"I want to suggest that the struggle against disease, and particularly infectious disease, has been a very important evolutionary agent."

J.B.S. Haldane 1949:68

Evolution & Human Health

Evolutionary epidemiology:

the application of Darwin's theory of NS to the study of disease in populations

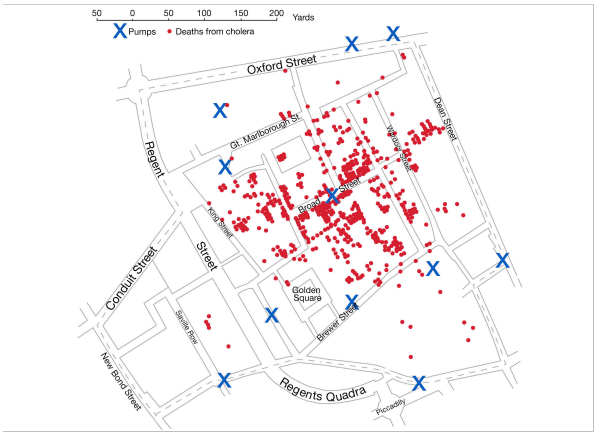
e.g. adaptive significance of pathogen virulence

Darwinian medicine:

the application of Darwin's theory of NS to the study of health-related phenomena

e.g. evolution of senescence

Cholera 1854 - John Snow

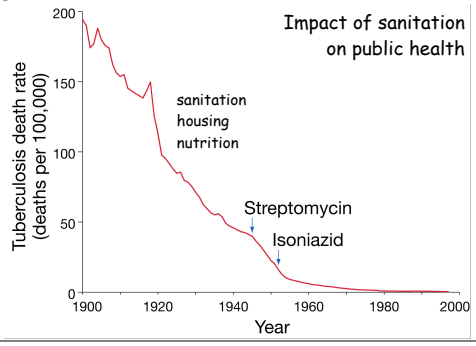


Pasteur 1858 - germ theory of disease

Koch 1858-1883- Vibrio cholorae, anthrax, typhoid etc

Lister 1860's- antiseptic surgery

Fleming 1928- antibiotics



0.4

Types of questions...

1. Medical consequences of the fact that pops evolve
   - Infectious diseases in human history
   - Disease ecology
   - Evolutionary Medicine

2. The human animal as it has been shaped by NS

√ Why have genetic diseases not been eliminated by natural selection?

√ Why does the evolutionary design of our bodies predispose us to certain illnesses (e.g. backaches)?

√ Why is it that treating some symptoms may neutralize our adaptive defenses (e.g. coughing, pain, fever, morning sickness) ?

√ Why has evolution not freed us from organisms that cause diseases?

√Why are some health problems worse today than in the past (e.g. heart disease, cancer, obesity)?

Leading Causes of Death 1900 vs 1967 (U.S.A.)

• Pneumonia & influenza	• Heart diseases
• Tuberculosis	• Cancer
• Diarrhea & enteritis	• Cerebral hemorrhage
• Diseases of the heart	• Accidents
• Nephritis	• Pneumonia & influenza
• Accidents	• Diseases of early infancy
• Cancer	• Arteriosclerosis
• Diphtheria	• Diabetes mellitus
• Meningitis	• Circulatory diseases

Mortality patterns shift significantly through time…..

Types of evidence

Human remains
- mummies
- skeletal &
  dental pathologies
- coprolites

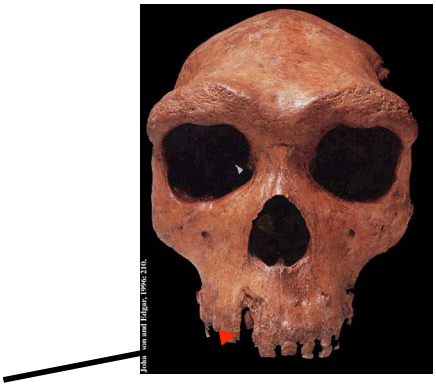
DNA from pathogens

Oetzi the Iceman 3300 BC
Schnalstal glacier, Oetztal Alps

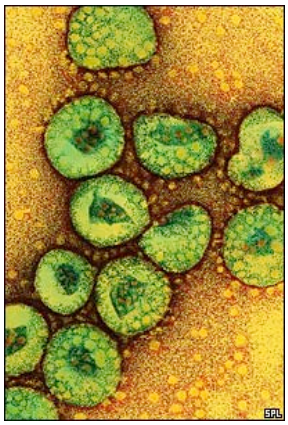
Possible lesions from tuberculosis

Paleopathology limited…

Infection in the Paleolithic
Broken Hill, Zambia (150,000 -125,000 ya)



