EVOLUTIONARY MEDICINE

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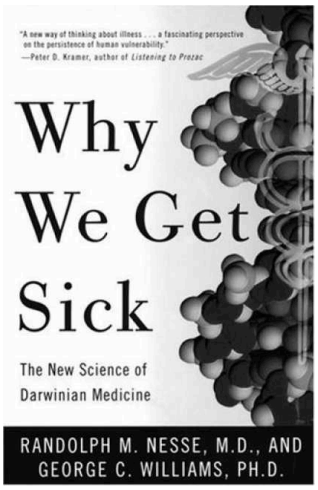
What is Evolutionary Medicine?

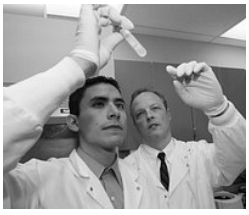
- Health and disease of humans
- Presents a distinction between proximate and ultimate levels of analysis
- Phylogeny - evolutionary history – phylogeny
- Adaptation – function or benefit

More than just genetics, more than development, more than just history.



Evolutionary Medicine

- Human vulnerabilities to diseases
- Research + Clinical Applications



Medicine

Older than the field of evolutionary biology.

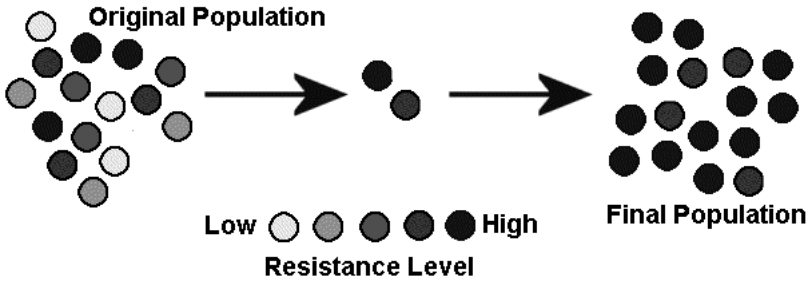
Medical "practice" may date to earliest social humans

Not quick to embrace evolutionary biology

Example

- Pathogens develop antibiotic resistance
- Multidrug resistant TB, Methacillin resistant Staph Aureus (MRSA). HIV
- Language of medicine: we don't talk about the ***evolution*** of resistance, we talk about bacteria ***developing*** resistance.
- In fact we are seeing evolution on action! How do bacteria become resistant?

Bacterial population



Natural Selection

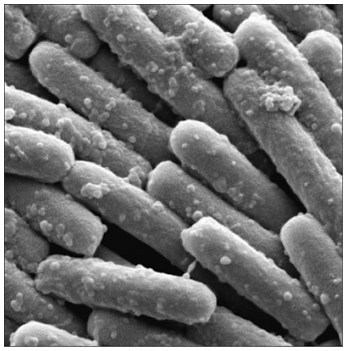
- Natural selection is the engine of evolution
- Natural selection was the insight of Darwin and Wallace back in the 1850s.
- When antibiotics are given to a human population natural selection favors resistant strains
- How?

VIST

- Variation
- Inheritance
- Selection
- Time

Change in gene frequencies

- Heritable variation + Selective pressure +Time
- Add antibiotics & mutant bacteria will reproduce much faster than bacteria without the mutation.



Clostridium difficile
binary toxin positive

Simple?

- Does this happen in people? You bet! It just happens a lot slower in people than bacteria
- Example: resistance to pathogens. Malaria infects 300 million yearly. 1 million die.
- RBC mutations are more prevalent in populations where malaria occurs.

Evolution by natural selection

- Changes in gene frequencies – changes in survival and reproduction.
- All you need is genetic variation and differences in reproduction

Key Questions

- Natural selection allows the healthiest and most disease-free individuals to survive and pass their genes. Wouldn't humans evolve towards health?
- Obviously this doesn't always happen
- Selection apparently maintains genetic "achilles heels" in generation after generation.
- Breast cancer genes, genes that cause Alzheimer's disease. !?

Key Insights

- You are product of innumerable ancestors who survived until reproduction
- Natural selection should promote survival during childhood and early adulthood
- Selection rewards reproductive success not longevity

Levels of analysis

- Most medicine is concerned with what and how questions.
- Evolution concerns itself with historical why questions.

