Neglected Respiratory Diseases in the Asia–Pacific

Parasites and the Lungs

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Neglected Tropical Diseases (NTDs)  
*Infectious Diseases of Poverty*

- Group of parasitic and bacterial diseases that cause significant impairment of physical and cognitive development (CDC, 2011)
- Has plagued humanity for centuries
- Affect an estimated two billion people in tropical and subtropical countries (WHO, 2013)
- All low-income countries are affected by at least five NTDs (CDC, 2011)
- Related to unsafe water, poor sanitation, and impoverished living conditions
The 17 Neglected Tropical Diseases

- **Virus**
  - Dengue/Severe dengue
  - Rabies

- **Protozoa**
  - Chagas disease
  - Human African trypanosomiasis
  - Leishmaniases

- **Helminth**
  - Cysticercosis/Taeniasis
  - Dracunculiasis
  - Echinococcosis
  - Foodborne trematodiases
  - Lymphatic filariasis
  - Onchocerciasis (river blindness)
  - Schistosomiasis
  - Soil-transmitted helminthiases

- **Bacteria**
  - Buruli ulcer
  - Leprosy (Hansen disease)
  - Trachoma
  - Yaws

(WHO, 2014)
Global NTD Burden Map

(United to Combated NTD, 2014)
Neglected Tropical Diseases

- In Southeast Asia and Western Pacific:
  - Soil–transmitted helminthiases (STH)
  - Schistosomiasis (SCH)
  - Lymphatic filariasis (LF)
  - Food–borne trematodiases (FBT)

- Morbidities include:
  - Anemia, malnutrition, poor mental and physical development (STH and SCH)
  - Chronic liver and pulmonary disease (SCH)
  - Physical disfigurement and disability (LF)
  - Diarrhea, anorexia, weight loss, peptic ulcer disease–like symptoms and chronic cough (FBT)
Parasites and the Lungs

- Not uncommon in tropical countries especially in Southeast Asia
- Manner of presentation
  - Focal lesions
    - cystic lung lesions
    - coin lesions
    - consolidation/pleural effusion
  - Diffuse lung disease
    - transient pulmonary infiltrates
    - alveolar/interstitial lung changes

(Kunst et al., 2010)
# Tropical Parasitic Lung Diseases

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(Kunst *et al.*, 2010)
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<td><em>Babesia microti</em></td>
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(Kunst et al., 2010)
Loeffler's syndrome

- Hypersensitivity response leading to respiratory symptoms including cough, wheezing, dyspnea, chest pain, fever and hemoptysis
- Characterized by transient pulmonary infiltrates associated with peripheral eosinophilia (Kunst et al., 2010)

Pathophysiology

- Damage to the respiratory epithelium, ciliastasis and mucus production
- Release of platelet activating factor and leukotrienes contributing to bronchospasm
- *Ascaris lumbricoides* and hookworms
- Other parasites such as *Strongyloides stercoralis*
- Can also be caused by nonsteroidal anti-inflammatory drug (NSAID) or infection with fungi (*Aspergillus fumigatus* or *Pneumocystis jirovecii*) (Sharma et al., 2014, NLM, 2013)
Soil transmitted helminthiasis

- **Causative agents**
  - *Ascaris lumbricoides* (round worm)
  - *Ancylostoma duodenale* or *Necator americanus*

- **Transmission**
  - Ingestion of eggs (*Ascaris*) or skin penetration by larvae from soil (hookworms)

- **Lung migration phase**

(CDC, 2011)
Soil transmitted helminthiases

- Major factors for exposure: poor environmental sanitation and poor personal hygiene
- Common worldwide in areas with poor sanitation
- Prevalence of STH in Southeast Asia
  - 59.7% in a rural community in Malaysia (Hakim et al, 2007)
  - 43.7% among PSAC and 44.7 % among SAC in the Philippines based from a sentinel surveillance in 2009 (Belizario et al., 2013)
- Definitive diagnosis: Microscopic examination of stool
STH Treatment

- Albendazole or Mebendazole
- WHO recommends preventive chemotherapy for morbidity control
  - Use of anthelminthic drugs, either alone or in combination, as a public health tool against helminth infections (WHO, 2006)
- Major mass drug administration (MDA) efforts ongoing in developing countries
- In the Philippines, MDA coverage rates generally very low at 15% (WHO, 2012)
**Strongyloides**

- *Strongyloides stercoralis*
- Infection rates in Southeast Asia:
  - 17.5% in Cambodia
  - 23.7% in Thailand
  - 26.2% in Lao PDR (Schar *et. al*, 2013)
  - 44.7% infection rate in a province in Northern Cambodia (Khieu *et. al*, 2014)
- Skin penetration of filariform larvae > entry to blood vessels > heart and lung migration > migration to alveoli (Kunst *et al*, 2010)
- Autoinfection leading to hyperinfection
- Disseminated strongyloidiasis – case-fatality rates near 90% (CDC, 2013)

Filariform larva of *Strongyloides stercoralis* (CDC, 2012)
Clinical Manifestations:
- Generally asymptomatic (latent phase)
- Mild symptoms during lung migration
- Respiratory symptoms may be non-specific
- Asthma-like symptoms
- In hyperinfection, pulmonary infiltrates are commonly seen on chest radiographs
- Eosinophilia in 75% of the cases
- Definitive diagnosis: demonstration of rhabditiform larvae in stool, sputum or duodenal aspirates
  - (Kunst et. al, 2010)
- Use of culture techniques such as Harada–Mori technique
Strongyloidiasis Treatment

- Ivermectin (first line therapy)
  single dose, 200 µg/kg orally for 1–2 days
- Albendazole (alternative)
  400 mg orally two times a day for 7 days