Pathogen <-> Host in conflict



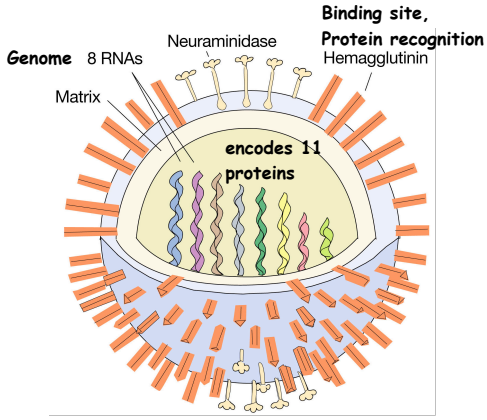
Coronavirus thought to be responsible for SARS

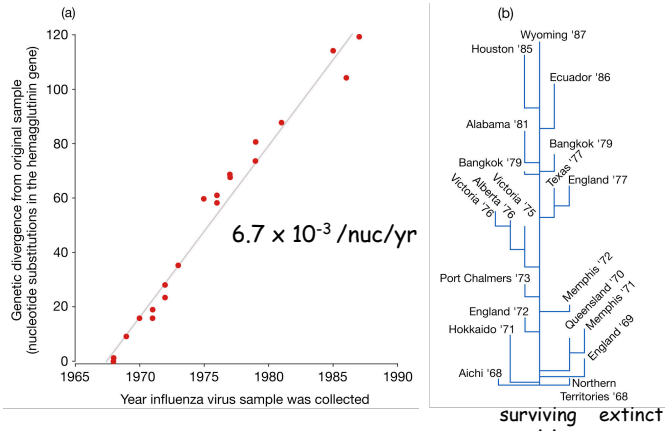
Detectable evolution in flu viruses - are humans responsible?

Influenza A

- global 1918, 1957, 1968
- US 30,000 -35,000 deaths/yr

Influenza A





		surviving	extinct
		**	
AA replacements:	Antigenic sites	33	31
	Non-antigenic sites	10	35

Fitch et al 1991

Follow up study....
357 strains (1985-1996)
331 substitutions (58% silent, 42% replacement mutations)
But..... non-neutral changes at 18 AA sites

Testing the action of NS at a protein....

ka = rate of non-synonymous substitution
ks = rate of synonymous substitution

ka/ks < 1 purifying selection
ka/ks > 1 positive selection

Follow up study....
357 strains (1985-1996)
331 substitutions (58% silent, 42% replacement mutations)

Testing the action of NS at a protein....

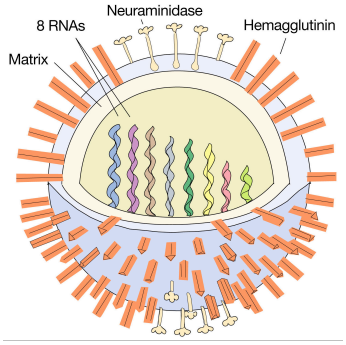
ka = rate of non-synonymous substitution mostly deleterious
ks = rate of synonymous substitution

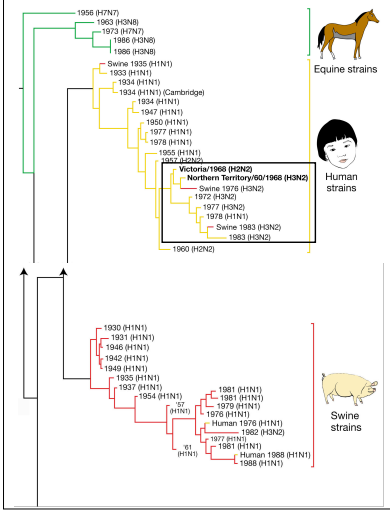
ka/ks < 1 purifying selection
ka/ks > 1 positive selection

Found.....
ka/ks > 1 at 18 sites in Hemagglutinin gene
all involved antigenic sites

