

## Evolution and Human Health

- Questions to Address:
  - 1. What are the medical consequences of the fact that populations evolve---for both patients and pathogens?
  - 2. How have these consequences resulting in puzzling aspects of human physiology and behavior? What adaptations have resulted?

## You and Pathogens in Conflict

- Immune System Cells: recognize and then remember billions of foreign proteins; are capable of killing the foreigners
- Pathogens: large population sizes, short generation times, high mutations rates---a perfect recipe for fast evolution; once a trait that thwarts the immune system shows up it's quickly and strongly selected for

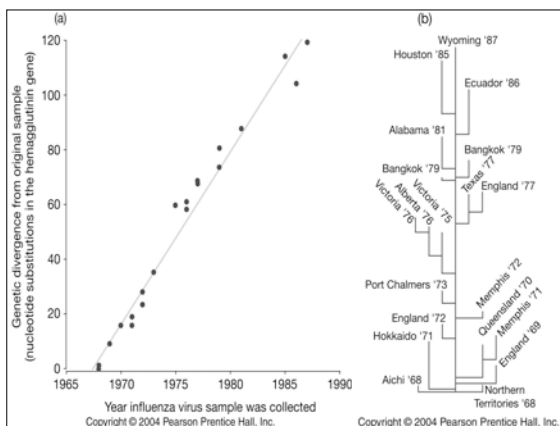
## The Influenza A Virus

- Responsible for annual flu epidemics and occasional pandemics (1918, 1957, 1968)
- In an ordinary flu season in the US, 20,000 Americans are killed by the virus
- The 1918 pandemic sickened about 20% of the world's population and killed between 50-100 million people

Does natural selection keep the virus potent?

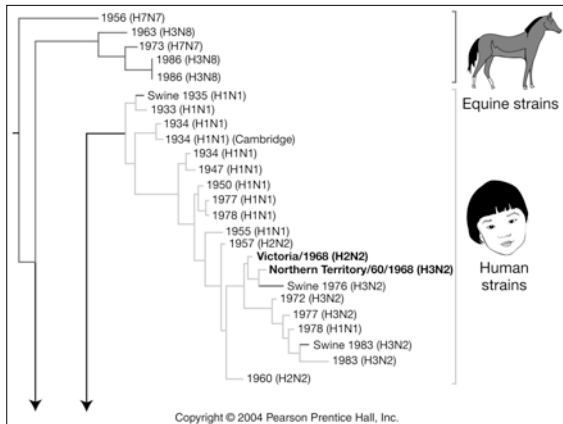
## How does the virus work?

- Initiates infection by having one of its coat proteins, hemagglutinin bind to the host cell
- Hemagglutinin is also the "antigenic site" which is recognized, attacked, and remembered by the host's immune system
- To stay alive, the virus has to find naïve hosts so it's hypothesized that flu strains with novel antigenic sites would have a selective advantage.



## What causes a pandemic?

- If a flu strain could radically alter the structure of its hemagglutinin such that no human immune system had ever seen it, it could potentially affect everyone alive
- It turns out that when two flu strains infect a cell at the same time, they can sort of combine and swap genes and these new combos can be unrecognizable



## Virulence of Pathogens

- Virulence is the harm done by the pathogen to the host during the course of an infection
- Some pathogens are lethal and some produce no symptoms at all.

How do you explain this evolutionarily?

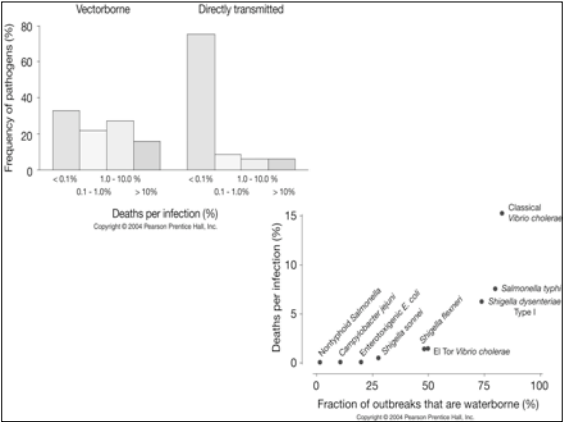
## How Virulence Evolves

1. **Coincidental Hypothesis:** virulence may not be a target of selection itself, but rather an accidental byproduct of selection on other traits  
 Tetanus is caused by a soil bacterium. In a human wound it produces a lethal neurotoxin. Since they don't normally live in humans though, this ability is probably a result of selection during their regular life in soil, not related to humans at all.

