NEGLECTED TROPICAL DISEASES AND ANEMIA - WHAT DO WE KNOW

18 October, 2016- Accelerated Reduction Efforts on Anaemia COP Webinar

Yaobi Zhang
1. What are the neglected tropical diseases (NTDs)?

2. Links between NTDs (focusing on soil-transmitted helminthiases and schistosomiasis) and anemia

3. Progress and gaps

4. Challenges and what NGDOs can do to help
What are the neglected tropical diseases (NTDs)?
• Viral infections
  – Dengue fever
  – Rabies

• Bacterial infections
  – Blinding trachoma
  – Buruli ulcer
  – Endemic treponematoses (Yaws)
  – Leprosy

• Protozoan infections
  – Chagas disease
  – Human African trypanosomiasis (HAT, sleeping sickness)
  – Leishmaniasis

• Helminth infections
  – Cysticercosis/taeniasis
  – Dracunculiasis (guinea-worm disease)
  – Echinococcosis/hydatidosis
  – Foodborne trematode infections (clonorchiasis, paragonimiasis, fasioliasis, etc)
  – Lymphatic filariasis
  – Onchocerciasis (river blindness)
  – Schistosomiasis
  – Soil-transmitted helminthiases (ascariasis, hookworm infection and trichuriasis)

WHO, NTD Roadmap, 2012

Preventive chemotherapy (PC)-NTDs

**NEGLECTED TROPICAL DISEASES**
are a diverse group of diseases with distinct characteristics found mainly among the poorest populations of the world.

The 17 diseases targeted by WHO share a common stranglehold on those populations left furthest behind by development: they perpetuate poverty. Most of those who suffer from more than one of these diseases at any given time are also mired in poverty, perpetuating a doubly intolerable and unacceptable situation destined to live in permanent disability.
5 Preventive chemotherapy (PC)-NTDs

- Blinding trachoma
- Onchocerciasis
- Lymphatic filariasis (LF)
- Schistosomiasis (SCH)
- Soil transmitted helminthiases (STH)

- Blindness
- Disfigurement
- Undernutrition / anemia
Disease Burden

Soil-transmitted helminthes

• Over 1 billion people infected or at the risk of being infected with soil-transmitted helminthes worldwide

• 266 million pre school age children require preventive chemotherapy

• 609 million school age children require preventive chemotherapy

• 37.7 million pregnant women in Africa

Schistosomiasis

• >770 million people estimated to be infected or at risk of infection globally

• 261 million people, including 121 million school age children, require preventive chemotherapy

• 20,000 to 200,000 deaths per year

Source: WHO 2015; others
Schistosomes (SCH)

- Caused by infection with parasite **Schistosoma**:  
  - Urogenital:  
    - *Schistosoma haematobium*  
  - Intestinal:  
    - *S. mansoni*  
    - *S. japonicum*

Map source: CDC
Soil-transmitted helminthes

Ascaris

Trichuris

Hookworm

Map source: CDC
Schistosomiasis and STH worm burden age profiles

Source: Weatherhead & Hotez 2015
Morbidity due to STH and schistosomiasis

Soil-transmitted helminthiases

• Under nutrition & anemia
  – Impaired growth
  – Impaired cognition
  – Weakness, fatigue
  – Poor school performance
  – Reduced productivity and earning ability

• Diarrhea and dysentery

Schistosomiasis

• Under nutrition & anemia
  – Impaired growth
  – Impaired cognition
    • Heavy infection - poor short-term memory and slower reaction times in schoolchildren
  – Weakness, fatigue

• Increased susceptibility to other infections (e.g. HIV)

• Chronic health problems: inflammation and fibrosis of the liver, spleen, lungs, bladder wall, colon

• Hematemesis (portal hypertension)

• Bladder cancer

Source: Various
Links of STH and SCH with anemia
Overlapping geographical distribution

Global estimates of the prevalence of anemia in infants and children aged 6–59 months, 2011