Marburg in Angola 2005

Global pandemics

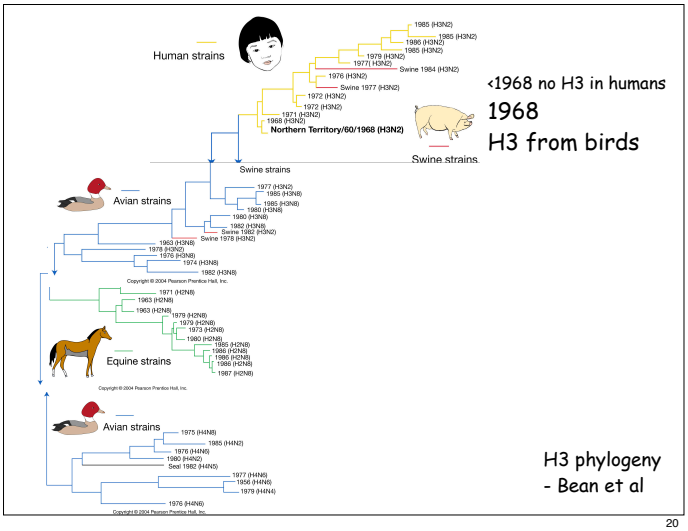




Flu strains do swap genes

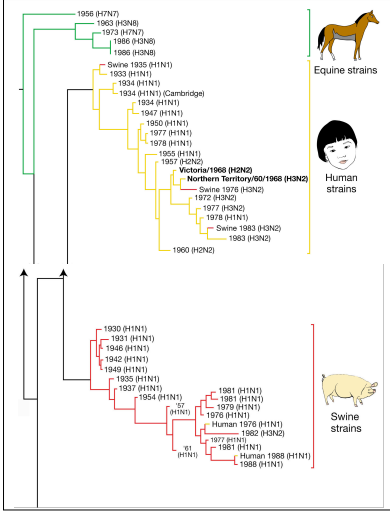
nucleoprotein tree
- ~host specificity
- distinct clades

H3N2
Hemagglutinin-3
Neuraminidase-2



<1968 no H3 in humans
1968
H3 from birds

H3 phylogeny
- Bean et al



Human + Bird in Swine

-> Human

(partial Nucleoprotein tree)

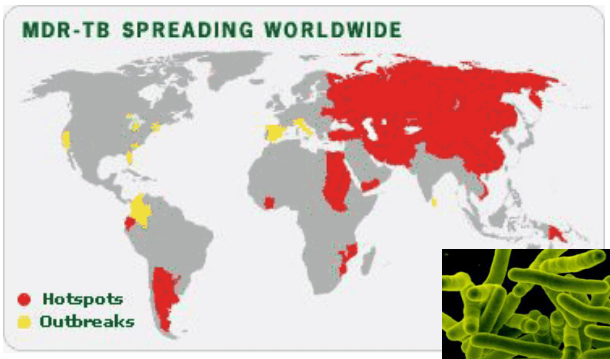
Avian flu threat (H5N1)

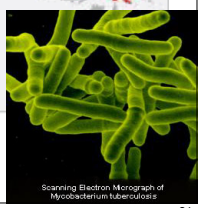
Hong Kong - May 1997
infected humans: ca. 50% mortality
1.5 million chickens slaughtered

Antibiotic resistance

	TB resistance to Isoniazid	
	New cases	Relapsed cases
# resistant cases	243	41
# susceptible bacteria	2728	150
Fraction resistant	8.2%	21.5%