(CDC, 2013)
Syndrome resulting from hypersensitivity reaction to *Wuchereria bancrofti* and *Brugia malayi*

- Occurs in Southeast Asia, China, India, and Africa
- Slow onset (over several months)
- Respiratory symptoms: cough, dyspnea and wheezing
- Systemic symptoms: fever, malaise and weight loss
- Seen in only <1% of filarial infection

(Kunst *et al.*, 2010, Vijayan, 2008)
Tropical Pulmonary Eosinophilia (TPE)

- **Diagnosis**
  - Demonstration of filarial parasite through microscopy
  - High titres of antifilarial antibodies
  - Peripheral blood eosinophilia
  - Elevated total serum IgE

- **Treatment**
  - Diethylcarbamazine (may be combined with albendazole to improve efficacy)

(Kunst *et al.*, 2010, Vijayan, 2008)
Paragonimiasis

- *Paragonimus westermani*
  Korea, Japan, China, Taiwan, Malaysia, Indonesia, Philippines and India

- *Paragonimus heterotremus*
  Southeast Asia and Southern China
  (WHO, 2014)

- 20 million people with paragonimiasis in Asia (90% of all cases) (Vijayan, 2008)

- 20.9% prevalence in children and 4.1% in adults in Arunachal Pradesh in India (Devi *et al.*, 2007)

- 0.2–11.3% prevalence in Vietnam, majority of whom are children (Doanh *et al.*, 2013)

- 15%–25% prevalence in Zamboanga del Norte and Sorsogon (Belizario *et al.*, 2000, 2007)
Known Endemic Areas for Paragonimiasis

Occidental Mindoro
Oriental Mindoro
Camarines Sur
Sorsogon
Samar
Leyte
Zamboanga del Norte
Compostela Valley
Davao del Norte
Davao Oriental
Cotabato
Basilan

(Cabrera, 1979; Belizario and Malte, 2004)
Paragonimiasis

- Major clinical manifestations:
  - Persistent cough
  - Hemoptysis
  - Chest pain
  - Back Pain
  - Dyspnea
  - Weight loss
  - Anorexia
  - Fever

- Manifestations and X-ray findings mimic pulmonary tuberculosis
  (Singh et al., 1986, 2005, Belizaro et al., 1997; Nagakura et al., 2002; Narain et al., 2004; Tay et al., 2005)

- 30% with TB as co-mobidity
- No significant different between males and females
  (Belizaro et al, 1997)
Paragonimiasis

Diagnosis
- Sputum examination (3% NaOH concentration technique)
- Immunological techniques and PCR not readily available (WHO, 2014)

Treatment:
- Triclabendazole
  20 mg/kg, in two divided doses on the same day
- Praziquantel
  25 mg/kg three times a day for three days

(WHO, 2014)
Schistosomiasis

- *Schistosoma japonicum* in China, Philippines, Indonesia
- *Schistosoma mekongi* in Cambodia, Lao PDR (WHO, 2014)
- Prevalent in Southeast Asia
  - Cambodia: <1%
  - Lao PDR: <1%
  - Philippines: 3%
(Zhou *et al.*, 2010; DOH, 2013)

www.cdc.gov/parasites
Schistosomiasis in the Philippines

- Endemic in 12 regions covering 28 provinces with focal distribution (DOH, 2007; Belizario et al., 2005)

- Prevalence of schistosomiasis in school-age children
  - Negros Occidental – 6.8%
  - Davao del Norte – 3.1%
  - Surigao del Norte – 4.8%
  - Agusan del Sur – 31.8% (5–70%) (Belizario et al., 2007, 2012, 2013)

- Major challenges with lab diagnostics (Belizario et al., 2004)

WHO/DOH Target
Prevalence: <1%
Pulmonary Schistosomiasis

- Schistosomiasis – maybe one of the most common causes of pulmonary hypertension
- Lack of data on disease burden (Butrous et al., 2008, Kolosionek, et al., 2010)
- Acute pulmonary schistosomiasis (Katayama syndrome)
  - Develop three to eight weeks after skin penetration
  - Fever, chills, weight loss, diarrhea, abdominal pain, myalgia, shortness of breath, wheezing, urticaria and dry cough
  - Small pulmonary nodules in CT

(Kunst et al., 2010, Vijayan, 2008)
Pulmonary Schistosomiasis

- Chronic pulmonary schistosomiasis
  - Features of pulmonary hypertension and cor pulmonale
  - Massive hemoptysis
  - Lobar consolidation and collapse (Kunst et. al, 2010, Vijayan, 2008)

- Pulmonary granulomas and fibrosis in S. japonicum infections reported in 80% Schistosoma japonicum egg of autopsied cases of advanced disease in China (Zheng et. al, 1981)

- Only 1 case of cor pulmonale in 65 patients with S. japonicum infections in Philippines (Watt et al, 1986)
Pulmonary Schistosomiasis

- Diagnosis
  - Microscopy
    - Kato Katz Technique
    - Formalin Ether Concentration Technique
  - Immunodiagnostic Tests
    - Circumoval Precipitin Test (COPT)
    - Enzyme–Linked Immunosorbent Assay
  - Rectal imprint
- Treatment: Praziquantel

(Kunst et. al, 2010, Vijayan, 2008)
Summary

- Neglected diseases, infectious diseases of poverty
- Parasitic infections affecting the lungs not uncommon in Southeast Asia
- Pulmonary manifestations coupled with evidence of parasitic infections provide basis for clinical diagnosis
- Treatment will include provision of appropriate anti-parasite drugs
Thank you
References: