

Genetics and Evolution IB 201 06- Lecture 15

Evolving Pathogens

One of the best examples of Natural Selection and Adaptation is the evolution of genetic resistance in disease-causing pathogens

- A major theme in the evolution of bacterial and viral pathogens is that of **resistance**.
- Bacteria that cause infection and disease **rapidly** develop resistance to antibiotics.
- The result is an **evolutionary arms race** between bacteria and humans, in which the participants are engaged in a continuous struggle against each other with no long-term reduction in extinction probability.

Example: *Staphylococcus aureus* is a bacterium that causes infections in humans in hospitals (burn victims, those recovering from operations).

- In 1941 *S. aureus* was successfully treated with **penicillin**, which inhibits synthesis of the bacterial cell wall
- By 1944 some strains had acquired _____ to penicillin
- By 1992 more than _____% of all *S. aureus* strains worldwide were resistant to penicillin
- Pharmaceutical industry responded by producing **methicillin**
- By 1980s *S. aureus* was resistance to methicillin + all drugs structurally similar to penicillin
- Resistance was caused by mutation in single gene that controls structure of a bacterial cell wall element, preventing the drugs from _____ to the wall
- Currently some *S. aureus* strains are resistant to most **other antibiotics** (erythromycin, tetracycline, etc.)
- 1980s **fluoroquinolones** killed *S. aureus* at low concentrations, curing serious infections
- By 1990s resistant strains appeared: 5% resistance increased to >80% resistance in one year in a New York hospital, and resistance quickly spread worldwide
- **Mupirocin** developed in UK works on *S. aureus* that are resistant to fluoroquinolones, but some strains have already developed resistance to mupirocin.
- Resistance is costly: treatment of non-resistant tuberculosis in 1992 cost \$12,000; treatment of a multidrug-resistant tuberculosis cost \$180,000
- Since antibiotics were invented, ~5 million tons have been used on humans and domestic animals, thus exerting massive selection on the world's bacteria, resulting in resistance
- Pharmaceutical companies prosper, but humans are at risk

Who will ultimately win the arms race?

I. Antibiotic Resistance

A. Mechanisms of rapid transfer of resistance

Bacteria rapidly evolve resistance to virtually all antibiotics. Hospitals are especially good breeding grounds for resistance because antibiotics are used intensively.

Resistance is caused by *genetic mutations*, which can be *horizontally transferred* from bacterium to bacterium by:

1. **Transformation:** bacteria acquire genes (e.g., resistance genes) by taking up free DNA molecules, released by dying bacteria into the surrounding medium, and incorporate it into their circular chromosome.
2. **Transduction:** A virus that infects bacteria picks up some bacterial DNA (including a resistance gene) from one host and carries it to another bacterial host, which can incorporate the resistance gene into its chromosome if it survives the viral infection.
3. **Conjugation:** A form of bacterial mating. Two bacteria construct a tube between them through which *plasmids* (small circular pieces of *extra-chromosomal DNA*) and chromosomal DNA can be exchanged.
4. **Transposons:** “jumping genes” that can pick up a resistance gene and move it into a plasmid.

Note: Plasmids and transposons can actually induce bacteria to conjugate, creating opportunities for horizontal transmission of themselves and the resistance gene!

In summary: resistance that evolves in one bacterium spreads horizontally through transformation, transduction, and conjugation. Strong selection (death of the bacterium) applied by antibiotics to large populations of bacteria with short generation times produces billions of cells in which many mutations occur every generation.

