

Pharmaceutical Research for Neglected Diseases

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Leading Infectious Causes of Death, 2001

Cause	Est. Number of Deaths
Respiratory infections	3,871,000
HIV/AIDS	2,866,000
Diarrheal diseases	2,001,000
Tuberculosis	1,644,000
Malaria	1,124,000
Measles	745,000
Pertussis	285,000
Tetanus	282,000
Meningitis	173,000
Syphilis	167,000

Table 1. The Major Neglected Tropical Diseases Ranked by Prevalence.*

Disease	Global Prevalence (millions)	Population at Risk	Regions of Highest Prevalence	Source
Ascariasis	807	4.2 billion	East Asia and Pacific Islands, sub-Saharan Africa, India, South Asia, China, Latin America and Caribbean	Bethony et al., ⁶ de Silva et al. ⁷
Trichuriasis	604	3.2 billion	Sub-Saharan Africa, East Asia and Pacific Islands, Latin America and Caribbean, India, South Asia	Bethony et al., ⁶ de Silva et al. ⁷
Hookworm infection	576	3.2 billion	Sub-Saharan Africa, East Asia and Pacific Islands, India, South Asia, Latin America and Caribbean	Bethony et al., ⁶ de Silva et al. ⁷
Schistosomiasis	207	779 million	Sub-Saharan Africa, Latin America and Caribbean	Steinmann et al. ⁸
Lymphatic filariasis	120	1.3 billion	India, South Asia, East Asia and Pacific Islands, sub-Saharan Africa	Ottesen, ⁹ WHO ¹⁰
Trachoma	84	590 million	Sub-Saharan Africa, Middle East and North Africa	International Trachoma Initiative, ¹¹ Médecins sans Frontières ¹²
Onchocerciasis	37	90 million	Sub-Saharan Africa, Latin America and Caribbean	Basáñez et al. ¹³
Leishmaniasis	12	350 million	India, South Asia, sub-Saharan Africa, Latin America and Caribbean	Desjeux ¹⁴
Chagas' disease	8–9	25 million	Latin America and Caribbean	WHO ¹⁵
Leprosy	0.4	ND	India, sub-Saharan Africa, Latin America and Caribbean	International Federation of Anti-Leprosy Associations ¹⁶
Human African trypanosomiasis	0.3	60 million	Sub-Saharan Africa	Fèvre et al. ¹⁷
Dracunculiasis	0.01	ND	Sub-Saharan Africa	Carter Center ¹⁸
Buruli ulcer	ND	ND	Sub-Saharan Africa	Global Buruli Ulcer Initiative ¹⁹

* ND denotes not determined.

Industry can focus its research platform on drugs for neglected diseases



- Different models are unfolding
 - Stand alone facilities
 - GlaxoSmithKline in Tres Contos, Spain
 - Novartis in Singapore
 - Integrated into existing facilities
 - Pfizer-WHO partnership for screening in Sandwich, England

Pfizer / WHO – Tropical Disease Research Partnership

What WHO-TDR Brings

- Expertise
 - Tropical parasitology
 - Desired target product profiles
- Screening Capability
 - Whole organism *in vitro* and lab animal *in vivo* screens
 - New mechanistic targets for high throughput screens
- Funding for FTE Support
 - Chemists to follow up hits and lead optimisation
 - Biologist for HTS development and implementation
 - Genomic work aimed at new target identification

What Pfizer Brings

- Compounds
 - Access to over 3 million compounds
 - Libraries of interesting drugs
 - Antiparasitic classes
 - Known drugs and mechanistic actives
- Medicinal Chemistry and Biology Expertise
 - Selecting the best compounds for follow up – AH parasitology + HH
 - Directing lead optimisation, e.g., input on likely toxicity, pharmacokinetics, etc.
 - Support for HTS development
 - Genomics and target selection expertise
 - Training and supervision for post-Docs