Evolving pathogens: antibiotic resistance

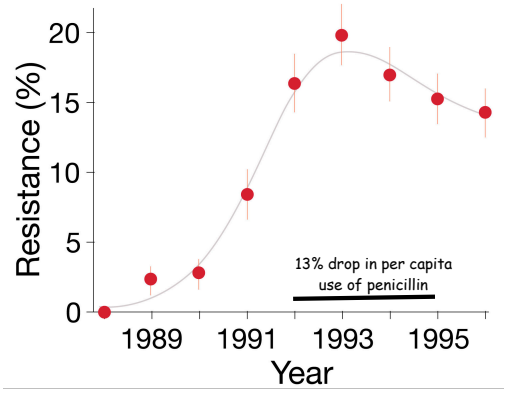




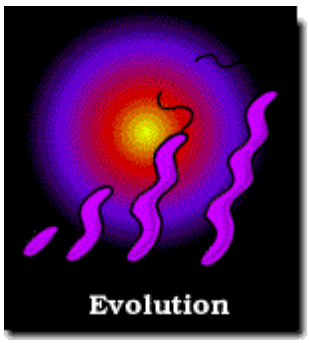
New patients 8%
Relapsed 21.5%

Population level……

Penicillin resistance among Pneumococcus bacteria in Iceland



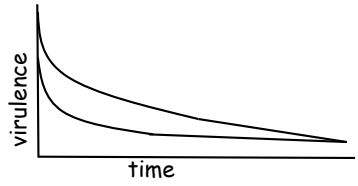
Why do pathogens vary in the severity of disease that they cause (i.e. virulence)?



Traditional view:

- inevitable loss of virulence with time

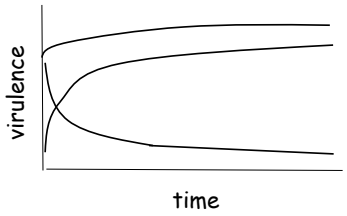
- a pathogen that harms its host will be "committing suicide" with respect to transmission



New view:

- pathogens will evolve towards optimal levels of virulence that maximize their probability of transmission

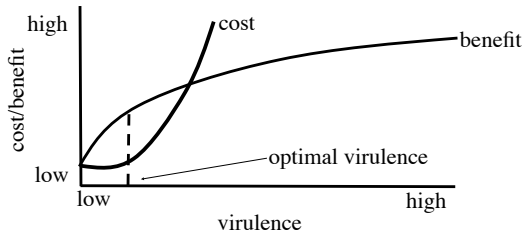
- these levels may be low or high



Imagine a hypothetical pathogen that is directly transmitted (sneezing, physical contact)….

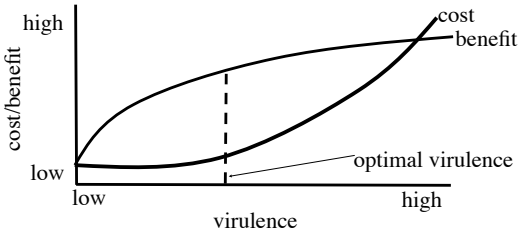
Virulence

- Benefit - more pathogen per sneeze
- Cost - host feels sick & contacts fewer susceptible hosts



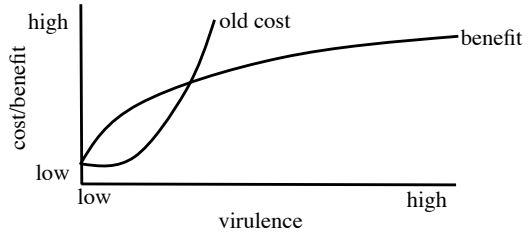
Imagine a hypothetical pathogen that is transmitted by an insect vector……..

- benefit of virulence - more pathogen eaten per insect bite
- cost of virulence - low. Even though the host feels sick, the insect can still bite and transmit the pathogen to new hosts



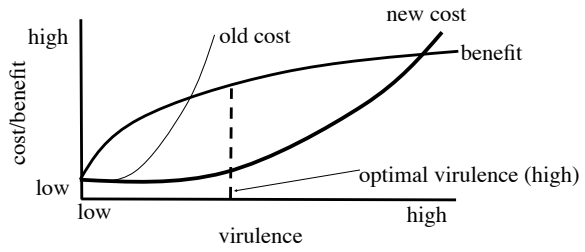
Imagine a virulent diarrhea-causing pathogen….

- invades new host & reproduces quickly; incapacitates host
- BUT, a dirty water supply (e.g. unprocessed sewage in a river used for drinking) allows new hosts to become infected anyway
- What happens to virulence?



Imagine a virulent diarrhea-causing pathogen….

