GLOBAL DISEASES:
Voices from the Vanguard

Bundling Grassroots Services to Battle Neglected Diseases in Africa

A Journey to Nigeria

Frank Richards Jr., MD
The Carter Center
March 18, 2008
“Four charismatic scientists invite you to help defeat infectious diseases that thrive in poverty and kill millions of people worldwide.”

Another (the third) ‘charismatic scientist’
The “P’s”

- Pediatrics
- Parasites
- (The) Poor
- Public Health
- Programs
- Pills (Tablets)
- Public Private Partnership
- Politics
- President Carter
  - Peace Prize
Den Norske Nobelskomite har overensstemmende med reglene i det av Alfred Nobel den 27. november 1895 opprettede testamentet tildelt Jimmy Carter Nobels Fredspris for 2002

Oslo, 19. desember 2002

Because of you, millions of people have better lives and hope for their families. We thank you for believing in our work.” — Jimmy Carter
“...I was asked to discuss here in Oslo the greatest challenge that the world faces. Among all the possible choices, I decided that the most serious and universal problem is the growing chasm between the richest and the poorest people on earth....The separation is increasing every year....The results of this disparity are the root causes of most of the world’s unresolved problems”

President Jimmy Carter
2002 Nobel address
• ‘Diseases of Poverty’
• ‘Forgotten Diseases of Forgotten People’
• ‘Neglected Diseases of the Tropics’
An Integrated Community-based MDA Program in Nigeria
Structure of my Talk

- Introduction
- Public Health Concepts
- Three neglected tropical diseases (RB, LF, Schisto)
- Nigeria
- Future challenges
Structure of my Talk

- Introduction
- **Concepts**
  - Control versus Elimination (Eradication) Strategies
  - Vertical versus Horizontal PH systems
- Three tropical diseases (RB, LF, Schisto)
- Nigeria
- Future challenges
Control versus Elimination (Eradication) Strategy

Control

Elimination

TIME
Vertical versus Horizontal PH systems

Focused Controlled Inputs Outputs

Polyvalent ‘Basket’ Decentralized decisions ‘Sustainable’

Donors Love It!
‘Integration of Programs means Integration of Problems’

Dr. Hans Remme, WHO/TDR
Structure of my Talk

- Introduction
- Concepts
  - Control versus Elimination (Eradication) Strategy
  - Vertical versus Horizontal PH systems
- **Three tropical diseases**
  - *Onchocerciasis* River Blindness
  - *Lymphatic Filariasis* (LF)
  - *Schistosomiasis* (‘Schisto’)
- Nigeria
- Future challenges
Neglected Tropical Diseases

WHO is currently focusing on 13 neglected tropical diseases:

- Buruli ulcer
- Chagas disease
- Cholera
- Dengue/dengue haemorrhagic fever
- Dracunculiasis (guinea-worm disease)
- Human African trypanosomiasis
- Leishmaniasis
- Leprosy
- Lymphatic filariasis
- Onchocerciasis
- Schistosomiasis
- Soil-transmitted helminthiasis
- Trachoma

Preventive Chemotherapy
(Mass Drug Administration-MDA)
Pharmaceutical Drug Donation Programs
UGA’s Center for Tropical and Emerging Global Diseases (www.ctegd.uga.edu)

- Leishmaniasis*
- Chagas’ Disease*
- African Trypanosomiasis*
- Schistosomiasis*
- Cryptosporidiosis
- Lymphatic Filariasis*
- Malaria

*NTDs
### DALY perspective (millions)

<table>
<thead>
<tr>
<th>Disease</th>
<th>DALY (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB</td>
<td>34.7</td>
</tr>
<tr>
<td>Malaria</td>
<td>46.5</td>
</tr>
<tr>
<td>‘Treatable’ NTDs</td>
<td>56.6</td>
</tr>
<tr>
<td>Diarrheal disease</td>
<td>62.0</td>
</tr>
<tr>
<td>HIV-AIDS</td>
<td>84.5</td>
</tr>
<tr>
<td>LRI</td>
<td>91.3</td>
</tr>
</tbody>
</table>

Control versus Elimination

- Onchocerciasis: Control
- Lymphatic Filariasis: Elimination
- Schistosomiasis: Control
- Trachoma: Elimination
- Soil Transmitted Helminths: Control
‘Nearness to rivers... Can eat the eyes’

African Proverb
Geographic Distribution of Onchocerciasis

WHO 1999
Microfilaria
Intensity (‘load’) of Infection
Who suffers from ‘oncho?’

