org/photoalbums/ellis_island_then.asp
In addition to antibiotic treatment, think of the environmental risk factors of trachoma to prevent infection and possible re-infection:

- The 6 D’s: Dryness, dust, dirt, dung, discharge, density (overcrowding)
- The 5 Fs: flies, feces, faces, fingers, and fomites

CarterCenter.org
INTERVENTION

Targeting the Mechanical Vector

Targeting Human Transmission

http://bjo.bmj.com/content/88/6/750.full

http://developmentmedia.net/success.html
PREVENTION IN CRISES

◆ Sanitation and Hygiene

◆ Contain fecal matter in latrines to limit fly population

◆ Include azithromycin in proposed “medical cocktail” of Ivermectin and Albendazole to prevent the seven neglected tropical diseases

CURRENT PREVENTION: S.A.F.E.

Management & Prevention Strategy as outlined by WHO and ITI:

S: simple surgery to create a slit in the eyelid and peel back a portion to prevent further corneal scarring.
A: antibiotics. Single dose of azithromycin
F: facial hygiene. Face washing, especially among children who may be outdoors playing with many other kids, is a great step in interrupting transmission.
E: environmental empowerment. Improve access to clean water, improve sanitation and latrines to reduce fly populations. Educational empowerment for community members also lends them the ability to prevent human-human transmission by better hygiene.
MOROCCO 1999: MANAGEMENT AND PREVENTION SUCCESS STORY!

- 5 government ministries partnered, including health and education, local NGOs and international organizations such as UNICEF and WHO
- Mobile surgery units
- Administer Zithromax
- Build wells and latrines
- Provide education
- SAFE strategy

ITI Morocco Report
TRACHOMA ELIMINATION

◆ 1997: WHO Alliance for the Global Elimination of Blinding Trachoma (GET 2020) created

◆ Greater Implementation of SAFE strategy

◆ Proven evidence of the effectiveness of mass treatment
  ◆ Case study in Tanzania

◆ Development of Point-Of-Care Tests

◆ Greater education