

ISID-NTD 2011 Boston MA

Future Trends in Vaccines for Neglected Tropical Diseases

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World Health Assembly Resolutions through MDA

- **Elimination of leprosy**
 - Dapsone/Rifampicin/Clofazimine
 - 1987 & 1998
- **Elimination of LF**
 - DEC + Albendazole
 - Ivermectin + Albendazole
 - 1997
- **Eradication of dracunculiasis**
 - 1997 & 2004
- **Elimination of blinding trachoma**
 - Azithromycin + SAFE
 - 1998
- **Elimination of avoidable blindness (trachoma and onchocerciasis)**
 - Ivermectin/Azithromycin + SAFE
 - 2003

USAID Goals

- **Reduce the prevalence of seven NTDs by 50% among 70% of affected population**
- **Contribute to:**
 - Elimination of onchocerciasis in the Americas by 2016
 - Elimination of LF globally by 2020
 - Elimination of leprosy

<http://www.neglecteddiseases.gov>

June 2, 2011



Integrating Neglected Tropical Diseases into AIDS, Tuberculosis, and Malaria Control

Hotez Peter H, MD, PhD, Hotez Maria M, MD, MPH, Juarez Robinson, G, MD, PhD, and Jeffrey D Sachs, PhD.

The present article reflects the growing commitment to bring the NTDs to support new efforts, which have included the development of a global strategy for NTDs, the adoption of a new paradigm for NTD control, and the launch of a new global strategy for NTD control. The authors discuss the importance of NTD control in the context of the global health agenda, and the need for a coordinated, multi-sectoral approach to NTD control. The authors also discuss the need for a coordinated, multi-sectoral approach to NTD control, and the need for a coordinated, multi-sectoral approach to NTD control.

“An Audacious Goal”: Malaria Eradication

- October 2007: the Bill & Melinda Gates Foundation called for a new global commitment to embrace “an audacious goal” for building a roadmap to eradicate malaria.
- Comprehensive set of strategies
 - Universal access to existing control tools
 - Expanded use of insecticide-treated bednets
 - Expanded use of IPT
 - Enhanced global procurement of artemisinin combination therapies
 - Parallel and large-scale program of R&D
 - New drugs
 - New vaccines
 - New insecticides

Enlarging the audacious goal? A launch to eliminate the NTDs?

- NTDs slated for elimination with existing technologies
 - Dracunculiasis
 - Just 3,000 cases left
 - Lymphatic Filariasis – MDA
 - Eliminated in 23 previously endemic countries
 - Trachoma – MDA
 - Eliminated in 12 previously endemic countries
 - Leprosy – MDT
 - Eliminated in 119 of 122 previously endemic countries
- Continuous need for operational research and implementation science to support the “endgame”

WHO List of 17 NTDs
PLoS NTDs List of 40 NTDs

- Helminth infections
 - Ascariasis/Trichuriasis
 - Hookworm infection
 - Dracunculiasis
 - Lymphatic Filariasis
 - Onchocerciasis
 - Cysticercosis
 - Echinococcosis
 - Food-borne trematodiasis
 - Schistosomiasis
- Protozoan infections
 - Chagas disease
 - HAT
 - Leishmaniasis
- Bacterial/Viral infections
 - Buruli
 - Leprosy
 - Trachoma
 - Dengue/Japanese Encephalitis
 - Rabies

THE QUESTION:
Do we need a similar rallying cry to support or galvanize the NTD community of scientists?

Should it be around tools needed for the “end game” promoting a comprehensive R&D initiative to tackle the “seventeen”?

