

Marisabel Jaramillo and Divya Sahore

**Professor Ebersole Class Discussion:**

*Disease Evolution and its Implications*

- NATURE OF VIRULANCE- Important with disease
  - How “Nasty” the disease is.
  - Measurement to do harm
  - Capacity to do harm

Connection of this could be Ebola – which has the capacity to do harm fairly quickly.

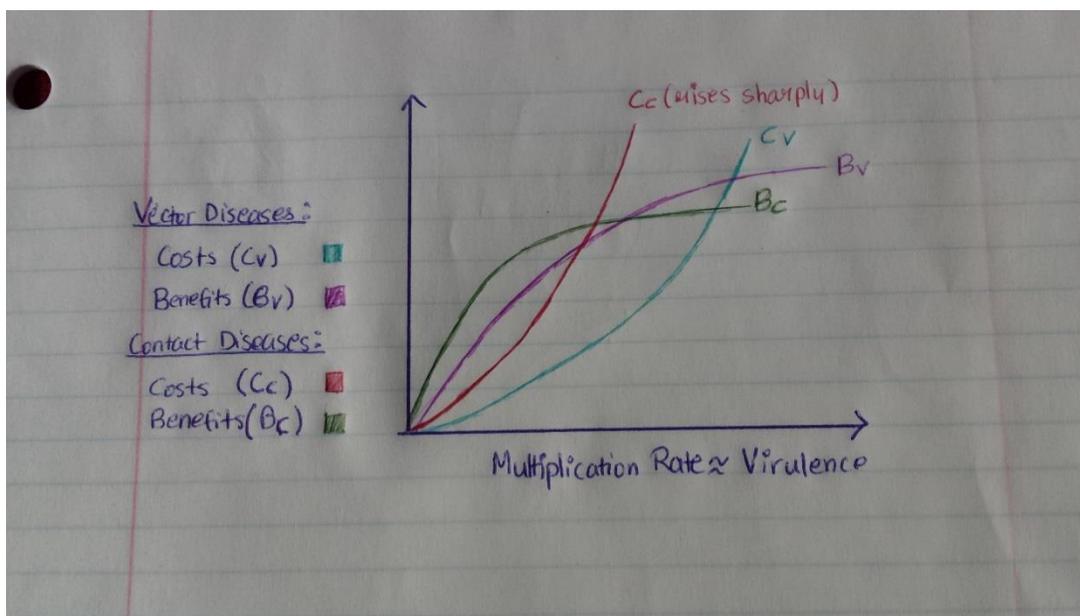
- What brings different levels of virulence in disease?
  - Disease as evil: represented through cultural history and art. Disease was seen as coming from nowhere. Examples of art from 14 century and 19 century related to Christian beliefs and the Apocalypse (end of the world) shows four men on horses: death, famine, war and conquest. However, conquest rapidly changed and pestilence took its place → personification of disease
  - Doctors were forced to see/realize the evolution for reproductive success of parasites (natural selection) around WWII
    - After wide spread of antibiotics (Penicillin – “miracle”), hospitals started to relax but result is the evolution of antibiotic resistant, a problem we still have today.
    - An example is some kinds of Tuberculosis strains that are totally resistant.
  - Germs that cause disease are parasites.
- What is a parasite?
  - In general has to live inside host.
  - It is not good to debilitate host because then the parasite cannot spread/reproduce.
  - Germs want to take advantage of host but not to the point of killing it
  - Back then, it was widely believed that germs that are doing harm are “evolutionary throwbacks” as maybe in time they will develop a mutualistic relationship with the host

Examples of deadly diseases that Professor Ebersole mentioned as being around since “God lost his sandal” are: Malaria, yellow fever, tetanus, typhus, and cholera. It has taken around 4,000 to 6,000 years for these to become benign through vaccinations, medications; they are still brutal today in parts of the world.

- ADAPTIVE VIRULENCE:

- It is not always best to put your host survival first.
- Three reasons why cholera is still nasty:
  1. Rate of multiplication: nasty germs multiply really fast.
  2. Nature of Parasite Fitness – how well one individual gets representation in the next generation.
    - a. If you are a parasite it is not enough to make successful babies. Eventually all hosts would die. As a parasite you have to also get your offspring into a new host → reproductive success
  3. Parasite fitness depends on transmission → higher transmission depends on the mode of transmission (vectors vs. non-vectors)

Cost-Benefit GRAPH: Display of difference between person-person contact diseases and vector diseases.