- A disease of rural poverty
- 90 million people at risk
- 34 million infected
- 37 countries
- Some 800,000 people are either blind or visually handicapped
- Rarely fatal
Clinical Manifestations

- Blindness
- Visual Impairment
- Skin rashes
- Intense itching
Microfilaria ('Microfilaricide')

Macrofilaria ('Macrofilaricide')
Treatments approved and shipped by the Mectizan\textsuperscript{R} Donation Program 1988-2006

Source: Annual Highlight
Mectizan Donation Program
www.mectizan.org
Treatments approved and shipped by the Mectizan® Donation Program 1988-2006, with UTG

Source: Mectizan Donation Program
www.mectizan.org
Carter Center-Assisted Mectizan Distribution

- Sudan
- Nigeria
- Cameroon
- Ethiopia
- Uganda
- Mexico
- Guatemala
- Colombia
- Ecuador
- Brazil
- Venezuela

Carter Center-Assisted Areas
Carter Center-Assisted Programs: Mectizan Treatments
1996 – 2007*

*Provisional
November 2007
The Carter Center celebrates

Over 100 Million assisted
Ivermectin treatments in 11 Countries in
Africa and the Americas since 1996

Thank you to our partners!
Cost per Treatment in Carter-assisted African RB Programs Averages $0.50 (range $0.10-1.50)
Impact of Eight Years of Mass Ivermectin Treatment in a Cohort of 411 persons in Imo State, Nigeria

Emukah, AJTMH 2004
Global distribution of lymphatic filariasis

World Health Organization
Global Programme for Elimination of Lymphatic Filariasis
Who suffers from ‘LF?’

- A disease of rural and periurban poverty
- Over 1 billion people at risk
- 120 million infected
- 80 countries
- Leading cause of disability
- Rarely fatal
Life Cycle of Lymphatic Filariasis

- Mosquito takes blood meal, infecting person with L3 larvae
- Larvae develop into adult worms in lymphatic vessels
- Blood microfilariae ingested by mosquito
- Adult female worms produce microfilariae which migrate to peripheral blood
War on worms and malnutrition
WORLD DISTRIBUTION OF SCHISTOSOMIASIS

S. mansoni
S. intercalatum
S. haematobium
S. japonicum

Source: Doumenge & Mott, 1984
Who suffers from ‘Schisto?’

- A disease of rural and periurban poverty
- Over 650 million people at risk
- 200 million infected
- 76 countries
- Major and subtle morbidity
- Rarely fatal
Intestinal Schistosomiasis
Control versus Elimination

- Onchocerciasis: Control
- Lymphatic Filariasis: Elimination
- Schistosomiasis: Control
Structure of my Talk

• Introduction
• Concepts
  ▪ Control versus Elimination (Eradication) Strategy
  ▪ Vertical versus Horizontal PH systems
• Three tropical diseases (RB, LF, Schisto)

• **Nigeria**
• Future challenges
Nigeria
Carter Center assisted States in Nigeria

Nigeria Integrated Project
GLOBAL DISEASES: Voices from the Vanguard

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Why ‘Bundling’ (Integration, Coimplementation) in Nigeria?

- Nigeria has the most River Blindness in the World (27 million in need of treatment) and the best Mectizan treatment program in the World
- Most LF (22% of Nigerians infected). 3rd globally (after India/Indonesia)
- For Schisto, greatest praziquantel tablet requirement of any country (60 million/yr)
- A lot of other diseases (Trachoma, Intestinal Worms, Malaria)
Integrated Onchocerciasis, Lymphatic Filariasis and Urinary Schistosomiasis Activities in Nigeria: A Case Study
We integrated three MDA programs at the LGA level by

- Building on the RB platform
- Mapping the distribution of LF and schisto
- Tailoring district level training and logistics based on the results of mapping exercises
- Implementing community based annual health education and mass treatment (with ivermectin, albendazole and/or praziquantel) where appropriate, per WHO guidelines
- Evaluating impact
Platform Programs and Integration Models
Plateau/Nasarawa ONCHO Program Map in 1998
Onchocerciasis Nodule Prevalences in 23 Villages