[at human body temps, bacteria have generation times of ~1 h, and can multiply rapidly]

B. Conditions for Rapid Evolution

Rate of evolution can be fast if there is:

- Strong selection-- when the result of the selective agent is death before reproduction
- Large populations
- Abundant genetic variation in a trait-- increases the potential for response to selection

C. Human Response to Resistance

- Most pathogens have much shorter generation times than their hosts, and will evolve more rapidly
- Part of the vertebrate defense response against pathogens is achieved by having an immune system whose response time is similar to the generation time of the pathogen

II. Coevolution [between pathogen and host]

When the evolution of a trait is affected not only by a) variation in reproductive success and b) a correlation between reproductive success and the variation in the trait, but also by c) **an interaction with an evolving partner** (also known as *reciprocal evolution*)

- **Reproductive success** of the pathogen can depend on the reproductive success of the _____.
- The **geographical pattern of the interaction** between pathogen and host is determined by the overlap between the geographical occurrence of the host and that of the _____:
 - overlap may be large, small, symmetric or asymmetric

1. Outcomes of host-pathogen interaction

- Stable coexistence
- _____ of one of the partners

Usually impact of the pathogen on the host species is negative and the interaction can be characterized as + -: **the pathogen benefits; the host suffers**

If it is not in the interest of a pathogen to make sure that the interaction between it and its host persists, then the pathogen could win the arms race and drive the host to extinction.

If a pathogen can attack several different hosts, then the disappearance of one makes little difference to its reproductive success.

Red Queen Interactions: No matter how much one species adapts to what the other is doing, the other will change just as much in response, with the result that there is no long-term improvement in fitness. They become locked in an arms race with no exit.

Example: Each time the bacterium improves its attack on its human hosts the human changes in a way that improves its defense, which then causes the bacterium to improve its attack.

Questions to Consider:

1. In the bacteria-human-antibiotic interaction described above, are humans actually adapting (responding) directly to the pathogen resistance?
2. Which two partners are actually in an arms race?

III. How Selection Shapes the Evolution of Virulence

Virulence: the property of pathogens of being highly malignant or deadly, causing disease or death in host

Virulence evolves to intermediate levels

- Tradeoff between immediate reproductive success (rapid growth) and impacts on host that can reduce long-term success of the pathogen—the tradeoff results *in intermediate levels of virulence*
- Doesn't pay pathogen to kill off the host before the pathogen has been transmitted

Too much will kill off host, too little will reduce transmission

Degree of virulence depends on mode of transmission

1. Vertical transmission of disease from parent to offspring (e.g., nematode worms that parasitize fig wasps) should evolve lower levels of virulence
2. Horizontal transmission can result in higher levels of virulence

Degree of virulence also depends on population density of host

1. High density hosts leads to easy transmission and higher levels of virulence (host is expendable)
2. Low density hosts leads to poor transmission of pathogens and lower levels of virulence: can't afford to kill off host if they are few and far between

IV. Role of Phylogenetic Methods in Tracking Pathogens

Phylogenetic methods allow reconstruction of trees from nucleic acid sequences, including DNA and RNA

One of the many contributions of phylogenetics is the clarification of the recent history of pathogens

In an infamous case involving the infection of dental patients with the **HIV** virus (an RNA virus), phylogenetic analysis allowed scientists to identify who transmitted the disease to specific patients.

The methods work because:

- the RNA virus can be sequenced from many individuals (patients and population at large)
- the RNA virus evolves so rapidly that each host has a new, unique strain after infection

V. HIV Evolution (Chap. 1, F&H)

HIV is proving to be one of the worst disease epidemics in history, particularly in the developing world, and especially in sub-Saharan Africa.

Please consider the following questions after reading F&H

- A. What is HIV?**

- B. How does HIV cause AIDS symptoms?**

- C. Have any drugs been developed to successfully combat HIV over the long term?**

- D. How have they been successful or why have they not been successful?**

- E. What are treatment cocktails and how do they work?**

- F. Compare HIV with Bacteria: What factors allow the rapid evolution of HIV strains?**

- G. Are there any similarities in the process of evolution of HIV-resistance to AZT and the evolution of beak size in Galapagos Finches?**

- H. Can HIV afford to kill off its host by being lethal? What is the tradeoff between lethality and transmission?**

- I. Where did HIV come from? (optional reading: Contaminated polio vaccine theory refuted, *Nature* 2004)**

Refs:

F&H: Chap. 1

Stearns, S. C. and R. F. Hoekstra. 2005. *Evolution: An Introduction* 2nd ed. Oxford Univ. Press, New York.