

## River Blindness: Winning the War Against a Neglected Tropical Disease – Dr. Ed Cupp

- a) History
  - i) 2nd leading cause of blindness worldwide
  - ii) Caused by a filarial nematode *Onchocera volvulus*
  - iii) First described in 1893 in sub-Saharan Africa
  - iv) Vectored by black fly (*Simulium* spp)
  - v) Humans are the only natural host
  - vi) Adult female worms occur in nodules
  - vii) Male worms move from nodule to nodule
  - viii) Microfilariae
    - (1) Cause skin and ocular disease
    - (2) Infect vector
- b) The vector
  - i) Larvae
    - (1) Stream habitat
    - (2) Riffle areas
  - ii) Adults
    - (1) Females are aggressive blood feeders
    - (2) Fly long distances
    - (3) Many species are migratory
  - iii) Species of interest
    - (1) Africa - *Simulium damnosum* complex
    - (2) Americas - primarily *S ochraceum*
- c) Transmission in Africa
  - i) In vector
    - (1) Female picks up microfilaria when feeding
    - (2) Larvae migrate to salivary glands
    - (3) When female feeds the larvae exit through the fly mouthparts
    - (4) Development in vector can be as little as 6-7 days
  - ii) In host
    - (1) Pre-patency is 12-18 months
      - (a) Worms form skin nodules
      - (b) Embedded in connective tissue
    - (2) Many nodules are not evident
    - (3) Microfilaria are released in bursts into the skin
    - (4) Move through skin by digesting skin
      - (a) Itching
      - (b) Destruction of skin architecture
    - (5) Move into eye, eventually causing blindness
      - (a) Slow process
      - (b) Blindness is caused by chronic exposure
      - (c) Rates have been as high as 8-12%
    - (6) Survey is by skin snip
    - (7) Calculate the community microfilaria load (CMFL)

- iii) Outcome
  - (1) Devastating to agrarian society
  - (2) Economic and social pressure
- iv) Transmission in the Americas - associated with coffee production
- d) Control
  - i) Nodulectomy
    - (1) Teams of lay surgeons visited villages
    - (2) Removed nodules under local anesthetic
    - (3) Went on for many years
    - (4) Not 100% effective as transmission can still continue
  - ii) Large scale vector control program
    - (1) Kill the larval flies
    - (2) Limit number of infected bites per person per year
    - (3) Need to reduce number of infectious stage larvae to <20 per person per year
    - (4) Demonstrated in Kenya in 1946-1955
      - (a) Vector eliminated after 18 years
      - (b) Used temephos
      - (c) Acres of land reopened
    - (5) Problems
      - (a) Insecticide resistance
      - (b) Switched to Bti
      - (c) Migration of parous infected flies during monsoon season
    - (6) Benefits
      - (a) Vector control worked
        - (i) Slow
        - (ii) Other issues
      - (b) In some place infection could not be prevented but blindness could
        - (i) Adults live a long time
        - (ii) Infectious larvae
        - (iii) Infectious larvae ~2 years
  - iii) Control of parasites using drugs
    - (1) Ivermectin was found to work against onchocerciasis in the 1980s
    - (2) Killed parasite with no side effects
    - (3) Study in Senegal (Lancet)
      - (a) Efficacious
      - (b) Safe
    - (4) In-depth studies done by WHO in Africa
    - (5) Greene et al, 1985, NE J Medicine 313: 133-138
      - (a) Study in the Americas
      - (b) Microfilaria gone in 2-3 days
      - (c) Fewer side effects than both the typical drug therapy and the placebo
    - (6) Ivermectin can reverse early eye disease
    - (7) Operational considerations
      - (a) Single treatment impacts seasonal transmission
      - (b) Clean for 4-6 months

- (c) Mass treatment can break the cycle
- (8) 1987 - Merck supplied ivermectin free of charge for treatment of onchocerciasis for as long as it was needed
  - (a) Other companies started doing the same for other diseases
  - (b) Established programs for drug distribution
  - (c) Regional programs
- (9) Strategy
  - (a) Treat 2x a year
  - (b) Treat at least 85% of the eligible people
  - (c) Surveillance occurs for three years after transmission is interrupted
- (10) Results
  - (a) Still some transmission occurring in the Americas
  - (b) Eliminated in 96% of risk area
  - (c) Remaining 4%
    - (i) 2 overlapping foci in Venezuela and Brazil
    - (ii) Aboriginal tribes infected
  - (d) In Africa
    - (i) Treat 1x per year
    - (ii) Disease control, not elimination
    - (iii) Problems
      1. Loa loa coinfection
      2. Worm moves into the brain when exposed to ivermectin
    - (iv) Biggest threat - resistance in female worms to ivermectin
      1. Continue to release microfilaria
      2. Need a macrofilaricide