WHO-Pfizer collaboration

- Progress to date
 - Screening of 12,000 compounds completed
 - against 6 parasitic targets
 - Approx 200 compounds being further assessed
 - Exposure of developing world post-doctoral students to industry
 - Enhanced relationships between multilateral organizations and industry

International Trachoma Initiative

Program

- Independent NGO created to support WHO goal to eliminate blinding trachoma by 2020
 - Founded by Pfizer and Edna McConnell Clark Foundation, Nov '98, in collaboration with WHO's Global Elimination of Trachoma
- Comprehensive public health strategy for prevention and treatment – “SAFE” Strategy (Surgery, Antibiotics, Face Washing, Environmental Change)
 - Zithromax is the preferred medicine



INTERNATIONAL TRACHOMA INITIATIVE

SAFE Strategy

SURGERY

ANTIBIOTICS

FACE
WASHING

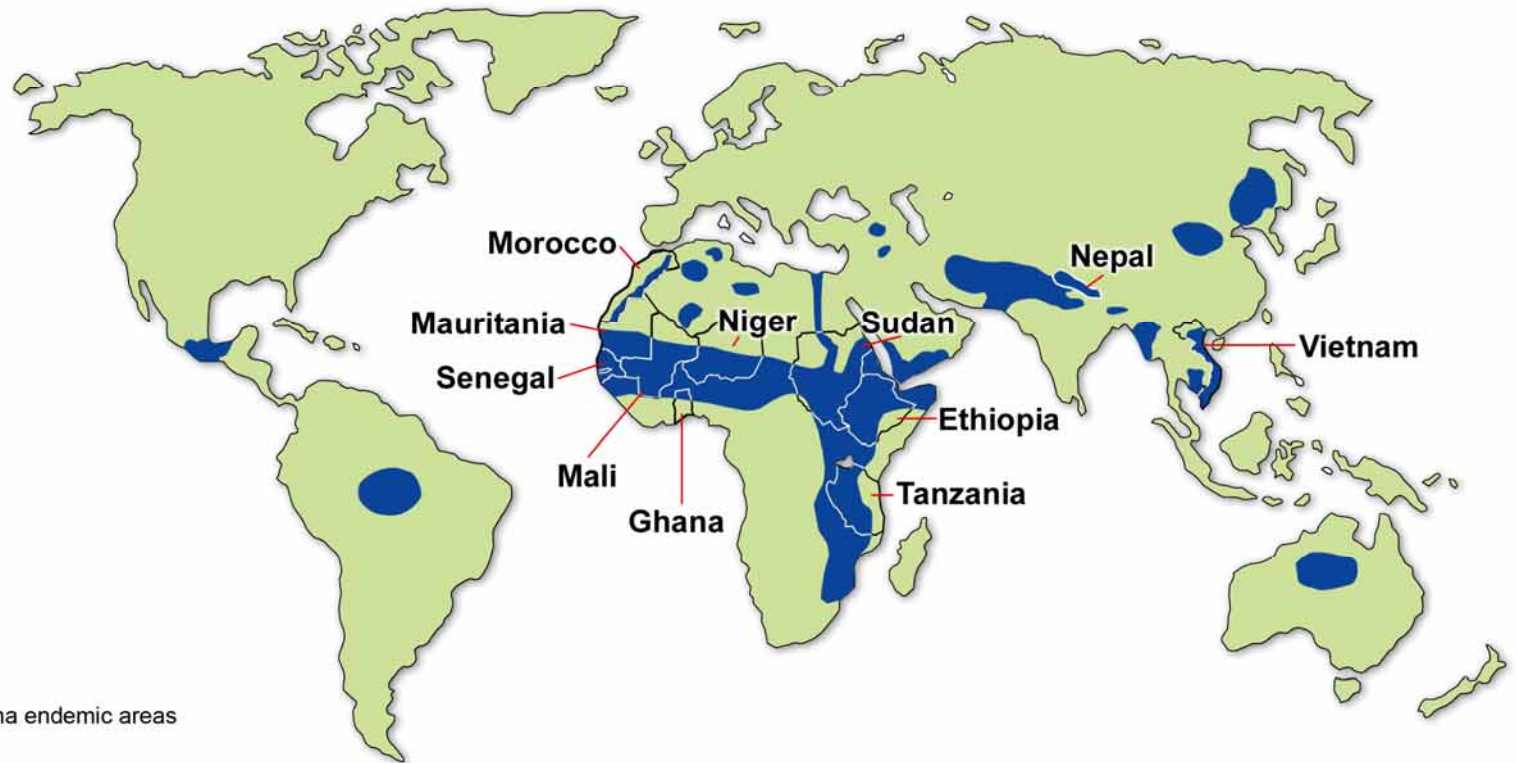
ENVIRONMENTAL
CHANGE



Trachoma Worldwide

Country Programs

ITI Supported Country Programs



International Trachoma Initiative

Metrics

