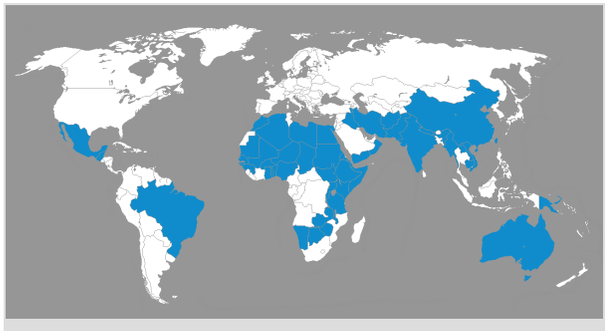
Background

Global Burden | Causative Agents & Transmission | Pathogenesis | Current Control Strategy | Existing Products | Get Involved

What is Trachoma?

Trachoma is a bacterial infection of the eye transmitted by close person-to-person contact. With frequent and repeated infections, trachoma infection can lead to permanent visual impairment.

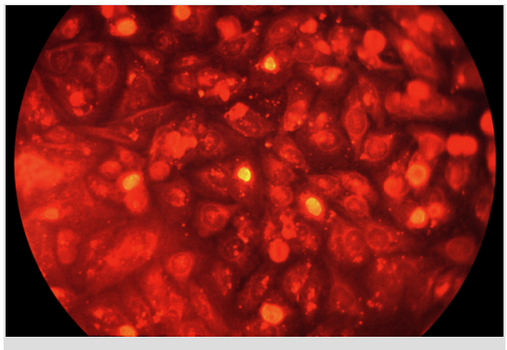
Global Burden



Distribution of trachoma worldwide, 2009 *(WHO)*

Trachoma has been eliminated from most of the developed world, but is still endemic in areas with poor sanitation, scarce water supply, and where people live in crowded conditions. It is especially prevalent in remote, rural areas of Africa, Asia, South America, and among aboriginal groups in Australia. Approximately 84 million people are currently infected with trachoma, of whom about 10% have some visual impairment.[1] It is the most common infectious cause of blindness worldwide.[2]

Causative Agent and Transmission



C. trachomatis-infected cells
(photo: CDC)

Trachoma is caused by infection of the ocular surface with the bacterium *Chlamydia trachomatis*. The infection is spread by mucus membrane contact with an infected person (or their secretions) and by mechanical transmission by flies. As such, it often affects members of the same family who live together in close quarters, and disproportionately affects women and children.[1]

Pathogenesis

A single infection with *C. trachomatis* causes inflammation that resolves, whereas repeated infection can result in permanent damage to the cornea and even blindness. The World Health Organization (WHO) divides the development of trachoma into stages.

1. Trachomatous inflammation - follicular
2. Trachomatous inflammation - intense
3. Trachomatous scarring
4. Trachomatous trichiasis (eyelashes rubbing and damaging the cornea)
5. Corneal Opacity[2]

The first two stages are 'active stages,' wherein the bacterial infection triggers a release of cytokines into the conjunctiva (the clear membrane that lines the eye and eyelid) causing swelling of the eyelid tissue. The later stages are the result of chronic inflammation and can lead to entropion (the formation of scar tissue that causes the eyelid to turn inward) with the lashes scratching and irreversibly damaging the corneal surface.[3] Children more often display the active stages of infection, whereas older people – who have suffered repeated reinfection – exhibit marked scarring of the conjunctiva and visual impairment.

The absence of active bacterial infection in the later stages of the disease has implications for the management of trachoma; although antibiotics can kill the C. trachomatis bacteria, antibiotic treatment does not cure the irreversible eye damage caused by years of repeated infections.

Current Control Strategy

In 1998, the WHO formed the GET2020 alliance, a coalition of NGOs, industry and academic experts, and field doctors, with the goal of global trachoma elimination by 2020. The control strategy for trachoma prevention adopted by the group is the SAFE strategy[1]:

- **S**urgery
- **A**ntibiotics to treat the reservoir of infection
- **F**ace washing
- **E**nvironmental Change

Surgery to correct trichiasis (lashes turned inward and scratching the cornea) has proven to be successful in clinical trials, but there are issues of access and feasibility in the low-resource settings where trachoma is endemic. Temporary non-surgical methods of preventing eye damage – such as sticky tape to hold open the eyelid, or epilation to remove inward-growing eyelashes – are also often employed. Antibiotics are used in mass drug administration to reduce the disease prevalence, and in individual cases to end the infection. Face washing and environmental change go hand-in-hand, and are both potentially effective at reducing the probability of transmission of the bacteria. Unfortunately, these solutions also require the most significant expansion of infrastructure, which may not be possible in the types of places where trachoma is endemic.[4]

