Emerging Diseases
Biosciences in the 21st Century
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Outline

• Disease emergence: a case study
• Introduction to phylogenetic trees
• Introduction to natural selection
• How do pathogens shift hosts?
• The evolution of virulence
Disease emergence: a case study

SARS: Severe Acute Respiratory Syndrome

• First detected in China, November 2002
• Spread quickly
• 10% fatality rate
Disease emergence: a case study
What was it? Where did SARS come from?

As laboratories worldwide home in on the virus responsible for the mysterious global outbreak of pneumonia, critics say that researchers could have been better prepared to anticipate the epidemic.

So far, 264 people worldwide are known to have been infected and 9 have been killed by Severe Acute Respiratory Syndrome (SARS). This flu-like condition is characterized by high fever and breathing problems. Fears began escalating after the World Health Organization put out an exceptional alert last week.

Laboratories in Hong Kong, Germany and Singapore have now found signs that the culprit may be a new type of...
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Phylogenetic tree: A visual representation of the evolutionary history of populations, genes, or species.
Constructing phylogenies with sequence data

DNA sequences in descendants:

ATTGCTATTC
ATTGCTTTTTC
ATTGCTTTTTC

DNA sequence changes to: ATTGCTTTTTC

Ancestral DNA sequence: ATTGCTATTC

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Reading a phylogenetic tree

- Ancestral population
- Four descendant populations, each with unique derived traits
- Two descendant populations, each with unique derived traits
No currently existing species is ancestral to any other.
Different arrangements show the same relationships.

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: the emergence of SARS
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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
Natural selection is one mechanism 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.
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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
• Host switching leads to strong selection:
  – Infection
  – Evade immune system and replicate
• What factors allow pathogens to evolve quickly?
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Evolution of virulence: a trade-off

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

Competition **within host** leads to Transmission to new hosts.

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

Direct transmission, vectorborne, waterborne
Mode of transmission affects virulence

![Bar chart showing frequency of pathogens and deaths per infection by mode of transmission.](chart.png)
Mode of transmission affects virulence

Deaths per infection (%) vs. Fraction of outbreaks that are waterborne (%)

- Classical *Vibrio cholerae*
- *Salmonella typhi*
- *Shigella dysenteriae* Type I
- El Tor *Vibrio cholerae*
Back to our case study: virulence in SARS

• Wanted: an animal model for SARS
• Problem: SARS slowly replicates in mice, but mice do not get sick
• Solution: create selection for increased virulence of SARS in mice
  1. Infect mouse with SARS
  2. After 2 days, purify virus from lungs and infect new mice
  3. Repeat, 14 times

Back to our case study: virulence in SARS

Evolution of virulence: implications for public health

Select for lower virulence by interfering with transmission

- Improve hygiene
- Wear masks
- Provide clean water
- Widespread vaccination

Selection within host favors rapid replication (increased virulence).

Selection across hosts favors reduced virulence.
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?
Key points

- New diseases are constantly arising
- Evolution can help us determine
  1. what they are
  2. where they came from
  3. how they infected humans
  4. how they become more/less virulent
  5. how best to fight them
- No currently existing species is ancestral to any other
- Virulence is a trade-off between fast replication and transmission
- Transmission mode affects virulence