Still a "Wormy World": The burden of helminthiasis in lesser developed countries

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“This Wormy World”

- Dr. Norman Stoll’s Presidential address to ASTMH 1947 @ Rockefeller

- 342 helminths associated with humans; 25 of greatest public health importance

- “However, each parasitologist is wont to live in his thinking in One World with the species which particularly interests *him*”
Overview

- Geohelminths and Schistosomiasis
- Still a wormy world
  - Quantification
  - Consequences
- Polyparasitism
- Interventions
- Hurdles
Adult *Trichuris trichiuria*
Ascaris lumbricoides

1. Eggs are ingested
2. Larvae hatch in small intestine, enter bloodstream, go to liver
3. Eggs pass out in feces embryonate in soil
4. Larvae migrate to heart
5. Larvae reach lung capillaries
6. Larvae enter alveolar spaces
7. Larvae migrate up trachea, are swallowed
8. Adults mature in small intestine
9. Obstruction

PATHOLOGY
“Jar-O-Worms”
Collected from one rural village in Bangladesh in a single day!
Child with Ascaris lumbricoides
Necator americanus

- Filariform larvae "quest" on blades of grass
- Larvae hatch and develop in soil
- Eggs pass out in feces
- Larvae enter bloodstream, reach heart
- Larvae enter lung capillaries
- Larvae enter alveolar spaces
- Larvae migrate up trachea, are swallowed
- Adults mature in small intestine

PATHOLOGY

Normal Anemia
Adult Ancylostoma duodenale
Hookworm in intestine

- Powerful anticoagulants released
- Increased blood loss in stool
Schistosomiasis life cycle

1. Infective Stage
2. Eggs hatch releasing miracidia
3. Miracidia penetrate snail tissue
4. Sporocysts in snail (successive generations)
5. Cercariae released by snail into water and free-swimming
6. Penetrate skin
7. Cercariae lose tails during penetration and become schistosomulae
8. Circulation
9. Migrate to portal blood in liver and mature into adults
10. Paired adult worms migrate to: mesenteric venules of bowel/rectum (laying eggs that circulate to the liver and shed in stools) and venous plexus of bladder

S. mansoni
S. japonicum
S. haematobium
Advanced hepatic schistosomiasis

- ascites
- splenomegaly
- collateral circulation
Helminthiasis GBD

- Ascaris - 1.2 billion infections globally, half in China
- Trichuriasis and hookworm: 700–800 million infections each
- Schistosomiasis: 200 million
- Together approach 2 billion infections
Trends

(a) *Ascaris lumbricoides*

(b) *Trichuris trichiura*

(c) Hookworm

**Key**
- Infections in LAC
- Infections in SSA
- Infections in Asia 1
- Infections in Asia 2
- Prevalence in LAC
- Prevalence in SSA
- Prevalence in Asia 1
- Prevalence in Asia 2

*TRENDs in Parasitology*
Quantifying burden: DALY

- Years Life Lost (YLL)
  - Doesn’t capture time lived in poor health, or disability
- Disability adjusted life year (WHO, Murray et al. Global Burden of Disease Series)
  - Considers length of “disability”, age at which occurs, and severity of morbidity
  - Includes equivalent years of ‘healthy’ life lost by virtue of being in states of poor health
  - Morbidity and mortality combined in one metric
Associated morbidities

- Malnutrition
- Anemia
- Decreased work capacity
- Poor pregnancy outcomes
- Cognition/school performance
Mechanisms mediating helminth infections and under-nutrition

TNF-alpha/ IL-1/ IL-6

Gastrointestinal symptoms → Cachexia/anorexia → Decreased intake and altered metabolism

Pain, nausea, vomiting, satiety

Mucosal inflammation or worm bulk → Malabsorption → Decreased intake

Fecal nutrient loss
Longitudinal study in Leyte, The Philippines

- **Timepoint 1**
  - Serum, nutritional assessment, eligibility determination, ultrasound, treat for S. japonicum
  - 6 weeks

- **Timepoint 2**
  - Stool screening
  - Timepoint 3
  - Serum cytokines, HGB, nutritional assessment
  - HGB

- **Timepoints 4-8** (18 months total)
  - as per Timepoint 3
  - 4-8 months

- **Timepoint 3**
  - Serum cytokines, HGB, nutritional assessment
  - HGB
Improvement in Nutritional Status after treatment with praziquantel
Improvement in long term growth 18 months after treatment for Schistosomiasis

Multivariate regression analysis, adjusted for sex, age and baseline height and weight, respectively. Least square means in growth from baseline are presented. Error bars represent 95% confidence intervals. Different letter represent significant differences between groups (P<0.05).
Significance of Protein Energy Malnutrition

- Potentiating effects of under-nutrition on mortality due to infectious diseases
  - PEM places children under age five at increased risk for mortality.
  - Approximately 56% of child deaths are attributable to malnutrition’s potentiating effects
  - Most attributable to mild-to-moderate, as opposed to severe malnutrition
- Associated with poor cognitive performance and school performance
- Stunting associated with decreased adult work capacity and reproductive risks
Anemia and helminths

Figure 1. Adjusted mean hemoglobin (Hgb) concentrations by intensity of helminth infection with 95% confidence intervals with least squared means analysis adjusted for the covariates specified. A, Hgb by intensity of Schistosoma japonicum infection adjusted for socioeconomic status (SES), moderate and heavy Trichuris trichuria infections, and moderate and heavy hookworm infections. B, Hgb by intensity of hookworm infection adjusted for SES, heavy S. japonicum infection, and moderate and heavy T. trichuria infections. C, Hgb by intensity of T. trichuria infection adjusted for SES, heavy S. japonicum infection, and moderate and heavy hookworm infections.
Least squared means analysis adjusted for the following covariates: age, sex, socio-economic status, hemoccult status, A. lumbricoides infection, T. trichuria infection, and N. americanus infection.
Improvement in hemoglobin after treatment w/ PZQ
Polyparasitism

- Most of the world’s children harbor more than one helminth
- Having multiple infections even all at low intensity causes morbidity expect for higher intensity single infection
- 5X chance of having anemia if harbor 2 or more low intensity infections compared to uninfected/one infection at low intensity
- Also synergistic effects
Interventions

• Sanitation
• Education
  – Shoes
  – Hand hygiene
• Ecologic
  – Snails
  – Dams
• Chemotherapy
  – School based anti-helmintic therapy
  – Mass treatment for schistosomiasis
• Science that is multi-disciplinary and across parasites
Pit Privy

- Distribution and installation in 1920’s with Rockefeller Sanitary Commission Report to Congress
- Hookworm larvae crawl 4 feet
Water
The burden here and now: Still a “wormy world”
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Music by Ayub Ogada “Kothbiro”
Dear children, the rain is coming, bring in the cattle, bring in our wealth