## How Virulence Evolves

1. **Short-Sighted Evolution Hypothesis:**  
 Pathogens may experience generations of evolution by natural selection within an individual host before they have an opportunity to move to a new host. Traits that enhance within-host fitness may rise to high frequencies even if they are detrimental to transmission of a pathogen to new hosts  
 Polio normally in intestinal cells; a problem only in nerve cells. Less competition in nerve cells but much less likely to get to a new host.

3. **Trade-Off Hypothesis:**  
 Traditionally biologists believed that pathogens would evolve toward ever lower virulence because damaging their host isn't good for them. But what if that damage enhances their ability to be transmitted? Natural selection must favor some optimal balance of costs/benefits



## Tissues as Evolving Populations of Cells

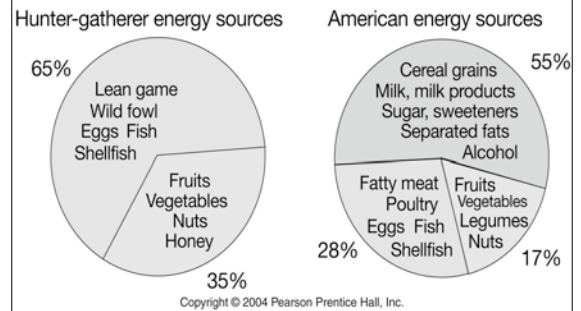
- All your cells are descended from a single ancestor--a zygote. During tissue development, as long as the somatic cells can divide, the tissue is a population of reproducing cells with heritable variation. If a mutation occurs and leads to improved survival or faster reproduction, then the tissue will evolve by natural selection
- Ex of ADA deficiency; implications for gene therapy

## Human Physiology/Behavior and Natural Selection

- If human physiology and behavior has been determined by evolution through natural selection, how do you explain quirks that seem to decrease fitness?
  - Nearsightedness (myopia)
  - Genes for breast cancer
  - Fevers
  - Parents harming kids

## Is the Modern World too New?

- Until the advent of agriculture about 10,000 years ago, our ancestors were hunter-gatherers who lived in a variety of habitats that mostly don't correspond to where and how we live now



## Myopia (nearsightedness)

- Myopia is at least partially heritable. Why does it persist? Surely a nearsighted hunter-gatherer would be in some trouble.
- Maybe the alleles that predispose us to myopia only cause that in a modern environment. Studies have shown that the shape of the growing eye is molded by visual experience

## The Inuits

Age	Fraction Myopic
6-35	42%
36-88	5%

The kids were the first generation to study in standard American schools where they had to do a lot of reading--close up work under artificial light.

## Breast Cancer

- If genes are responsible for a substantial fraction of breast cancer, natural selection should have eliminated those alleles.
- If it's caused by long-standing environmental factors, natural selection should have favored those immune to the effects

So why do 1 in 8 North American women get breast cancer today?

## Two possibilities...

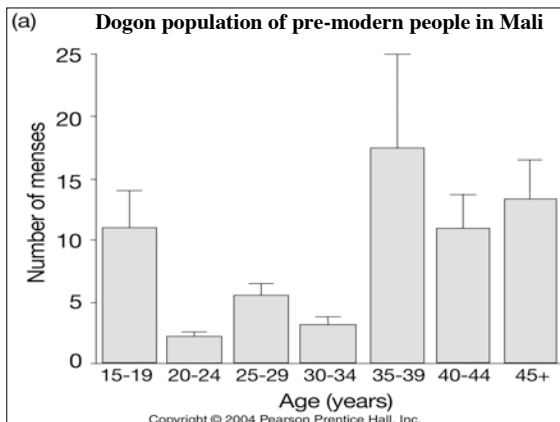
1. Breast cancer may be caused by a pathogen which changes as it evolves so everyone is not immune
2. Breast cancer is a disease of civilization. It may be caused by interaction between genes and novel environments to which our ancestors were never exposed.

## Evidence for #1

- Mice carry a mouse mammary tumor virus (MMTV) that causes the equivalent of breast cancer in mice. Do humans have this?
- First researchers looked for gene sequences similar to MMTV in humans and found them in 38% of cancerous *vs.* 2% of normal tissue---but they've not found MMTV itself

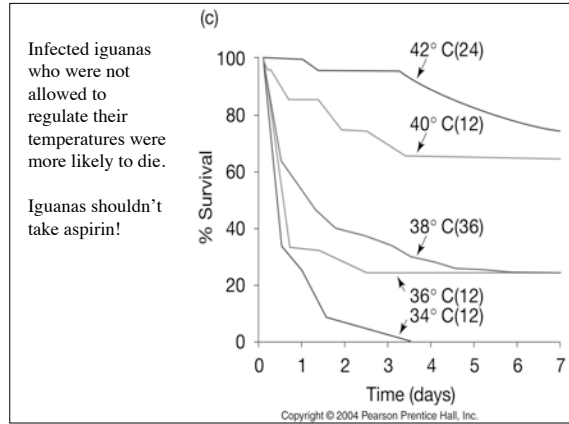
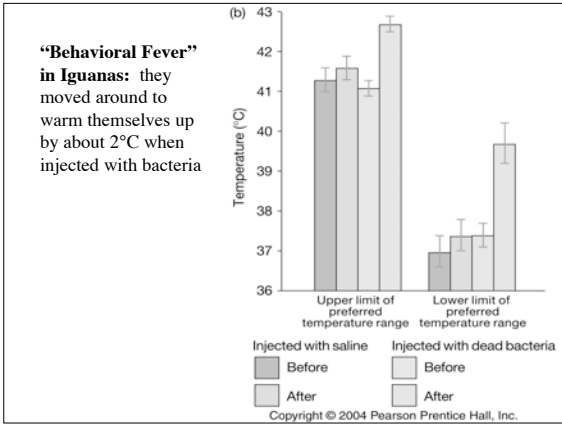
## Evidence for #2

- Modern women have very steady monthly menstrual cycle patterns compared to primitive cultures which lack birth control
- Studies suggest that the more menstrual cycles you have (start early, have children late, don't nurse) the higher your risk of breast cancer. This apparently has to do with levels of estrogen and progesterone.



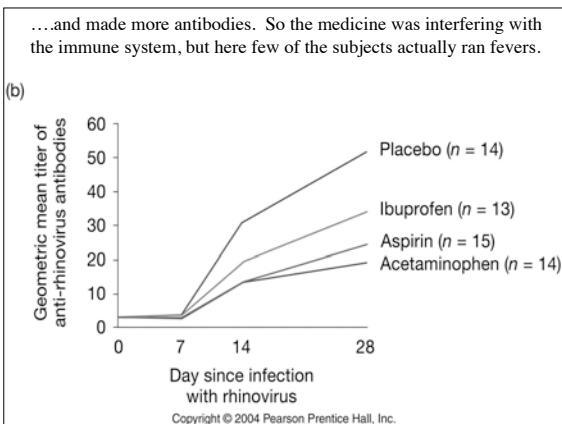
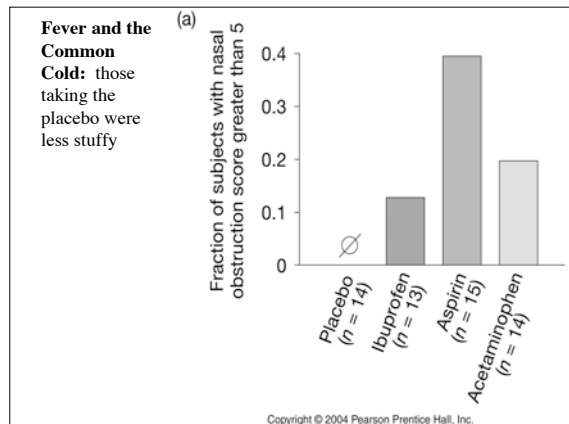
## Fevers--Adaptive or not?