Levels of analysis

- Proximate answers - Physiology and Pathophysiology
- Ultimate answers: reproductive advantages & disadvantages of traits.

Levels of analysis

- During this semester we will ask ourselves lots of "why" questions about diseases.
- Why do illnesses exist?
- What makes certain diseases common?
- Why hasn't natural selection eliminated the genes that cause diseases?
- What are the implications of asking these questions?!

Example: Pain

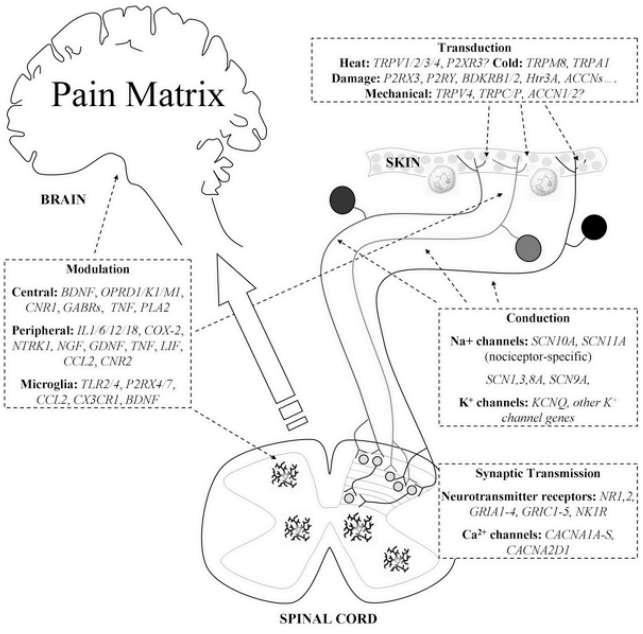
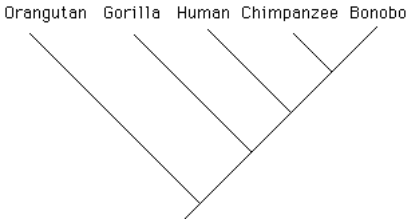


Figure 1. Genes Involved in Pain Perception and Modulation.

Examp
Pain

Evolutionary Explanations for Diseases

- Trade-offs and Constraints
- Evolved host defenses
- Evolution of virulence
- Gene-environment mismatch
- Host-pathogen arms race
- Genetic conflict in reproduction
- Antagonistic pleiotropy

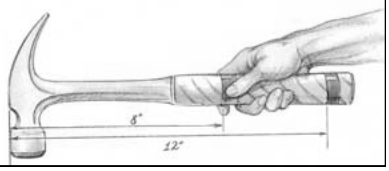


Evo Med Hypotheses

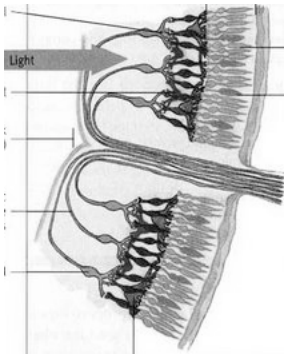
- Two main categories:
- Phylogeny (history)

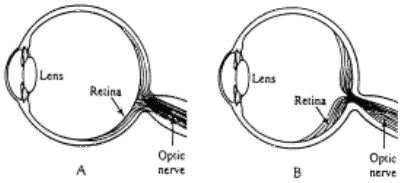
  what series of historical events led to predominance of a particular set of traits?
- Adaptation

  what (function) reproductive benefit does an inherited trait confer?



