

Vectors and Virulence



UNM Evolutionary Medicine 2009
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Goals

- Understand disease severity in relation to modes of transmission
- Appreciate clinical applications of virulence evolution
- Answer the question: are medical professionals are like blood-sucking insects?
- Find value in asking "Why?"

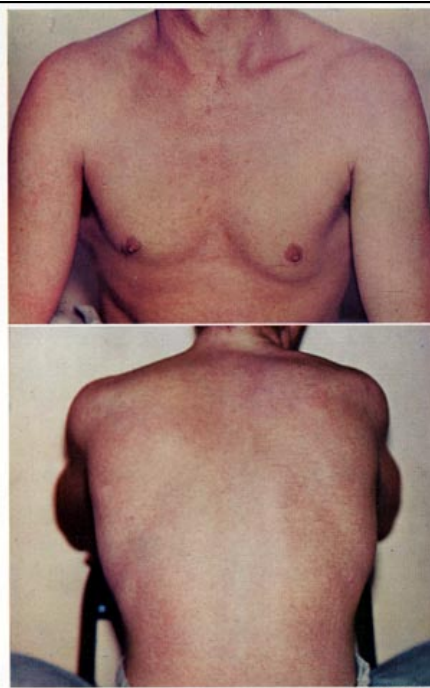
Spring Break

Diver returns from trip to Roatan Honduras, 3 days later - fever 104, retro-orbital headache

- Doesn't want to move
- Persistent nausea & vomiting

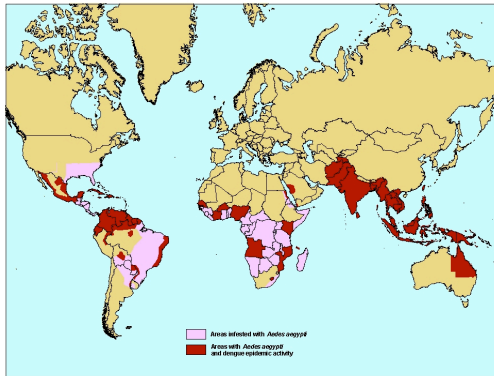


- Exam shows erythematous macular rash that soon becomes confluent.



AFIP D-44-58-5, 7
FIGURE 7.—Rash of dengue fever on chest and back.

Dengue (Breakbone) fever



- Flavivirus
- Single-stranded RNA
- Widespread in tropics
- 50-100 mil cases/yr
- 250-500K hemorrhagic
- 24K deaths

Aedes aegypti



- Patas blancas
- Day biter
- Restless feeder
- Multiple hosts
- Anthrophilic
- ½ world population
- Between 30°N & 20°S

Classic Dengue Fever



- Older kids and adults
- Sudden onset fever
- Headache, muscle aches, pain in shoulders and knees
- Weakness
- By 3rd day: rash

San Salvador, El Salvador

- Female, 11, falls ill with fever, rash, muscle aches, vomiting
- 4 days into illness fever decreases
- Confusion/somnolence.
- Blood concentration
- Swelling
- Low blood pressure
- CXR: large effusions
- Coma briefly precedes death.

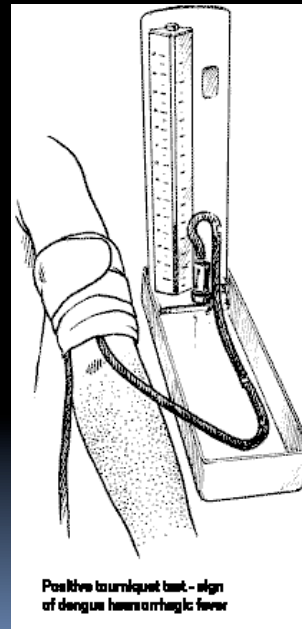


Dengue Hemorrhagic Fever

- 24,000 deaths
- Re-infection with another of 4 serotypes of dengue
- Diagnostic criteria include:
 - Low platelets
 - Capillary leak
 - Hemorrhage

Tourniquet Test

- Checks for hemorrhagic manifestations
- Inflate blood pressure cuff to median B/P for 5 min or until burst blood vessels are seen: $> 3/\text{sq cm}$



Dengue Outbreaks

- Epidemic Disease requires population center > 10,000
- Lack of screened enclosures, piped water
- *But* → increased severity of DHF with increasing interval of exposure to different serotypes

Experimental Vaccine

- Walter Reed laboratory
- All 4 dengue serotypes
- Live attenuated virus
- Incomplete immunity can lead to hemorrhagic fever



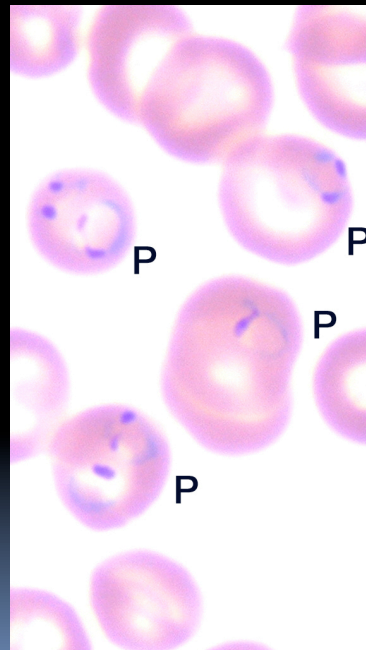






Malaria

- Parasites invade red blood cells: some rupture
- Patients have:
 - Fever
 - Decreased alertness
 - Low blood sugar
 - Anemia
 - Yellow eyes



Malaria kills 1,500,000 /year

- 30,000 travelers get malaria yearly



- Do mosquito borne diseases have high virulence?