“Seventeen by 2017”

FUNDING SPREAD ACROSS DISEASES >\$3 Billion

G-FINDER: YEAR 3

❖ Funding more evenly spread across the neglected diseases since first G-FINDER survey

- HIV/AIDS, malaria and TB share down from 77% to 72%
- Diarrhoeal diseases, dengue and kinetoplastids share > 5% for the first time
- Leprosy, rheumatic fever, trachoma and Buruli ulcer each received less than \$11m (0.3%)

Enlarging the “audacious” goal:

- Eliminating all of the 17 NTDs (40 NTDs?)
- Comprehensive research effort to develop new diagnostics, drugs, vaccines for the NTDs
- Coupled with implementation research to fold these tools into control and elimination strategies
- And *basic research* on these conditions
- Scale up of international funding

Hotez PJ. PLoS NTDs May 2011

PLoS ONE

New Antipoverty Drugs, Vaccines, and Diagnostics: A Research Agenda for the US President's Global Health Initiative (GHI)

Author: Hotez PJ, et al.

Abstract: Allocating just 1%–2% of Global Health Initiative funds to conduct research and development for neglected tropical diseases drugs, vaccines, and diagnostics would create a new generation of tools to eliminate our planet's greatest scourges and help shape United States foreign policy.

A Handful Of 'Antipoverty' Vaccines Exist For Neglected Diseases, But The World's Poorest Billion People Need More

Health Affairs (Millwood) June 2011

Human Vaccines
Buruli Ulcer
Chagas Disease
Dengue
Food-borne Trematodiasis
Hookworm
Leishmaniasis
Leprosy
Onchocerciasis
Schistosomiasis

Veterinary Transmission Blocking
Cysticercosis
Echinococcosis
Food-borne Trematodiasis
HAT
Rabies

NTDs Requiring Vaccines
Health Affairs (Millwood) June 2011


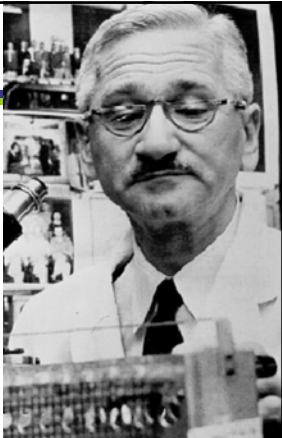
NTDs Requiring Vaccines
Health Affairs (Millwood) June 2011

NTDs Requiring Vaccines
Health Affairs (Millwood) June 2011

NTD Antipoverty Vaccines
The Decade of Vaccines: “Outside Looking In”

- Of the 17 Pharma only produces dengue vaccine and rabies vaccine
- AMCs and PRVs have not accelerated antipoverty vaccines
- Conspicuous by their absence
 - High morbidity (112 million DALYs)
 - but low mortality (200,000-600,000 deaths)
 - Hidden in remote rural areas LMICs (Zero market)
 - Expensive R&D
- Different model:
 - PDPs
 - Developing Country Manufacturers
 - Public Sector Vaccine Manufacturers in Brazil, Cuba, Mexico

“The Business Plan from Hell”

THE RIGHT OF ACCESS TO INNOVATION


"A scientist who is also a human being cannot rest while knowledge which might reduce suffering rests on the shelf."
 —Dr. Albert B. Sabin

Sabin Vaccine Development

PDP for NTD "Antipoverty Vaccines"




Process Development: Bridging the "Valley of Death"