- For Person to person contact (cold, STDs): Germs have good reason not to make host too miserable (in case of STDs, can be silent for a long time).
  - Not highly virulent as the host has to be mobile and make contact in order to transfer the disease
  - Common cold – Stays in the nasal region- it has done enough, there is no much more benefit by doing more. Costs of making host sick are avoided. Costs go up really fast from person to person contact transmission
- VECTOR DISEASE:
  - Mosquito takes blood of host, it has better chances
  - Continual gradual improvement
  - Debilitation of host partly beneficial, but the cost increases gradually.
  - Example: Common cold – Stays in the nasal region- it has done enough, there is no much more benefit by doing more. Costs of making host sick are avoidance. Costs go up really fast from person to person contact transmission.
- Typhus, malaria, sleeping sickness, yellow fever are carried by vector

CONTINGENCY TABLE by Ewald

Records to find out mortality rates.

	<u>Contact</u>	<u>Vector</u>	
<u>Virulent</u> (with mortality rate >1%)	5	10	
<u>Not virulent</u>	40	8	
<u>Total</u>	<b>45</b>	<b>18</b>	<b><u>Grand Total: 63</u></b>

1/9<sup>th</sup> of contact diseases were virulent, whereas, more than 1/2 of vector were virulent

Additional Notes:

Small pox is an exception that proves the rule of higher virulence. It does not matter if host is sick, or death. It can persist for long periods outside host and still infect. It makes it more of a vector disease.

HIV is another exception. Terribly virulent, although there is some evidence that is becoming less virulent.

## Thoughts:

The class discussion really helped us understand the concept of virulence and why some diseases are highly virulent → vector presence. The theory of parasites eventually forming a mutualistic relationship with host is very interesting. I can see why it was prominent as in order to be successful a parasite's goal is to not debilitate the host, however, what the scientists did not take into account was that there is a co-evolution of the parasites and host. The host's evolutionary goal is to be immune to the parasite whereas the parasite evolves to become more virulent so it can attack the immune system. It is a race between the host and the parasite.

## Chapter 5 from Ewald: When Water Moves like a Mosquito

1. Waterborne Transmission and Virulence
  - a. Diarrhea is the cause of one of the greatest death tolls (4-20 million deaths annually)
    - i. Some organisms (like ones that cause typhoid and cholera) have a better reproductive success and evolutionary rate.
    - ii. Waterborne pathogens use us as pathogen production machines just like mosquitos
    - iii. "Transmission by a cultural vector" – set of characteristics (at least one being a human aspect) that allow transmission from immobile hosts to susceptibles
      1. Examples: any material utilized by the infected, immobilized host: tainted bed sheets, sewage system, streams.
      2. Waterborne pathogens may have high fitness benefits because it has the high potential of infecting many people (large susceptible pool) due to the cultural vectors
      3. In contrast, person-person contact has lower fitness because of higher immobilization → leading to less virulent pathogens compared to waterborne pathogens
      4. Figure 5.1: higher mortality is seen (high virulence) in pathogens that are waterborne

WATERBORNE TRANSMISSION

TABLE 5.1 Waterborne Transmission and Lethality of Diarrheal Diseases

Pathogen	Mortality (%)	Waterborne (%)
<i>Vibrio cholerae</i> , classical biotype	15.2	83.3
<i>Shigella dysenteriae</i> , type 1	7.5	80.0
<i>Salmonella typhi</i>	6.2	74.0
<i>Vibrio cholerae</i> , el tor biotype	1.42	50.0
<i>Shigella flexneri</i>	1.35	48.3
<i>Shigella sonnei</i>	0.45	27.8
Enterotoxigenic <i>Escherichia coli</i>	<0.1	20.0
<i>Campylobacter jejuni</i>	<0.1	10.7
Nontyphoid <i>Salmonella</i>	<0.1	1.6