Virulence Definition

- Trait of pathogen that increases its reproduction within a host
- Can increase pathogens transmission rate
- Virulence negatively affects host fitness
- High virulence associated with increased disease severity

Virulence

- Virulence = α
- Transmission rate = β
- Duration of infectiveness = v (nu)
- $\uparrow\alpha\uparrow\beta$
 - As virulence increases transmission increases
- $\uparrow\alpha\downarrow v$
 - As virulence increases survival decreases

Outbreak

- Rho = number of new infections in a new outbreak = $\beta*v$
- Ebola - duration of infectivity is low
- Leprosy – transmission rate is low
- H1N1?

Transmission

- 3 types of infectious disease spread:
- Direct Contact
- Vector Borne
- Environmental

Rhinovirus

- Common cold
- Mortality rate:
0.0001
- Disease severity
low
- How is it
transmitted?



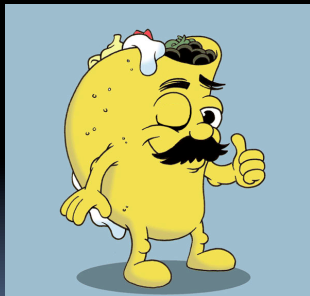
Direct Contact

- Flu
- Rhinovirus
- Travelers Diarrhea



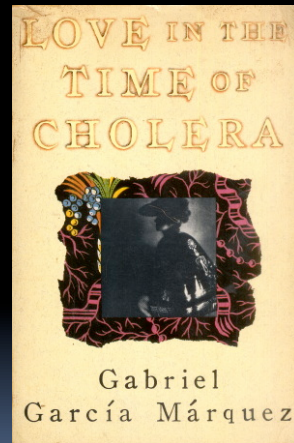
Travelers diarrhea

- Enterotoxigenic E. coli
- Mortality = 0.0025



Cholera

- Untreated mortality rate = 50-90%
- Cholera is more virulent and deadly than traveler's diarrhea – why?



Anthrax

- *Bacillus anthracis*
- Mortality rate = 20 to 90%



Environmental Transmission

- Anthrax
- Spores spread disease readily even after host death



Vector borne diseases

- Anopheles
- Aedes
- Do these pathogens require mobility or contact between victims?



Photo: Doug Valentine

Incapacitation

- Dengue
- Malaria
- Benefits pathogen
- Pathogens should not incapacitate the vector



Humans as vectors

PSEUDOMONAS OUTBREAK LINKED TO NURSES' FINGERNAILS.

Infectious Disease

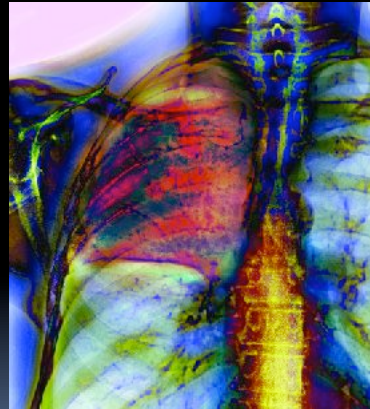
AJN, American Journal of Nursing. 100(7):17, July 2000.

- Artificial nails and hospital setting benefit pathogens
- Easy transmission leads to more virulent bugs
- Hospital acquired pneumonia



Hospital acquired pneumonia

- Mortality rate 15-40%
- Why different from community acquired bugs?



Community Acquired Pneumonia

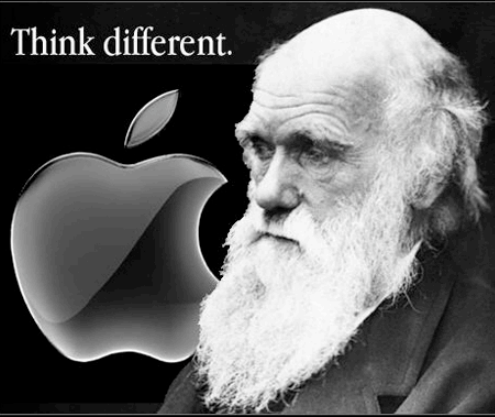
- Mortality rate (hospitalized patients) 12%



Mac vs. PC

- Why aren't there many viruses for Mac computers?
- Email programs are the vector
- What is the likelihood of PC to PC transmission?
- Mac to Mac?

Think different.



Competition

- Competition increases virulence
- Dengue has 4 serotypes
- Multiple serotypes competing for reproduction within same human population.
- Slight increment in virulence for one serotype can give it a fitness advantage.

Can public health interventions alter pathogen evolution?

- Handwashing can decrease likelihood of disease transmission, elimination human vector transmission
- More benign Staph strain might replace virulent hospital acquired pneumonia

HIV

- Sit and wait pathogen
- Relies on slow progression of disease and long duration of infectivity
- Infrequent change in sexual partners (1 in 3 years), selects for less virulent strains
- Populations with overlapping and frequent partner changes (30 in 1 year), selects for more virulent strains

- Virulence = α
- Transmission rate = β
- Duration of infectiveness = v (ν)
- $\uparrow\beta\uparrow\alpha$
 - transmission increases, gives opportunities for strains with increased virulence
- $\uparrow v\downarrow\beta\downarrow\alpha$
 - Duration of infectiveness increases in setting of decreased transmission. virulence decreases.

HIV



- $\downarrow\beta$
 - Reduces transmission
- $\uparrow v$
 - Duration of infectiveness increases
- $\downarrow\alpha$
 - virulence decreases



Goals

- Understand virulence in relation to modes of transmission: direct contact (low) vector (moderate to high), and environmental (highest).
- Clinical applications of virulence evolution: Epidemiologic factors as well as actions taken by hospital staff influence disease severity
- Are medical professionals are like blood-sucking insects? Yes. Attendant borne illness.