World Bank Presentation

The Prevention and Control of Human Hookworm Infection

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The 2000 Millennium Declaration

The Millennium Development Goals (MDGs)

1. Eradicate extreme poverty and hunger.
2. Achieve universal primary education.
3. Promote gender equality and empower women.
4. Reduce child mortality.
5. Improve maternal health.
7. Ensure environmental sustainability.
8. Develop a global partnership for development.
Human Hookworm Infection

• Hookworm occurs in 20-25% of the world’s poorest people living on less than $2 per day
• 576-740 million cases worldwide
  – 198 million SSA
  – 149 million EAP
  – 71 million India
  – 59 million SAS
  – 50 million LAC
  – 39 million China*
The Global Distribution of Human Hookworm Infection

Wherever Rural Poverty and Adequate Climate Overlap
Chronic hookworm infection in childhood reduces future wage-earning by 40%
Hoyt Bleakeley UCSD
<table>
<thead>
<tr>
<th>Disease</th>
<th>DALYS</th>
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<tbody>
<tr>
<td>HIV/AIDS</td>
<td>46.5 million</td>
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<tr>
<td>Malaria</td>
<td>46.5 million</td>
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<tr>
<td>Tuberculosis</td>
<td>34.7 million</td>
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<tr>
<td>Hookworm</td>
<td>22.1 million</td>
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<tr>
<td>Measles</td>
<td>21.4 million</td>
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</tbody>
</table>
The Human Hookworms

Necator americanus
Ancylostoma duodenale
Ancylostoma ceylanicum
Ancylostoma caninum
Ancylostoma brazilianense
Human Hookworm Infection

Leading cause of malnutrition and anemia
Adult hookworms injure by causing intestinal blood loss

25 *Necator americanus* Hookworms = 1 ml blood daily = 0.55 mg Fe
37% of Iron Deficiency Anemia in Brazil
22-73% of Severe Anemia Africa
Children and Pregnant Women (44 million)

Hookworm Anemia

Hemoglobin concentration in children (Zanzibar) and prevalence of anaemia in women (Vietnam) by intensity of hookworm infection.
Hookworm Disease

- Anasarca
- Pallor and Facial Edema
At-risk Populations for Hookworm Disease

• Women and Children: Low Iron Stores
• Children:
  – Physical growth stunting
  – Cognitive deficits and intellectual retardation
• Women of Child-bearing age
  – Puberty
  – Menstruation
  – Pregnancy (Adverse fetal outcomes)
Malaria and Hookworm

Geographic Overlap

“The Perfect Storm” of Anemia

• Opportunities for joint control
• IPT and Deworming in Pregnancy/Childhood

Will hookworm/schisto thwart new malaria vaccines?
WHA Resolution 54.19

• Endorses as the best means of reducing mortality and morbidity and improving health and development in infected communities, the regular treatment of high-risk groups, particularly school-aged children, and ensured access to single-dose drugs against schistosomiasis and STH infections in primary health care services, complemented by the simultaneous implementation of plans for basic sanitation and adequate safe water supplies

• Goal of attaining a minimum target of regular administration of chemotherapy to at least 75% and up to 100% of all school-age children at risk of morbidity by 2010
Benzimidazole derivative C\textsubscript{12}H\textsubscript{15}N\textsubscript{3}O\textsubscript{2}S, synthetic.

Albendazole 400 mg single dose (sometimes requires repeating)
Mebendazole 500 mg single dose (does not work as well)
Mebendazole 100 mg b.i.d. for three days

Benzimidazole Anthelminthics
MDA Coverage 2006

- **STH/Schisto**
  - At risk population treated: 10%
  - Untreated: 90%

- **Lymphatic Filariasis**
  - At risk population treated: 38%
  - Untreated: 63%

- **Onchocerciasis**
  - At risk population treated: 44%
  - Untreated: 56%
Integrating Neglected Tropical Disease Control

Countries with 5 or more NTDs
- 5 NTDs
- 6 NTDs
- 7 NTDs

Range of treatment costs per person per year

- HIV/AIDS
- TB
- Malaria
- 'Rapid Impact' Package

Cost per patient treatment per year (US dollars)
Drug Failure: Mebendazole for Hookworm

Figure 1. Cure rates after treatment with single dose mebendazole 500 mg
Sustainability of Deworming
BZAs Do Not Prevent Hookworm Infection

1. Low Mebendazole Cure Rates = 9-21%

2. Hookworm infected patients reacquire hookworm to pre-treatment levels within 4-12 months following anthelmintic chemoRx

3. Efficacy of BZAs diminishes with increasing use
Necator americanus Life Cycle

1. Eggs pass out in feces
2. Eggs hatch and develop in soil
3. Larvae penetrate skin, enter bloodstream, reach heart
4. Larvae enter lung capillaries
5. Larvae enter alveolar spaces
6. Larvae migrate up trachea, are swallowed
7. Adults mature in small intestine
Papers on Sanitation and Hookworm

Sanitation

- Change in hookworm prevalence before & after Sanitation interventions in Iran:
- Reduction in prevalence from 71% to 68% (4.2%)
- Reduction in mean intensity from 1549 epgs to 1143 (26%)
- Asaolu and Ofoezie, 2003
Sanitation and Water Supply