Existing Products

Drugs

While there are no drugs specifically targeted to *C. trachomatis* infection, azithromycin and tetracycline are the antibiotics of choice. Oral formulations of the drugs are often given in mass drug administrations, while topical ointments or eye drops are used to treat existing infections.[5]

Vaccines

There are currently no vaccines in use to prevent trachoma

Diagnostics

Diagnosis in the field is generally made based on clinical presentation in endemic areas, and treatment is therefore usually presumptive. A definitive diagnosis of active infection is made in the laboratory using enzyme immunoassays, serology, or identification of the C. trachomatis bacteria in microscopic evaluation of conjunctival tissue.[6]

A dipstick immunoassay rapid diagnostic test (RDT) developed by Cambridge researchers has been shown to be more effective for

diagnosis of trachoma than the WHO grading system.[7] Clinical diagnosis of late-stage visual impairment caused by trachoma using the WHO system allows health care workers to arrange for surgery or another physical interventions to prevent further corneal damage. However, diagnosis of active C. trachomatis infection allows health care workers to prescribe antibiotics, clearing the bacterial infection and potentially preventing eye damage at an earlier stage. Rolling out the C. trachomatis RDT in endemic areas therefore has the potential to improve the early detection of infections and improve the correct use of antibiotics to prevent permanent eye damage.[7]

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References

1. WHO trachoma fact sheet.
2. Thylefors et al (1987) “A Simple System for the Assessment of Trachoma and its Complications.” Bulletin of the World Health Organization 65(4).
3. Burton M et al. (2009) “The Global Burden of Trachoma: A Review.” PLoS Neglected Tropical Diseases 3(10): e460.
4. Sumamo et al. (2007) “The Cochrane Library and trachoma: an overview of reviews.” Evidence-Based Child Health: A Cochrane Review Journal 2(3).
5. Schachter et al. (1999) “Azithromycin in control of trachoma.” The Lancet 354 (9179).
6. Solomon et al (2004) “Diagnosis and Assessment of Trachoma.” Clinical Microbiology Reviews 17(4).
7. Michel et al (2006). “Field Evaluation of a rapid point-of-care assay for targeting antibiotic treatment for trachoma control: a comparative study.” The Lancet 367.

Get Involved

To learn how you can get involved in neglected disease drug, vaccine or diagnostic research and development, or to provide updates, changes, or corrections to the Global Health Primer website, please view our FAQs or contact us at globalhealthprimer@bvgh.org.

Pipeline & Analysis

Drugs | Vaccines | Diagnostics | Get Involved

Drugs

Although drug resistance to common antibiotics is a concern, numerous antibiotics are available to treat *C. trachomatis* infection. Vaccine development is the primary focus of new trachoma products

Vaccines

PIPELINE

Product/Research Program	Developers	Discovery	Pre-clinical	Phase I	Phase II	Phase III
Oral Chlamydia vaccine	Wayne State University					
PmpD multivalent chlamydia vaccine	National Institute of Allergy and Infectious Diseases					
rMOMP vaccine	National Institute of Allergy and Infectious Diseases University of California, Irvine					
Chlamydia vaccine research program	Queensland University Sanofi Pasteur					

ANALYSIS

Because the bacterium *C. trachomatis* also causes sexually-transmitted chlamydia infections, which are common in both the developed and developing worlds, there is potential to develop a vaccine that prevents both diseases. Although the two diseases are caused by different bacterial serotypes, there is potential to co-develop a vaccine using common protein antigens.

The immunogenic major outer membrane protein (MOMP) is common to all chlamydia strains and therefore represents a promising vaccine antigen. Studies using this protein have seen a reduction in bacterial shedding and an induction of both cellular and humoral immune response against *C. muridarum*, the mouse strain of chlamydia[8]. However, despite evoking an antibody response, recombinant vaccine candidates using this protein have not been successful at providing total protection against infection. Early research into a MOMP-based DNA vaccine has yielded mixed results, but a DNA prime and immune-stimulating boost combination is the most promising vaccine candidate thus far.[9]

Diagnostics

Early detection of the disease is crucial to prevent the damaging long-term effects of repeated trachoma exposure. An RDT that enables targeted detection of new cases and rapid antibiotic treatment could vastly improve disease outcomes in endemic areas. A rapid diagnostic ‘dipstick’ test is currently in the process of being distributed and applied for this use

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References

1. Michel et al (2006). “Field Evaluation of a rapid point-of-care assay for targeting antibiotic treatment for trachoma control: a comparative study.” The Lancet 367.
2. Carmichael et al (2011). “Induction of protection against vaginal shedding and infertility by a recombinant Chlamydia vaccine.” Vaccine.
3. Schautteet et al (2011). “Chlamydia trachomatis vaccine research through the years.” Infectious Diseases in Obstetrics and Gynecology.