Source: WHO
Overlapping geographical distribution

Distribution of schistosomiasis, 2011
Overlapping geographical distribution

Distribution of STH and proportion of children (1-14 years) in each endemic country requiring PC, 2011

Source: WHO
Anemia in moderate or heavy hookworm infection
- Even light infection can significantly decrease Hb level in pregnant women

Pregnant women with moderate or heavy *Trichuris* infection in their 2\(^{nd}\) trimester had significantly lower Hb levels

Anemia and schistosome infection is well established

Sources: Stoltzfus et al 1997; Hotez 2004; Brooker et al 2008; Pullan et al 2013; Gyorkos et al 2011; King 2008; Colley et al 2014; Charmi et al 2015; and others
Schisto, hookworm and anemia in Ugandan communities

- Heavy infection, 1.65 times more likely to have anemia
- Moderate infection, 56% more likely to have anemia
- Heavy infection, anemia risk increased by 2.86 fold

Source: Charmi et al 2015
How do SCH/STH infections cause anemia?

• **Iron deficiency anemia**
  – Blood loss:
    • Blood in urine – 2.6 -126 ml/day – urogenital schistosomiasis
    • Blood in stools – 7.5 - 25.9 ml/day – intestinal schistosomiasis
    • 0.14 - 0.26 ml/worm/day for *A. duodenale*,
    • 0.02 - 0.07 ml/worm/day for *N. americanus*
    • ?? *Trichuris trichiura*

• **Anemia attributable to schistosomiasis:**
  - 3.7% to *S. haematobium*
  - 3.6% to *S. mansoni* in whole population (4.5% in school-age children and pregnant women vs 2.4% in adults)
  - 32% to *S. mansoni* in population with heavy infection

• **Anemia attributable to hookworm infection:**
  - 4.2-18% in preschool children
  - 5%-25% in school-aged individuals
  - 28% in pregnant women
  - 3% in whole population (4.6% in adults vs 1.8% in school age children and pregnant women)
  - 23.7% in population with heavy infection (more in adults)

• **Anemia attributable to trichuriasis:**
  - ?? *Trichuris trichiura*

Sources: Soares Magalhães and Clements, 2011; Stoltzfus et al 1997; Pullan et al 2013; Charmi et al 2015
After deworming, treating anemic schoolchildren in Tanzania for 3 months
- with vitamin A increased Hb by 13.5 g/L
- with iron + vitamin A increased Hb by 18.5 g/L
- With placebo (deworming alone) increased Hb level by 3.5 g/L

Weekly iron-folic acid supplementation and regular de-worming increased and stabilized Hb level in women of childbearing age in Vietnam

Single or repeated treatment of children with albendazole and praziquantel significantly improved Hb level from 123 g/L and 122 g/L to 136.8 g/L and 136 g/L in 24 months

Sources: Mwanri et al 2000; Casey et al 2013; Kinung’hi et al 2015
Controversy

Systematic reviews of Cochrane & Campbell Collaboration on mass deworming!

Key negative findings:
- Little to no improvement in weight, height or school attendance
- Little to no difference in stunting, short-term cognition or mortality
- No evidence on spillover benefit

Some facts:
- Worm infection is not a good thing and deworming is beneficial
- Absolute effects on reducing worm prevalence...
- Small effects on Hb level (of less than 3 g/L) unless mass deworming was combined with iron or praziquantel.

- Removing worms is not end of the game, but the beginning of recovery
- It takes much longer for recovery after removing worms without addressing nutritional deficits
- Drugs are donated and can be added to other intervention platforms, e.g. school health program, child health days, etc.

Sources: Taylor-Robinson et al 2015; Welch et al 2016
“Mass deworming alone is insufficient to improve growth, cognition, school performance or school attendance for children living in endemic areas. These findings suggest that in addition to a reconsideration of mass deworming programs in their current form, additional policy options need to be explored to improve child health and nutrition in worm-endemic areas. These include the needs for investing in interventions to address basic determinants of worm infestations such as poverty, living conditions, sanitation and inequities. Decisions on public health approaches in such settings need to be taken on the basis of human rights, ethics and evidence-based, sustainable cost-effective approaches. For schistosomiasis, policy implications are that mass deworming may be effective at improving weight.”