- Impressive reduction in active infections
 - Morocco in certification process for elimination of trachoma
 - Tanzania (75%), Vietnam (75%)
- 54 million antibiotic treatments in 13 countries in Africa & Asia
- 276,000 surgeries performed = 276,000 cases of blindness averted
- Added Burkina Faso and Uganda as new countries in conjunction with country Oncho and LF distribution programs
- “SAFE” strategy
 - Ethiopia: Exceeded 2004 targets in face washing education, surgery training and latrine building (target 10k latrines, actuals closer to 90k latrines)
 - Tanzania: Clean faces increased from 9% to 33% in one year

International Trachoma Initiative

Preventing and Eliminating Disease

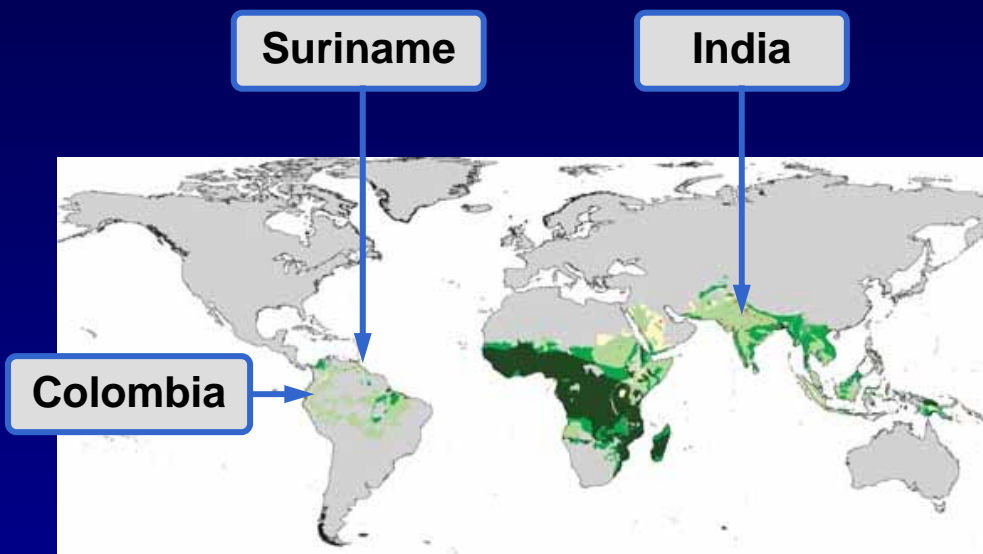
“We have seen what Pfizer is doing around the world with Zithromax in dealing with Trachoma, which is by far the number one cause of preventable blindness. You have been able to reduce the incidence of Trachoma dramatically, in some cases approaching 100 percent. This is, to me, an earthshaking accomplishment.”