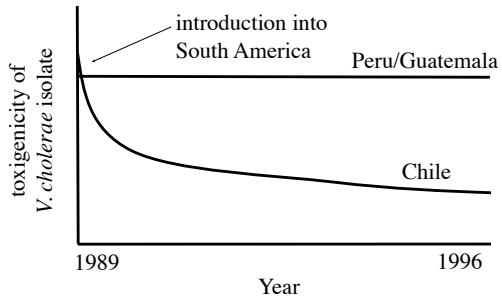
- invades new host & reproduces quickly; incapacitates host
- BUT, a dirty water supply (e.g. unprocessed sewage in a river used for drinking) allows new hosts to become infected anyway
- over time, pathogens like this out-compete less virulent types



A natural experiment

- In the early 1990's, Vibrio cholerae, the bacterium that causes human cholera, was introduced into South America
- Certain countries (e.g. Guatemala) had "dirty" water supplies
- Certain countries (e.g. Chile) had "clean" water supplies
- Prediction:
  - V. cholerae should evolve to lower virulence over time in countries with clean water supplies, but should remain virulent in countries with dirty water supplies.

Vibrio cholerae in South America



Moral of the story…

- Things that facilitate transmission from an infected host will LOWER THE COSTS of virulence for the pathogen and lead to the evolution of increased virulence:
  - Biological or mechanical vectors
  - Overcrowding
  - "Sit-and-wait" pathogens
  - Cultural vectors

'Cultural vectors'

- cultural practices that inadvertently carry pathogens from infected, debilitated hosts to susceptible, healthy hosts
- = "like a mosquito"
- favor the evolution of increased virulence

e.g. Washing dirty sheets near drinking water supply

Moving between hospital patients without washing hands

Social pressure to go to work when feeling sick

Big, Fat Moral

- There is a "hidden" evolutionary benefit to decreasing pathogen transmission rates
  - Obvious benefit: decreased incidence of infectious disease
  - Hidden benefit: confers a selective advantage on benign variants of pathogens
    - will cause pathogens to evolve towards decreased virulence

Evolutionary Medicine

- Traditional view of disease control
  - Goal: eradicate pathogens
  - or, at least confine them and limit their transmission
- Evolutionary view of disease control
  - Goal: select for benign variants of pathogens
  - Do NOT eliminate pathogens, but allow benign forms to circulate freely
  - Use evolutionary interventions to "domesticate" pathogens

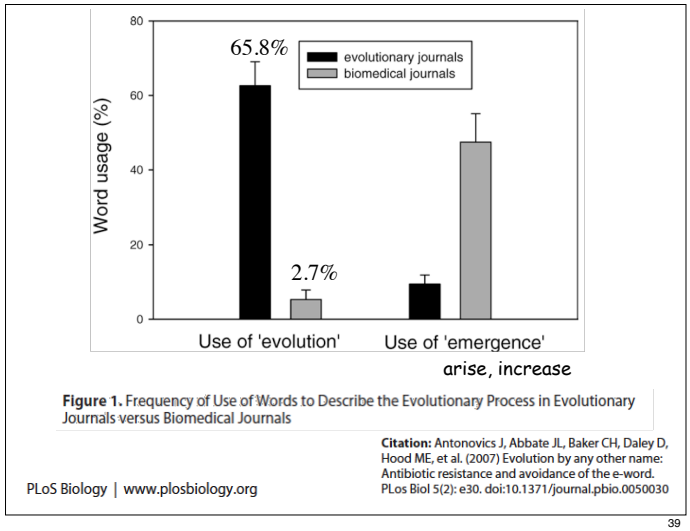


Figure 1. Frequency of Use of Words to Describe the Evolutionary Process in Evolutionary Journals versus Biomedical Journals

Citation: Antonovics J, Abbate JL, Baker CH, Daley D, Hood ME, et al. (2007) Evolution by any other name: Antibiotic resistance and avoidance of the e-word. PLos Biol 5(2): e30. doi:10.1371/journal.pbio.0050030

Impact on the public perception of science.....

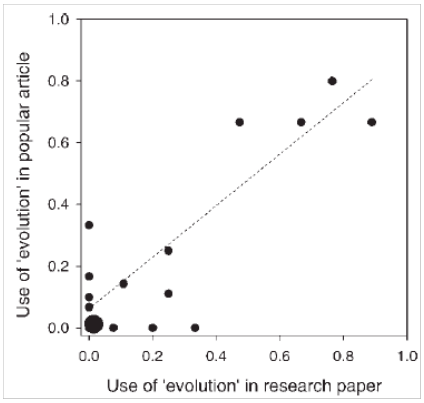


Figure 2. Use of "Evolution" in Popular Articles Based on Research Papers