2. Geographic Patterns

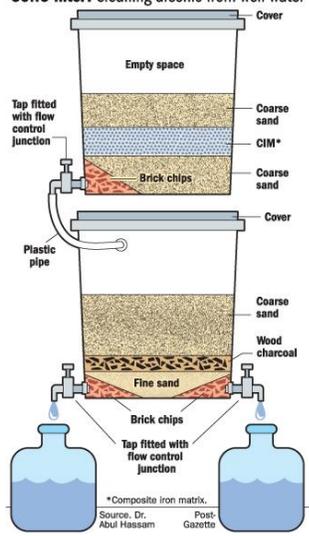
- a. Antibiotic resistance is a prime example of how pathogens are capable of evolving for their survival to “cultural changes” – aka antibiotics.
- b. Hypothesis: “introduction of uncontaminated drinking water should result in an evolutionary reduction in virulence.”
  - i. Comparing closely related species (within a genus) do display a correlation between purification of water and the reduction of virulence.
  - ii. Example: US → purification of water occurred around first quarter of 20<sup>th</sup> century. As a result by 1930s, the deadly bacterial strain *Shigella dysenteriae* type 1 was replaced by moderately severe *Shigella flexneri* and eventually to an even more benign *Shigella sonnei*.
  - iii. This was verified further by comparing regions that had initiated purification later/earlier than the US.
    1. The strains of *Shigella* had already transitioned to benign in the UK three decades before US, since they had initiated purification earlier than the US.
  - iv. *Vibrio cholerae*: the mild version called el tor replaced the classical strain during the 1960s and 1970s.
    1. Bangladesh is one country that still see endemics of classical *V. cholerae*
    2. Cholera is caused by the release of toxins by the bacteria that expels all other competitors from the intestine → extreme diarrhea.
      - a. The classic *V. cholerae* releases more toxins compared to el tor type → more voluminous diarrhea → pathogens are shed in the environment at a greater rate compared to el tor.
    3. If el tor largely replaced the classic strain, then how come Bangladesh sees the resurgence of the classic type?

- a. The strains cross-react: intense infection of one type provide immunity to the other type.
  - b. When immunity to el tor was low, the moderate improvements in water purification favored el tor over classic strain.
    - i. This led to increase in immunity to el tor and a decrease in immunity to the classic strain (plus the lack of sustained water purification) → resurgence of classic *V. cholerae*
    - ii. The cycle of oscillation of strains continues
  - c. Studying Bangladesh has shown that the classic strain is highly dependent on water-borne transmission, hence it spreads really fast, but dies off quickly after exhausting the supply of susceptibles. The el tor type is prevalent in non-water borne transmission → less explosive spread.
3. The Origin of Cholera
- a. Harappan civilization (3000 to 1800 BC) in Pakistan and India
    - i. Inhabitants fetched water from open wells with the drain openings near the well openings → high possibility of oral-fecal infections.
    - ii. Deurbanization of major cities within a century → possibility of spread of water-borne disease like cholera.
  - b. Cultural vector hypothesis also suggests an explanation on how cholera largely remained in South Asia and did not spread to Europe
    - i. Classic virulent strain would die out even before reaching Europe plus a water-borne vector needs to be maintained
4. Waterborne Transmission, Research, and Public Health Policy
- a. Cultural vector hypothesis verifies that variation in virulence can be explained by variation in waterborne transmission (classic vs. el tor)
  - b. Alternative policies: some policies do not regard the evolution of the strains
    - i. Purification of water in Bangladesh has taken a back drop compared to providing immunizations, when it can be seen that by just purifying the water, highly virulent strains die out.
    - ii. The net cost would be about 1/10<sup>th</sup> the cost per life saved by vaccination
    - iii. Another benefit: the benign strain would provide immunization against possible virulent strains that are left.
    - iv. Water purification complements the oral rehydration (providing electrolytes) therapy.

**Thoughts:** Very detailed and scientific analysis of the difference between waterborne vectors and non-waterborne parasites like the Cholera strains and how it relates to virulence really clarified the concept of vectors and virulence. It was shocking to see how purification efforts in Bangladesh were not given as much importance as vaccinations. As I read up online, even after tube wells were installed in Bangladesh (1970s-1980s), arsenic poisoning became a big problem. This has really affected the poor population as they cannot afford the purification filters. New systems are being developed though like in 2006 Sono

filters were distributed which utilizes little materials and can be made locally. Also the Bangladesh Water Purification and Distribution Company Ltd has a vision to set up Satellite Water Purification Plant. So, it looks like more importance is definitely being given to purifying water now. After the classic strain of Cholera is diminished from countries like Bangladesh, it would be interesting to see what type of affect it has on the overall fitness of the Cholera strains. Would the el tor type evolve to become more virulent? Or acquire a different mode of transmission since parasites evolve more rapidly compared to us.