<table>
<thead>
<tr>
<th>Year</th>
<th>Percent Nodule Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992</td>
<td>51.2%</td>
</tr>
<tr>
<td>1999/2000</td>
<td>2.9%</td>
</tr>
</tbody>
</table>
Distribution of Lymphatic Filariasis (LF) in Plateau / Nasarawa States
Results in Villages Sampled for LF Antigen Testing (Numbers are % positive Antigenemia)

Phases 2000 - 2003
- 2000 Phase 1 Oncho Endemic
- 2001 Phase 2 Oncho Endemic
- 2002 Phase 3 Non-Oncho endemic
- 2003 Phase 4 Non-Oncho endemic

LF Prevalence (Sample)
- WHO Villages: % ICT (2000)
- LF Pilot Villages: % ELISA (1998)
Carter Center-assisted Onchocerciasis and Lymphatic Filariasis Treatments, Plateau & Nasarawa States, Nigeria

LF is now the ‘Platform Program’
LF/Oncho Treatments in Plateau and Nasarawa States, Nigeria, by Year

The graph shows the number of LF/Oncho treatments over the years from 1999 to 2007. The number of treatments has increased significantly over the years, reaching a peak in 2007 with over 3,000,000 treatments.

Yearly treatments:
- 1999: 0
- 2000: 100,000
- 2001: 500,000
- 2002: 2,000,000
- 2003: 3,000,000
- 2004: 3,500,000
- 2005: 3,500,000
- 2006: 3,500,000
- 2007: 3,500,000

The data indicates a steady increase in treatments, reflecting a growing effort to combat LF/Oncho in these states.
Integration of LF with RB was fast and ‘easy’
Top indicator of success for the Nigeria LF Effort as a ‘Demonstration Project’

We will attempt to show that annual treatment with the ivermectin and albendazole combination can demonstrate, on a large scale, the feasibility of eliminating lymphatic filariasis from Africa.
Impact on Onchocerciasis, Schistosomiasis and Lymphatic Filariasis in Plateau and Nasarawa States of Nigeria

Average Lymphatic Filariasis ICT Results in Seven Sentinel Villages

Average Lymphatic Filariasis Mosquito Infection Rate (*W. bancrofti*) in 9 Sentinel Villages
Onchocerciasis and Lymphatic Filariasis Treatments:* Plateau and Nasarawa States; Past and Projected Future through 2014

What happened to our platform??
Schistosomiasis
>1 million PZQ treatments celebrated in 2007
Integration of schisto with LF/RB has been problematic and ‘slow’
Urinary Schistosomiasis

Photo credit Emily Staub
Impact on schistosomiasis haematobium prevalence in school aged children: Hematuria* (blood in urine) prevalence before (1999) and after two annual rounds of praziquantel treatment in two villages in Nigeria (Bars show 95% Confidence Intervals)

*Based on heme positive urine dipstick testing
Intestinal Schistosomiasis
April 2007: The first big donation

DG M Chan and Merck KGaA (E-Merck) Exec Board member Elmar Schnee announce 200 million tablet, 10 year PZQ donation (20 million/year)
WHO Nigeria Pledge

- 1.5 million PZQ tablets/year for Carter Center assisted programs in Nigeria
- Targeted for School aged children
- Tablets are now in Port of Lagos
Integration of mass drug administration programmes in Nigeria: the challenge of schistosomiasis
Frank O Richards Jr, Abel Eigge, Emmanuel S Miri, My Jinadu, & Donald R Hopkins

Costs of extra TX rounds

Cost of PZQ

Cost of Mapping

Bull WHO Aug 2006
Triple Co-Administration of Ivermectin, Albendazole and Praziquantel in Zanzibar: A Safety Study

Khalfan A. Mohammed¹,², Hamad J. Haji³, Albis-Francesco Gabrielli⁴, Likezo Mubila⁵, Gautam Biswas⁴, Lester Chitsulo⁴, Mark H. Bradley⁶, Dirk Engels⁴, Lorenzo Savioli⁴, David H. Molyneux²*

Abstract

Background: Public health interventions based on distribution of anthelminthic drugs against lymphatic filariasis (LF), onchocerciasis, soil-transmitted helminthiasis (STH) and schistosomiasis have been implemented separately to date. A better use of available resources might be facilitated by a more coordinated approach to control such infections, including the possibility of co-administering the three recommended anthelminthic drugs through a single, large-scale intervention.