Sabin-Brazil Technology Transfer



Bio-Manguinhos



FIOCRUZ

CDTS


Sabin PDP Clinical Field Site: Americaninhas, Minas Gerais, Brazil

Hookworm
32 million cases
68% Minas Gerais

Schistosomiasis
2-7 million cases
45% Minas Gerais

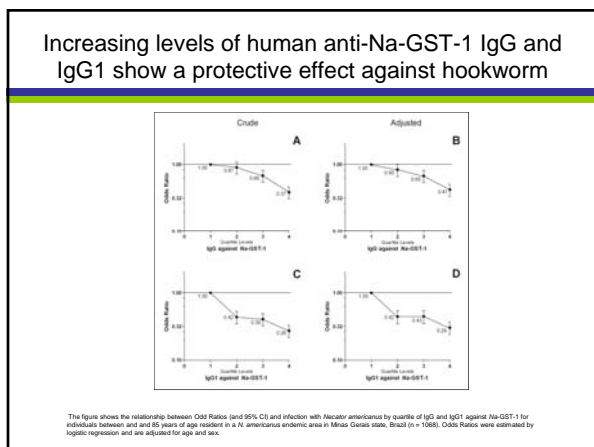
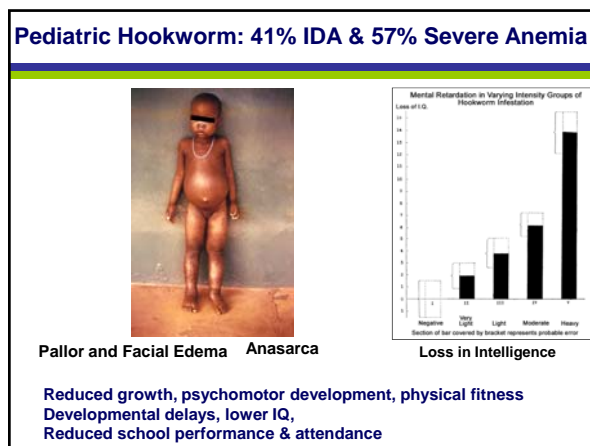
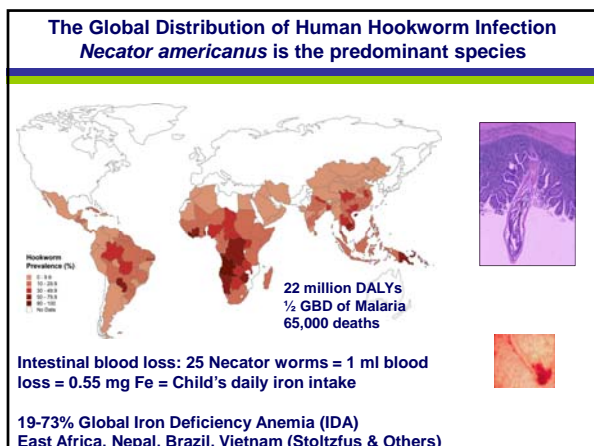
Hookworm and Schistosomiasis Co-Infections



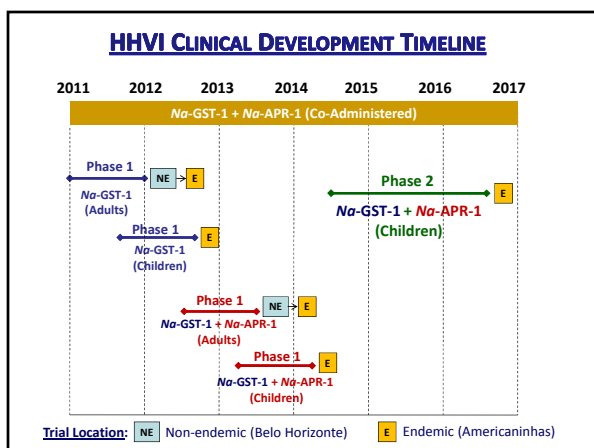
Sabin Portfolio of Vaccines

- Human Hookworm Vaccine**
 - Bivalent recombinant protein vaccine: Na-GST-1 and Na-APR-1
 - Alhydrogel formulation ± synthetic lipid A
 - IND filing FDA – Phase 1 testing Brazil (FIOCRUZ Biomanguinhos)
- Human Schistosomiasis Vaccine**
 - Monovalent recombinant protein vaccine: Sm-TSP-2
 - Alhydrogel formulation ± synthetic lipid A
 - cGMP pilot manufacture Brazil (Instituto Butantan)
- Cruxmexvax® and Leishmexvax®**
 - Bivalent recombinant protein vaccines
 - Alhydrogel formulation + synthetic lipid A
 - Possible Nanoparticle-based vaccines
 - cGMP pilot manufacture Mexico (Birmex)

Support: B&M Gates Foundation, NIH, Dutch Ministry of Foreign Affairs, Carlos Slim Inst Health, Other Private Support