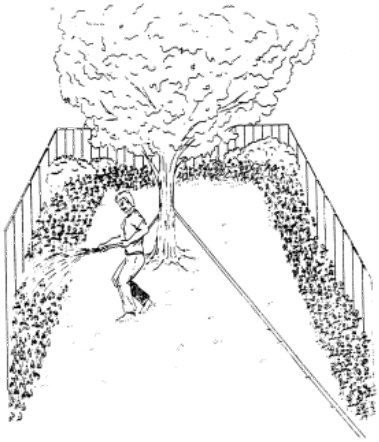
Phylogeny can explain puzzling phenomena – blind spot

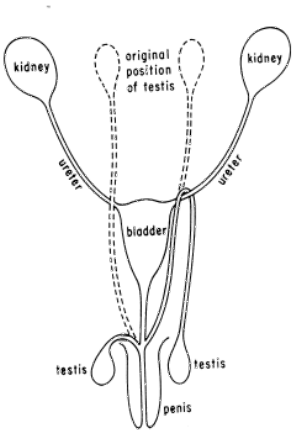




- Constraint of history
- Human Inverted Retina – optic nerve has to puncture the retina

Phylogeny can explain puzzling phenomena – hernias





(from G. C. Williams, Plan and purpose in nature, p. 144)

Tradeoffs and Constraints

- Large neonate head size vs limits of maternal pelvis – cause some childbirth injuries/deaths
- Why can't female pelvis accommodate a larger head size?

Unnecessary anatomy?

- <- Tonsils surgery becoming much rarer.

- Appendix –>

Surgery for Appendicitis: Is It Necessary? Surg Infect (Larchmt). 2008 Aug 7.

Concept: Cryptic Function - Benefit

- Some diseases might be explained by a hidden benefit
- Benefit does not have to be to the person suffering from the disease
- Might accrue to a pathogen
- Or to a sexual partner
- Or to a person in a different environment
- Or to individuals with a different combination of genes

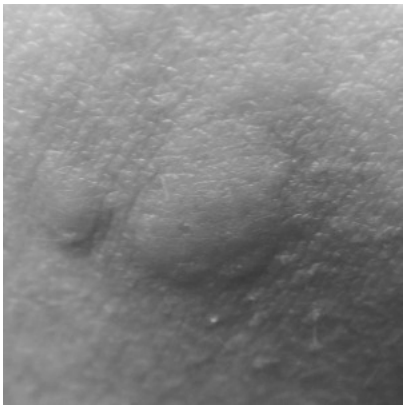
Evolved Host Defenses

- Cough
- Fever
- Nausea
- Diarrhea

- Symptoms may give pathogens a reproductive advantage– or may help humans survive infections

Example: Itch

- Why does a mosquito bite itch?
- Does itch have a function?



Evolution of Virulence

PSEUDOMONAS OUTBREAK LINKED TO NURSES' FINGERNAILS.

Infectious Disease

AJN, American Journal of Nursing. 100(7):17, July 2000.

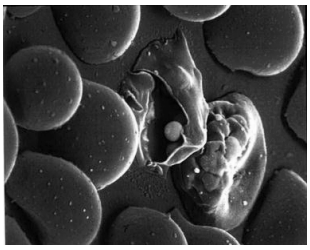
- Artificial nails and hospital setting benefit pathogens
- Easy transmission leads to more virulent bugs
- Community acquired and Hospital acquired pneumonia

Heterozygote advantage

- In Sickle cell, benefit accrues to heterozygotes in malarial areas
- Others suffer disease

Host-Pathogen Arms Race

- Defense against pathogens becomes increasingly costly as bugs learn to evade defenses.



Genetic Conflicts in Pregnancy

- Gestational Diabetes
- Cryptic benefit accrues to paternal genes

Evolution of Aging

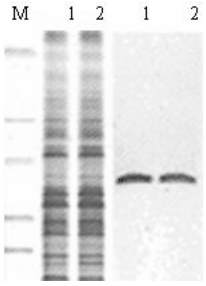
- Declining power of natural selection
- Genes with more than one effect.

Why bother?

- Hidden assumptions.
- Important insights.

Evolutionary Viewpoint - Research

- Leads to new hypotheses
- Helps explain existing findings
- Can inform directions for future work



Education

- Education:
- Gives a framework for understanding normal and abnormal physiology
- Has potential to place lots of disparate facts in context

Evolutionary Viewpoint

- Clinical medicine
- Healthy skepticism

- Helps define "disease" and "normal"
- Default: *most* "normal" physiology reflects selection for beneficial processes

Evolutionary Medicine Summary

- Incorporates well accepted basic principles of natural selection
- Asks "why" questions of disease
- Evolutionary explanations fall into discrete categories
- Can help guide clinical medicine, research and medical education