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Tools

The following series of tables describe the availability of tools for research, discovery, and development of novel drugs, vaccines, and diagnostics for trachoma. The tools listed in the following tables are not intended to be an all-inclusive list but rather capture the most common tools used for drug, vaccine, and diagnostic development. The tools for trachoma are not well developed. However, trachoma benefits from tools developed to study the related sexually transmitted form of the disease.

Drug Development Tools

Basic Research: Target Identification	Target Validation	Screening: Hit/Lead Identification Optimization	Pre-clinical Validation	Clinical Validation
Genome: *C. trachomatis* GenBank library available **Key databases:** GenBank ***In vitro culture:*** Yes	**Gene knock-outs:** No **Conditional gene knock-outs:** No **Transposon mutagenesis:** No **RNAi:** No **Other antisense technology:** No **Viability assays:** Yes **Transcription microarrays:** Yes **Proteomics: Yes** **Crystal structures:** Yes	**Whole-cell screening assays:** Yes **Enzymatic screening assays:** Yes	**Animal models:** Yes Monkeys and mice are most common	**Monitoring treatment efficacy:** Yes **Availability of endpoints:** Resolution of disease signs is considered a 'clinical cure' of *C. trachomatis* infection, but there is no endpoint for Trachoma. **Availability of surrogate endpoints:** No **Access to clinical trial patients/sites:** Yes

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Vaccine Development Tools

Basic Research: Antigen Identification	Immune Response Characterization	Clinical Validation
See drug development tools above	**Predictive animal models:** Murine models are most commonly used in sexually transmitted *C. trachomatis* studies and in genetic studies. Primates are a more relevant human analogue for clinical symptoms in Trachoma	**Surrogate markers of protection:** No

	studies. **Detection of endogenous antigen specific response in clinical samples:** Yes, antibodies to C. trachomatis Major Outer Membrane Protein (MOMP). **Natural immunity well characterized:** No	**Challenge studies possible:** No

Diagnostic Development Tools

Basic Research: Biomarker Identification	Biomarker Validation	Clinical Validation
See drug development tools above	**Biomarkers known:** Yes **Access to clinical samples:** Yes **Possible sample types:** Eye fluids, blood	**Access to clinical trial patients/sites:** Yes **Treatment available if diagnosed:** Yes (treatment of infection, not of eye damage)

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Product Details

Chlamydia vaccine research program

Synonyms:
Chlamydia vaccine research program

Disease:
Trachoma

Specific Indication:

Product Type:
Vaccine

PRV Elegible?
Yes

Target/Technology:
Unknown

Mechanism of Action:

Molecule Class:

Administration Route:

Notes:

Clinical Trials:

Publications:

Oral Chlamydia vaccine

Synonyms:
Oral Chlamydia vaccine

Disease:
Trachoma

Specific Indication:

Product Type:
Vaccine

PRV Elegible?
Yes

Target/Technology:
Unknown

Mechanism of Action:

Molecule Class:

Administration Route:
Oral

Notes:

This early-stage preclinical vaccine candidate is based on novel peptide immunogens that are intended to induce protective immunity against all Chlamydia serotypes.

Clinical Trials:

Publications:

PmpD multivalent chlamydia vaccine

Synonyms:
PmpD multivalent chlamydia vaccine

Disease:
Trachoma

Specific Indication:

Product Type:
Vaccine

PRV Elegible?
Yes

Target/Technology:
Polysaccharide protein conjugate vaccines

Mechanism of Action:

Molecule Class:

Administration Route:

Notes:

Clinical Trials:

Publications:

rMOMP vaccine

Synonyms:
rMOMP vaccine

Disease:
Trachoma

Specific Indication:

Product Type:
Vaccine

PRV Elegible?
Yes

Target/Technology:
Recombinant/purified protein vaccines

Mechanism of Action:
recombinant prime + protein subunit boost

Molecule Class:

Administration Route:

Notes:

Clinical Trials:

Publications:

Developer Details

Wayne State University (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Trachoma	Oral Chlamydia vaccine	Pre-clinical

Sanofi Pasteur (France)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Trachoma	Chlamydia vaccine research program	Discovery

Queensland University (Australia)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Trachoma	Chlamydia vaccine research program	Discovery

National Institute of Allergy and Infectious Diseases (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Trachoma	PmpD multivalent chlamydia vaccine	Pre-clinical

National Institute of Allergy and Infectious Diseases (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Trachoma	rMOMP vaccine	Pre-clinical

University of California, Irvine (United States)

Type	Disease	Product/Research Program	Current Phase
Vaccine	Trachoma	rMOMP vaccine	Pre-clinical