- Welch et al 2016, Campbell Collaboration
Progress and gaps
Control/elimination strategies

Schistosomiasis (elimination):
- Repeated mass drug administration with praziquantel
- Behavioral change communication
- Hygiene & sanitation
- Clean water supply
- Snail management

Soil-transmitted helminthiases (control):
- Repeated mass drug administration with albendazole or mebendazole
- Behavioral change communication
- Hygiene & sanitation
- Clean water supply

Effective but does not prevent reinfection
Global status of preventive chemotherapy in 2014 – soil-transmitted helminthiases

<table>
<thead>
<tr>
<th>Preschool-aged children (1–4 years)</th>
<th>AFR</th>
<th>AMR</th>
<th>EMR</th>
<th>EUR</th>
<th>SEAR</th>
<th>WPR</th>
<th>GLOBAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of countries requiring PC¹</td>
<td>42</td>
<td>25</td>
<td>7</td>
<td>5</td>
<td>8</td>
<td>15</td>
<td>102</td>
</tr>
<tr>
<td>Number of people requiring PC</td>
<td>102M</td>
<td>13.3M</td>
<td>22.6M</td>
<td>844K</td>
<td>105.9M</td>
<td>24.9M</td>
<td>269.5M</td>
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<tr>
<td>Number of countries reporting²</td>
<td>29</td>
<td>10</td>
<td>4</td>
<td>0</td>
<td>8</td>
<td>15</td>
<td>66</td>
</tr>
<tr>
<td>Number of people treated</td>
<td>90.7M</td>
<td>8.1M</td>
<td>14.2M</td>
<td>0</td>
<td>43M</td>
<td>13.1M</td>
<td>169.1M</td>
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<tr>
<td>Coverage (%)³</td>
<td>63.1</td>
<td>38.7</td>
<td>56.2</td>
<td>0</td>
<td>40.6</td>
<td>52.5</td>
<td>51.3</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>School-aged children (5–14 years)</th>
<th>AFR</th>
<th>AMR</th>
<th>EMR</th>
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<td>102</td>
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<tr>
<td>Number of people requiring PC</td>
<td>191.5M</td>
<td>33.7M</td>
<td>51.8M</td>
<td>1.5M</td>
<td>248.5M</td>
<td>50.4M</td>
<td>577.5M</td>
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<tr>
<td>Number of countries reporting²</td>
<td>23</td>
<td>12</td>
<td>2</td>
<td>3</td>
<td>6</td>
<td>17</td>
<td>63</td>
</tr>
<tr>
<td>Number of people treated</td>
<td>88.9M</td>
<td>27.1M</td>
<td>5.2M</td>
<td>2.3M</td>
<td>129.2M</td>
<td>19.4M</td>
<td>272.2M</td>
</tr>
<tr>
<td>Coverage (%)³</td>
<td>44.6</td>
<td>57.0</td>
<td>10.1</td>
<td>36.2</td>
<td>52.0</td>
<td>38.4</td>
<td>44.8</td>
</tr>
</tbody>
</table>

¹ Number of endemic countries moved to post-treatment surveillance stage is not included in total.
² Number of countries reporting data on PC implementation. Countries submitting blank reports are not included in total.
³ Coverage is calculated as number of people in need of PC and treated out of population requiring PC.