- ### Goals of Anti-Hookworm Vaccine
- Reduction of 80% of moderate/heavy hookworm infections
 - Worm burden reduction
 - Egg reduction
 - Reduced intestinal blood loss
 - Reduction in anemia and malnutrition
-

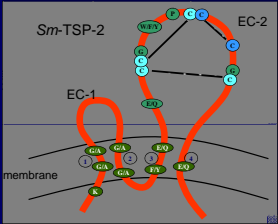


Countries with High Hookworm & Schistosomiasis

Country	Hookworm	Schistosomiasis
Angola	11.3 million	6.1 million
Brazil	32.3 million	2-7 million
Cote d'Ivoire	10.0 million	6.6 million
DR Congo	31.0 million	14.9 million
Ethiopia	11.2 million	5.0 million
Ghana	5.5 million	15.1 million
Kenya	9.2 million	7.4 million
Nigeria	37.8 million	28.8 million
Sudan	8.1 million	5.0 million
Tanzania	9.9 million	19.0 million
Uganda	9.1 million	5.3 million
Zimbabwe	8.1 million	5.2 million

Completed Genome Projects & Additional Vaccine

- Buruli Ulcer
- Chagas Disease
- Afr. Trypanosomiasis
- Leishmaniasis
- Leprosy
- Leptospirosis
- Lymphatic Filariasis
- **Schistosomiasis**
- Trachoma

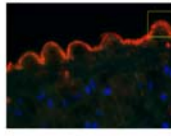


The Schistosome Tetraspanins

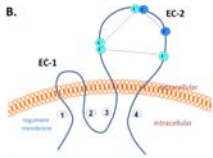
Hotez PJ, Ferris M. The antipoverty vaccines. *Vaccine* 2006

Suppression of *tsp-2* mRNA expression results in impaired tegument turnover *in vitro*

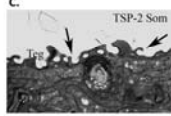
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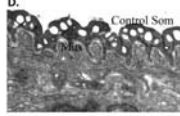


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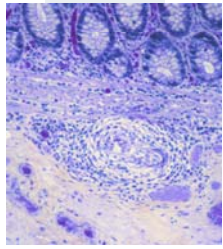


Control Som

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Goals of Anti-schistosome Vaccine

- Worm burden reduction
- Egg reduction
- Reduced end-organ pathology
- Reduction in inflammation
- Reduction in anemia and malnutrition





Cruzmxvax: Therapeutic Vaccine for Chagas disease

Mexico




6 million cases in Mexico: Chiapas, Oaxaca, Puebla, Veracruz, Yucatan



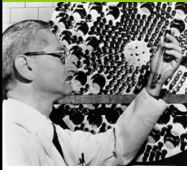

Up to one million cases in U.S.
267,000 cases in Texas

Bivalent vaccine: Tc24 + TSA-1

Joint venture with Birmex



Opportunity for "Vaccine Diplomacy"

"There are no better grounds on which we can meet other nations and demonstrate our own concern for peace and the betterment of mankind than in a common battle against disease" John Gardner

Hotez PJ. *SCIENCE* 2010

Sabin's New Home Sabin Vaccine Institute & Texas Children's Hospital Center for Vaccine Development



Baylor College of Medicine
Texas Medical Center





Feigin Center for Medical Research
Texas Children's Hospital
Baylor College of Medicine



100+ years of translational research & training
in Tropical Medicine



No Equivalent School in U.S.

Vision Statement

- The National School of Tropical Medicine will harness the scientific horsepower of the Texas Medical Center and apply it to solving global public health problems affecting the world's poorest people



Roy and Lillie Cullen Building
Baylor College of Medicine

Thank You

- Donor Support
 - Bill & Melinda Gates Foundation
 - Dutch Ministry of Foreign Affairs
 - Carlos Slim Institute of Health
 - NIAID, NIH
 - Brazilian Ministry of Health
 - Texas Children's Hospital-Baylor Coll. Medicine
 - Blavatnik Charitable Foundation
 - Mort and Chris Hyman