Emerging Diseases

Biosciences in the 21st Century

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Outline

• Disease emergence: a case study
• How do pathogens shift hosts?
• Evolution within hosts: The evolution of virulence
• Treatments: the evolution of drug resistance
Disease emergence: a case study

Ebola Virus

- First identified in Zaire, 1976
- Outbreaks in mid-90s, early 2000s, mid 2000s, 2014
- Average 50% fatality rate

Gire et al. 2014, Science
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Reading a phylogenetic tree

Four descendant populations, each with unique derived traits

Two descendant populations, each with unique derived traits

Ancestral population
No currently existing species is ancestral to any other

There is no linear ancestor-descendant relationship! Humans did not evolve from cats or fish!
Phylogeny of HIV

Three separate introductions from chimpanzees
Back to our case study: Ebola’s natural reservoir

Ebola isolates from fruit bats

Ebola isolate from fruit bats

Shifting to another host species

- phi 6: virus that infects bacteria (bacteriophage)
- phi 6 only infects *Pseudomonas syringae*
Shifting to another host species

- Could phi 6 switch hosts?
- Plated on 14 different *Pseudomonas* species
- A few viruses infected and survived
- All had mutation in protein for attaching to host

Duffy et al. 2007
Shifting to another host species

- Once in a new host, must adapt quickly
- Slow growth can lead to extinction
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What is evolution?

Evolution is a change in a population’s allele frequencies over time.

- Generation t:
  - 70% A
  - 30% a

- Generation t+1:
  - 60% A
  - 40% a
Mechanisms of evolution: sources of variation

**Mutation**: a change in DNA sequence, gene order, or chromosome number

- Random
- Increases genetic variation within populations

- Types of mutations:
  - Point mutations
  - Insertions
  - Deletions
  - Gene duplications
  - Chromosomal inversions
  - Polyploidy
Mechanisms of evolution: sources of variation

Gene flow (or migration): movement of genes between populations
- Increases genetic variation within populations
- Makes populations more similar to each other

Figure: Univ. of Calif. Mus. of Paleontology’s Understanding Evolution Site
Mechanisms of evolution

Natural selection: differential reproductive success
  – Non-random
  – Not forward-looking, can only work with existing variation
  – Only adaptive mechanism of evolution

Figure: Univ. of Calif. Mus. of Paleontology's Understanding Evolution Site
Evolution by natural selection

Ingredients needed for evolution by natural selection

• Variation in traits
• Inheritance
• Differential reproduction (natural selection)

End result: Traits that increase reproductive success increase in frequency in a population.

Figure: Univ. of Calif. Mus. of Paleontology's Understanding Evolution Site
Evolution within the host species

• Once in a new host, must adapt quickly
• Slow growth can lead to extinction
• Host switching leads to strong selection:
  – Infection
  – Evade immune system and replicate
• What factors allow pathogens to evolve quickly?
Back to our case study: the transmission of Ebola, 2014-15

262 patient samples
Full Ebola genome sequences

Carroll et al. 2015, Nature
Evolution of virulence: a trade-off

Selection *within host* favors rapid replication (increased virulence).

Competition *within host*  

Transmission to new hosts

Selection *across hosts* favors reduced virulence.
Mode of transmission affects virulence

Direct transmission, vectorborne, waterborne
Mode of transmission affects virulence

![Graph showing the relationship between fraction of outbreaks that are waterborne and deaths per infection. The x-axis represents the fraction of outbreaks that are waterborne (%) ranging from 0 to 100, and the y-axis represents deaths per infection (%) ranging from 0 to 15. The graph includes data points for Nontyphoid Salmonella, Campylobacter jejuni, Enterotoxigenic E. coli, Shigella sonnei, Shigella flexneri, Classical Vibrio cholerae, Salmonella typhi, Shigella dysenteriae Type I, and El Tor Vibrio cholerae.]

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Evolution of virulence: implications for public health

Select for lower virulence by interfering with transmission
• Improve hygiene
• Wear masks
• Provide clean water
• Widespread vaccination
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Evolution within the host species

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- Host switching leads to strong selection:
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  - Evade immune system and replicate
- What’s another source of strong selection?
The evolution of drug resistance by natural selection

- AZT-susceptible
- Partially susceptible
- AZT-resistant
The evolution of antibiotic resistance before your eyes

• https://youtu.be/plVk4NVIUh8
• 11 day time-lapse video
Avoiding more widespread resistance

1. Avoid contracting infections
2. Minimize transmission of resistant microbes
3. Improve use of antimicrobial drugs
   - Take only when appropriate (i.e., don’t take an antibiotic for the flu!)
   - Use antibacterial soaps/cleaners ONLY around people with weakened immune systems
   - Avoid broad-spectrum antibiotics if possible.
   - Take ALL of the medication
   - Reduce agricultural use of antibiotics
Why can reducing inappropriate use of antimicrobial drugs combat resistance?

- Resistant bacteria escape livestock, spread to humans
Current research aims

- Can we predict which pathogens are more likely to shift to humans?
- What makes some strains so much more deadly than others?
- How can we develop effective new vaccines and drugs?
- What is the mechanism of resistance?
- How can we develop better and faster diagnostic tools?