- 20 programs evaluated sanitation in combination with water supply
- 13 – longitudinal trial approach
  - None specifically looked at hookworm
  - Reduction ascariasis prevalence 18% to 31%
  - Reduction trichuriasis prevalence 16% to 58%
  - One study the ascariasis prev. increased 13.5%
  - Intensity of infections same or increased
- 7- cohort design (only one for ascariasis)
- Asaolu & Ofoezie, 2003
Sanitation and Chemotherapy

• 9 programs total (Asaolu & Ofoezie, 2003)
• 2 hookworm programs
  – Dezful, Iran
    • 69% reduction in prevalence (62% to 19%)
    • 88% reduction in intensity
  – Nigeria
    • 86% reduction in prevalence (31% to 4%)
Conclusions

• Sanitation reduces the prevalence of soil-transmitted helminth infections
• Reduction rates are not rapid and no impact on intensity
• Does sanitation increase heterogeneity of exposure?
• Rates are comparable to health education
• Reduction rates of both are improved considerably when combined with chemotherapy
• Sanitation may help to sustain control over long periods
• Choice of helminth infection adopted for assessment may not matter
• Asaoulu and Ofoezie, 2003
Wastewater farmers in Pakistan
Ensink et al, 2005

• Main health risk to wastewater irrigation is Hookworm/Ascaris
  – Risks reduced by treating wastewater prior to use
  – Prohibitively expensive
  – Two-thirds of wastewater in the world receives no treatment

• Study in Faisalabad
  – Wastewater treatment plant located next to wastewater use sights – farmers prefer the use of raw sewage because of the higher nutrient content and lower salinity compared with treatment effluent
  – Wastewater farmers vs. textile workers
  – Hookworm was the main risk associated with wastewater irrigation
  – Absence of a toilet OR = 1.9 (hookworm)
  – Poor house construction OR = 2.3
  – Adult wastewater farmers vs. textile laborers OR = 4.0
  – Children of wastewater farmers OR = 9.3
WHO Wastewater Use Guidelines

- Intestinal nematode water quality standard (<1 egg/L) was included in WHO guidelines in 1989
- Controversy whether to decrease or increase limit
- In Pakistan wastewater 558 hookworm eggs/L
- Lower than expected hookworm rate thought to be wide availability of cheap anthelminthic medication vs. rapid die off (urban environment?)
Salvador, Brazil
Moraes et al, 2004

- 3 neighborhoods
  - Group 1 – control (no community sanitation)
  - Group 2 – rainwater drainage
  - Group 3 – rainwater drainage and a separate sewerage system
- Urban area
- Trichuriasis
  - 88% Group 1; 72% Group 2; 68% Group 3
- Ascariasis
  - 66% Group 1; 47% Group 2; 38% Group 3
- Hookworm
  - 25% Group 1; 9% group 2; 9% Group 3
  - 191 epgs Group 1; 158 epgs Group 2; 302 epgs Group 3
- Significant difference in prevalence all three
- No difference in intensity of ascaris and hookworm
- No self-medication
- Does sanitation increase the heterogeneity of exposure?
NEW TOOLS FOR DISEASE CONTROL
THE ANTIPOVERTY VACCINES

Product Development Partnership

Sabin Vaccine Institute
George Washington University
FIOCRUZ
Instituto Butantan
The Na-ASP-2 Hookworm Vaccine

21.3 kDa Recombinant Protein
Expressed in Yeast (*Pichia pastoris*)
Isolated by IEC
Adsorbed to Alhydrogel®
i.m. injectable

X-ray crystal structure of Na-ASP-2

Goud et al. Vaccine 2005; 23: 4754-64
INSTITUTO BUTANTAN

Created in 1901 to produce Antiplague and Antivenom Sera

1985: National Program for Self-Sufficiency in Immunobiologics

2005: One of Two Major Vaccine Producers in Brazil - 483 million doses of vaccines: DPT, BCG, Pneumococcal, H5N1, Hepatitis B, Rabies

The Innovative Developing Countries:
Brazil, China, Cuba, India, Indonesia, Iran, Senegal
The Antipoverty Vaccines

• Helminth Infections
  – Hookworm \((Na-ASP-2 + Na-APR-1)\)
  – Onchocerciasis \((Ov-ASP-1)\)
  – Schistosomiasis \((Sh28GST, Sm-TMP-2)\)
  – Cysticercosis (Transmission Blocking)
  – Echinococcosis (Transmission Blocking)
  – Fascioliasis \((Fh-Cys Protease)\)

• Protozoan Infections
  – Chagas Diseases (Sialidase/Trans-Sialidase)
  – Leishmaniasis (Leish-111f-MPL-SE)

• Bacterial Infections
  – Buruli Ulcer & Leprosy \((HSP65, Ag85, Mycolactone)\)
  – Chlamydia Infections \((MOMP, POMP)\)
  – Leptospirosis \((Ligs, OMPs)\)
  – Trepanematoses \((OMPs)\)

Hotez PJ, Ferris M. Vaccine 2006
Future Trends in
Neglected Tropical Disease Control

• Develop new control tools
• Fold them into existing structures, i.e., rapid impact package
• Drugs + Vaccines in Integrated Framework
• Human Vaccine-Linked Chemotherapy
• School-based Health and Child-Health Day Systems