1. Fever may represent manipulation of the host by the pathogen. They could grow and reproduce more quickly at a higher temperature.
  2. Fever is a defense against a pathogen. The immune system may work faster at higher temperatures.
- So which is it? Should you take fever-reducers or not?



### Fevers and Chickenpox

- Two groups of kids with chickenpox were given acetaminophen or a placebo.
- Those taking placebos scabbed over and had their itching subside more quickly
- BUT there was no difference in the fever levels of the groups so????



### So????

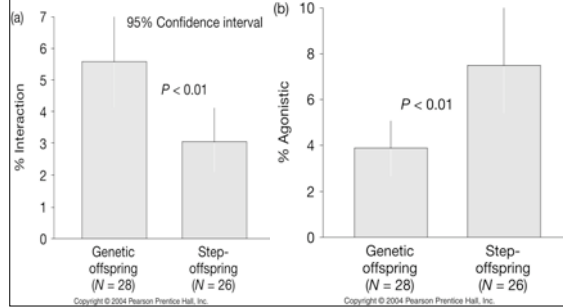
- So it looks like it MIGHT not be a good idea to suppress a fever but....
- It might depend on which pathogen you have
- There are other costs to fevers to consider: being able to function normally might be an acceptable trade-off and very high fevers deplete nutrient reserves and damage tissue

## Human Behavior

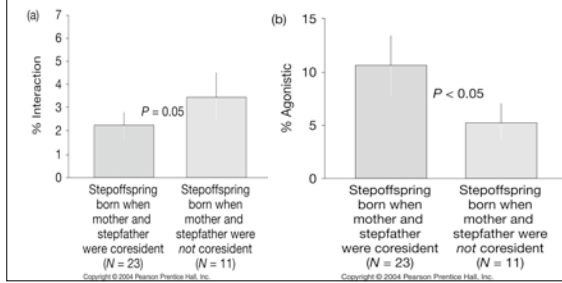
- Human behavior is so strongly influenced by culture that it's often unrealistic to try to look at it in terms of selection for fitness
- Additionally, some things we do now our ancestors simply could not have done---skiing, race car driving, watching TV etc---so there's no point at all in looking at these in terms of adaptive value (or lack thereof)

### Parenting of Genetic vs. Stepchildren

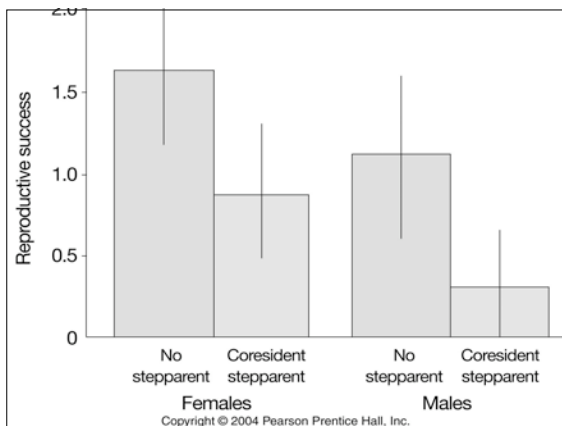
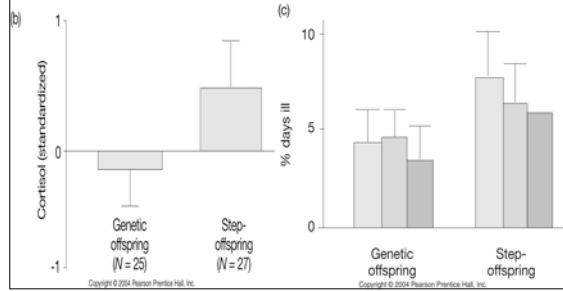
(studied in a primitive Caribbean town where the homes had open walls so the researcher could randomly walk through town and observe interactions)



This looked at whether it was just that the father arrived in the family after the child was older such that a lack of parental bonding might be the problem



Levels of cortisol in the kids saliva was measured as an indicator of stress. Days of illness was also recorded as an indicator of stress levels.



Likelihood of child being killed by parent. (has the odd sounding dependent variable to compare relative rates because most children, especially young children live with biological parents so numerically, many more of those are killed than stepchildren)