Methodology/Principal Findings: Ivermectin, albendazole and praziquantel were co-administered to 5,055 children and adults living in areas endemic for LF, STH and schistosomiasis in Zanzibar, United Republic of Tanzania, during a pilot intervention aimed at elucidating and quantifying possible side-effects. Subsequently, these drugs were co-administered to about 700,000 individuals during a countrywide intervention targeting a large part of the total population of Zanzibar. Passive and active surveillance measures carried out during both interventions showed that side-effects attributable to the three drugs given at the same time were mild and self-limiting events.

Conclusions/Significance: Our data suggest that co-administration of ivermectin, albendazole and praziquantel is safe in areas where lymphatic filariasis, soil-transmitted helminthiasis and schistosomiasis are co-endemic and where several rounds of treatment with one or two drugs have been implemented in the past. Passive surveillance measures, however, should be continued and detection, management and reporting of possible side-effects should be considered a key component of any health intervention administering drugs.


Editor: Juerg Utzinger, Swiss Tropical Institute, Switzerland

Received May 31, 2007; Accepted December 21, 2007; Published January 23, 2008
TRIPLE DRUG ADMINISTRATION (TDA)
Treating 3 diseases at once in Nigeria

Treating three diseases (Schisto, LF and river blindness) with PZQ, albendazole and ivermectin administered at the same time. Eigege, Annals Trop Med Parasit 2008
Cost of PZQ

Costs of extra TX rounds

Cost of Mapping

Integration of mass drug administration programmes in Nigeria: the challenge of schistosomiasis

Frank O Richards Jr, Abel Eigege, Emmanuel S Miri, My J inadu, & Donald R Hopkins

Bull WHO Aug 2006

Integration of schistosomiasis into other MDA programmes would be helped by amended guidelines leading to simpler mapping, more liberal use of praziquantel and the ability to administer praziquantel simultaneously with Ivermectin and albendazole.
### WHO PZQ MDA Treatment Guidelines (1993)

<table>
<thead>
<tr>
<th>Prevalence*</th>
<th>Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyper &gt;50%</td>
<td>Entire Population</td>
</tr>
<tr>
<td>Meso 20- 49%</td>
<td>School aged children</td>
</tr>
<tr>
<td>Hypo &lt;20%</td>
<td>Infected children only</td>
</tr>
</tbody>
</table>

*Prevalence in sample of school aged children
NIGERIA CARTER CENTER-ASSISTED SCHISTOSOMIASIS VILLAGE PREVALENCE ASSESSMENT

Assessed: 747
Need PZQ: 358
School Age: 233
Mass Tx: 125

N=22,402
Intestinal Schistosomiasis
Missed Treatment Opportunities for *Schistosomiasis mansoni* in Plateau and Nasarawa States

Julie R. Gutman, Ayodele Fagbemi, Kal Alphonsus, Abel Eigege, Emmanuel S. Miri, Frank O. Richards

1Emory University, Atlanta, GA, United States
2The Carter Center, Jos, Nigeria
3The Carter Center, Atlanta, GA, United States

In press AJTMH (2008)
NIGERIA CARTER CENTER-ASSISTED URINARY SCHISTO VILLAGE PREVALENCE ASSESSMENT

N=22,402

Assessed: 747
Need PZQ: 358
School Age: 233
Mass Tx: 125

‘Mesoendemic’ ‘Hyperendemic’
Enrolled Subjects

924 Children
25% have intestinal Schisto
Missed opportunities

- Of the 50% of communities not needing treatment for Urinary Schisto, over half need treatment for Intestinal Schisto
- Overall, 80% of villages need treatment for some form of Schisto (urinary and/or intest)

Why, then, are we mapping????
Integration of mass drug administration programmes in Nigeria: the challenge of schistosomiasis

Frank O Richards Jr, Abel Eigege, Emmanuel S Miri, My Jinadu, & Donald R Hopkins

Cost of PZQ
Costs of extra TX rounds
Cost of Mapping

Bull WHO Aug 2006
New Ideas with New Resources
Simplify, Simplify, Simplify, Simplify

Ralph Waldo Emerson
What should we do?

