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, 2014-2016, 2018
- Average 50% fatality rate

Gire et al. 2014, Science
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Reading a phylogenetic tree

- Ancestral population
- Two descendant populations, each with unique derived traits
- Four descendant populations, each with unique derived traits
No currently existing species is ancestral to any other.

There is no linear ancestor-descendent 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

Leroy et al. 2005, Nature
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 $t$
- AA
- Aa
- aa

70% A
30% a

Generation $t+1$
- AA
- Aa
- aa

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?**
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 for different bacterial species.]

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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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- What’s another source of strong selection?
The evolution of drug resistance by natural selection
The evolution of antibiotic resistance before your eyes

- [https://youtu.be/plVk4NVIUh8](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?