**SONO filter: Cleaning arsenic from well water**



[http://www.irinnews.org/report/76176/bangladesh-new-water-filter-to-combat-](http://www.irinnews.org/report/76176/bangladesh-new-water-filter-to-combat-arsenic-poisoning)

arsenic-poisoning

## Chapter 6

### **Attendant-Borne Transmission**

**(Or How are Doctors and Nurses like Mosquitoes, Machetes and Moving Water?)**

- ATTENDANTS AS CULTURAL VECTORS
  - Attendant-borne transmission- Attendants do not become infected but carry pathogens from patient to patient. This can happen in hospitals and in other institutions.
  - Hospital nurseries diarrheal diseases
    - ◆ Neonates are susceptible to infection, they do not have the same immunity that adults have acquired.
    - ◆ Healthy attendants resistant to infection. Hospital strains of diarrheal pathogens present on attendant's hands → persist and multiply even after washing hands with disinfectants.
    - ◆ Extensive pathogen reproduction in nursery wards neonates should give pathogen high fitness benefits. (babies are touched by nurses at least 20-25 times per day)
    - ◆ Studies show that contaminated hands of attendants is a major source of hospital acquired diarrheal pathogens even though attendants do not suffer from infection.
    - ◆ Severe symptoms facilitate attendant-borne transmission when hygienic standards are negligent.
    - ◆ Sick babies release more pathogens; stay in hospital longer and have to be attended more closely.
    - ◆ Virulence increases with continuous institutional transmission increase.
    - ◆ Pathogens can evolve from months to years in hospital environments.

#### Escherichia Coli and Neonatal diarrhea

- Escherichia Coli – Little or no negative effect on human host, but some strains can kill or immobilize infected people.

- Large-scale community-wide epidemics happened, transmission in hospitals was strongly implicated. Explosive outbreaks were limited to hospital wards, newborn nurseries, and institutions.
- Neonatal infections are less severe when mothers have been infected outside the hospital (acquired immunity).
- If attendant-borne transmission increases virulence → infections should increase with institutional transmission increase.
- Stopping outbreaks on time is important. Each patient tends to be infected with a larger number of pathogens.
- Wards sometimes have to be closed in order to terminate severe outbreaks. Comprehensive cleaning with disinfectants is important.

### E. Coli

- Even with high improvement in hygiene virulence continued.

### Staphylococcus

- Severity of endocardial infections can show how virulent a hospital strain of staphylococcus can be.
- Death might be lowered if attendant-borne transmission was blocked.
- Betterment of hospital policies on precautions, usage of soap/sanitizer, cleaning of the patient rooms

## ATTENDANT-BORNE TRANSMISSION AND ANTIBIOTICS

- Modern medical science analyze in host resistance, antibiotic resistance, or random variation resistance, or random variation in pathogen virulence.
- Little to no discussion about hospital-acquired infections. Hospital-acquired infections of staphylococcal are more severe than community-acquired.
- Medical science explanations: Patients are ill and debilitated in hospital → weak immune systems
- Author argues that there is a possibility that hospital environments have exceptionally virulent strains of pathogens.
- Compromised states in patient are not the only factor to the severity of hospital-acquired infections.

- Strong-vested interest behind the reason why hospitals do not offer information about microbiological records. It is easier to say that it is the compromised status of patients.
- There is a lack of understanding in medical researchers about evolutionary processes and how to apply these processes to hospital settings.
- Antibiotic treatment should impose fitness attention of hospital personnel.
  
- Prevention of attendant-borne transmission can reduce virulent hospital-acquired pathogens.
  
- Pathogen population controlled with antibiotics may evolve resistance and increase virulence.
  
- Most of the dangerous attendant- borne pathogens are of little consequence outside of hospitals.
- Hospital might be especially dangerous for AIDS patients; because their compromised immune systems make them vulnerable to infection that are often attendant-borne.
  
- ALTERING THE EVOLUTIONARY COURSE OF HOSPITAL-ACQUIRED PATHOGENS:

*Hygienic Standards*

*Maternal Contact:* Lower hygienic standards that inhibit transmission from people outside the attendant-borne transmission cycle. Mothers harbor organism from the community that favor benign variants. Mothers could inhibit infection by colonizing infants with benign bacteria.

- Support breastfeeding policies.

Even moderate reductions in the virulence of hospital-acquired pathogens might therefore translate into many thousands of lives saved each year.

## OUTSIDE THE HOSPITAL

### *Homes for the elderly*

*Attendant-borne transmission in kennels-* Hypothesis about cultural vectors can be apply also to non-human hosts' attendant-borne transmission. Example: canine parvovirus.

*Agricultural attendant-borne transmission-* Even without mobility plants can also be applicable to attendant-borne transmission. Pathogens transmitted via seeds or pollen causes additional fitness costs from high virulence.

### **Thoughts:**

- It is important to consider the evolutionary findings of attendant-borne transmission when creating policies for hospitals.
- Records of attendant-borne transmission outbreaks should be open and subject to more regulations.
- Deaths could be saved if hospital become more accountable of infections caused by attendant-borne transmission.