- Use donation to treat all the school aged population (approximately 1 million) in two state area
- Use Triple Drug Administration (TDA)
- Get it done in a single round
- Less focus on mapping results
- Forgo community-wide PZQ treatment for now and evaluate impact in higher prevalence areas
Community based treatment
SCHISTO TREATMENTS, 1999 – SEPTEMBER 2007 IN PLATEAU, NASARAWA AND DELTA STATES
Conclusions

• Integrating LF and RB programs at district level was easy
• LF took over from RB as the ‘platform program’ due to size
• Control vs Elimination strategies. Stopping LF MDA after 5-6 years (2008)? Do we lose our platform program?
Conclusions

• Schistosomiasis integration was difficult, not only because PZQ is not donated, but:
  ▪ Slow and costly LGA level mapping and village stratification
  ▪ Delivery of praziquantel separately from ivermectin and albendazole
• Going for 1,000,000 PZQ treatments in 2008
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MOBILE DISTRIBUTION
COMMUNITY DIRECTED TREATMENT (ComDT, CDTI)
Community-based vs. Facility-based
“That’s the difference between government and individuals. Governments don’t care, individuals do.”

Mark Twain
In rural Ugandan communities the traditional kinship/clan system is vital to the success and sustainment of the African Programme for Onchocerciasis Control

BY N. M. KATABARWA*
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Ministry of Health, P.O. Box 1661, Kampala, Uganda

Received 5 April 2000, Revised 5 May 2000, Accepted 8 May 2000
Controlling onchocerciasis by community-directed, ivermectin-treatment programmes in Uganda: why do some communities succeed and others fail?

By N. M. KATABARWA*, D. MUTABAZI
Global 2000 River Blindness Program, Carter Center, P.O. Box 12027, Kampala, Uganda

AND F. O. RICHARDS Jr
Global 2000 River Blindness Program, Carter Center, One Copenhill, Atlanta, GA 30307, U.S.A.

Received 8 March 2000, Accepted 14 March 2000
Key Hypothesis of new BMGF Grants on Integration

Integration of community based disease control programs will increase effectiveness and reduce cost, easing the strain on public health systems in African countries. Integration will therefore improve the health of as many people as possible at a cost that can be sustained for as long as necessary.
A Nigerian woman and her baby show their insecticide-treated bed net.
The Carter Center Turns 25

Human rights, conflict resolution, election monitoring, and locally even the Atlanta Project. During his presidency from 1977 to 1981, then with the establishment of the Carter Center and Jimmy Carter Library and Museum — housed from 1982 to 1986 at Emory before the latter year's opening on what is now Freedom Parkway — Jimmy Carter has added much to the vernacular, and more to the 70 countries the center has targeted for its humanitarian efforts.

On Oct. 1, the non-profit Carter Center turns 23 and Carter himself turns 83, an exhibit and reflective book, "Beyond the Presidency: 25 Years of The Carter Center," recognizes the anniversary of achievements.

"I think we have demonstrated that a very small, nongovernmental organization can be highly effective," says the 2002 Nobel Peace Prize recipient. "I believe we also have shown that although it is not easy we can cross the chasm between the rich and poor on earth. Potential donors have come to see that people in Africa and other distant regions deserve our help."

With a permanent staff of only 160, philanthropy as to the Carter Center goes both ways; how it is helped and how it then can help, only 76 percent of the center's funding comes from corporate and individual giving, and another 14.4 percent from foundations like The Turner Foundation and the Gates Foundation, which this year pledged $5 million and matching dollars up to $20 million for the Guine worm eradication program, another term few of us would know if not for the Carter Center, which uses 81.2 percent of all donations for its worldwide health programs.

Here are some examples of what the Carter Center has achieved the past 23 years — Greg Palast
GLOBAL DISEASES: Voices from the Vanguard

Bundling Grassroots Services to Battle Neglected Diseases in Africa

A Journey to Nigeria
THANKS

- Governments of Plateau/Nasarawa States
- Federal Government of Nigeria (FMOH)
- University of Jos
- CDC
- Emory University
- The Gates Foundation
- Merck & Mectizan Donation Programme
- GlaxoSmithKline (GSK)
- Izumi Foundation
- Lions International
- APOC/WHO/World Bank
Reflections for Students
“Never Go Back the Way You Came”
From: A Profile of Dr. Ben Kean,”
CUMC Alumni News, 1985

‘When a student asks me today about going into tropical medicine, I tell him or her this: Decide what field you want to go into; master the specialty; then, when you go into the tropics, you can bring that special knowledge with you….

The basis for eventual success in tropical medicine is temporary restraint of enthusiasm...’
Don’t be afraid to be a ‘Globalist’

• Be an Activist
• Be a Practical Scientist
• Seek Simple Solutions
• Be Confident
• Be Focused
Thanks!