Source: WHO/NTD 2016

AFR – African Region; AMR – Region of the Americas; EMR – Eastern Mediterranean Region; EUR – European Region; SEAR – South-East Asia Region; WPR – Western Pacific Region

Graph showing coverage percentage trends from 2008 to 2014 for Pre-SAC and SAC periods.
Global status of preventive chemotherapy in 2014 – schistosomiasis

<table>
<thead>
<tr>
<th>PC implementation</th>
<th>AFR SAC/Adults</th>
<th>AMR SAC</th>
<th>EMR SAC/Adults</th>
<th>EUR</th>
<th>SEAR SAC/Adults</th>
<th>WPR SAC/Adults</th>
<th>GLOBAL SAC/Adults</th>
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</thead>
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<td>Number of countries requiring PC¹</td>
<td>41</td>
<td>2</td>
<td>4</td>
<td>-</td>
<td>1</td>
<td>4</td>
<td>52</td>
</tr>
<tr>
<td>Number of people requiring PC</td>
<td>111.4M/125.2M</td>
<td>1.6M</td>
<td>8.1M/10.3M</td>
<td>-</td>
<td>28K/0</td>
<td>2.1M/67K</td>
<td>123.3M/135.5M</td>
</tr>
<tr>
<td>Number of countries reporting²</td>
<td>23/10</td>
<td>0</td>
<td>3</td>
<td>-</td>
<td>1</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>Number of people treated</td>
<td>43.7M/8.7M</td>
<td>ND</td>
<td>5.2M/2.7M</td>
<td>-</td>
<td>31/161</td>
<td>327K/1.1M</td>
<td>49.2M/12.4M</td>
</tr>
<tr>
<td>Coverage (%)³</td>
<td>20.1</td>
<td>0</td>
<td>30.9</td>
<td>-</td>
<td>&lt;1</td>
<td>16.9</td>
<td>20.7</td>
</tr>
</tbody>
</table>

1 Number of endemic countries moved to post-treatment surveillance stage is not included in total.
2 Number of countries reporting data on PC implementation. Countries submitting blank reports are not included in total.
3 Coverage is calculated as number of people in need of PC and treated out of population requiring PC.

Regional coverage is calculated starting from 2010 when new country estimates by age group were published.

AFR – African Region; AMR – Region of the Americas; EMR – Eastern Mediterranean Region; EUR – European Region; SEAR – South-East Asia Region; WPR – Western Pacific Region

Source: WHO/NTD 2016
Challenges and what we can do to help
Challenges

- **Commitment of the endemic governments**
  - Political
  - Financial
- **Lack of guidelines for schisto elimination**
- **STH elimination – lack of clear program endpoint and guidelines**
- **Drug donations**
- **Lymphatic filariasis mass treatment scaling down**
- **Donor priority shift**
- **Country capacity**
  - Human resources (national, regional, local, CDDs etc)
  - Coordination of activities by partners and by sectors (e.g. education, rural development, WASH etc)
  - Weak health systems
What we (NGDOs) can do to help

• Advocacy
• Technical support and training
• Financial support
• Coordination and partnership among selves
• Health system strengthening – institutionalizing deworming

• Integrate deworming with nutrition programs at all levels, e.g.
  – Essential Nutrition Action (ENA) framework
  – School health/school feeding programs
  – Micronutrient supplementation programs
  – Child health days/weeks
  – Maternal health
  – …
WHO documents and resources

- WHA resolutions: WHA54.19 (SCH/STH), WHA65.21 (SCH), WHA66.12 (NTDs)
- WHO NTD Roadmap: Accelerating work to overcome the global impact of neglected tropical diseases, 2012
- WHO Preventive chemotherapy guidelines 2006
- WHO Helminth Control in SAC 2012

- WHO PCT databank
- NTDmap.org [www.ntdmap.org](http://www.ntdmap.org)
- Thiswormyworld.org [www.thiswormyworld.org](http://www.thiswormyworld.org)
- InfoNTD.org [www.infontd.org](http://www.infontd.org)
- WHO/AFRO NTD Mapping Project (to be made available)
Acknowledgements
Questions/comments/contributions?
THANK YOU/JE VOUS REMERCIE.

“Although the world is full of suffering, it is also full of overcoming it.”
-Helen Keller