Jimmy Carter

Former U. S. President

Azithromycin and Chloroquine: Treatment of Uncomplicated Malaria in Adults



ex-African Program

- Phase 2b/3 study
 - ◆ Two Doses Levels
 - > 500 mg AZ +600 mg CQ
 - > 1 g AZ + 600 mg CQ
 - ◆ Phase 2 Conclusion
 - > 500 mg AZ arm ineffective
 - > Regional efficacy differences
 - > Dose-response seen
 - > Well tolerated

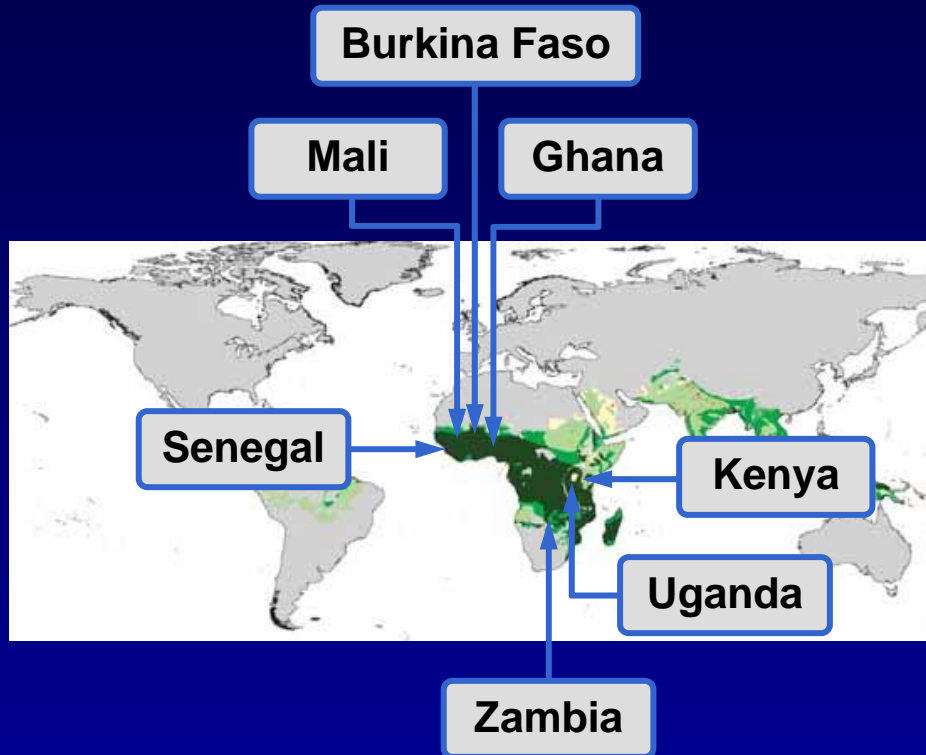
South America (57 %)	
Suriname	25%
Tumaco	64%
Guapi/Tado	91%

Note: A yellow arrow points from the 91% efficacy in Guapi/Tado to the 64% efficacy in Tumaco, with a question mark next to it.

India (84%)	
Guwahati	94%
Rourkela	89%
Mumbai	79%
Nagpur/Indore	100%
Goa	71%

- Phase 2 follow-up
 - ◆ 2 gm AZ + CQ
 - ◆ Status
 - > Tumaco= 96% efficacy
 - > India site enrolling

Azithromycin and Chloroquine: Treatment of Uncomplicated Malaria in Adults



African Program

- Phase 2b/3 study
 - ◆ 3 arms studied
 - > 500 mg AZ + 600 mg CQ
 - > 1 g AZ + 600 mg CQ
 - > Mefloquine
 - ◆ Results
 - > 500 mg arm dropped
 - > 1gm AZ/CQ = 98% efficacy
- Phase 3 Study
 - ◆ 2 arms compared
 - > 1gm AZ + 600 mg CQ
 - > Mefloquine
 - ◆ Status
 - > Enrollment complete
 - > Preliminary results supportive

**Next Steps: Intermittent Preventive Treatment
Pediatric Treatment Trials**

Much work to be done

“.....the successful translation of basic scientific discoveries into new treatments is a long, complex and expensive process.”

David O'Connell

Chief Editor, *Nature Reviews Microbiology*

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