Fall 2026

ANTH B317 Disease & Human Evolution

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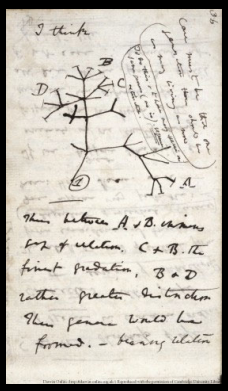
Dalton 310
OH: Thursdays 2:30-4:30
and by appt



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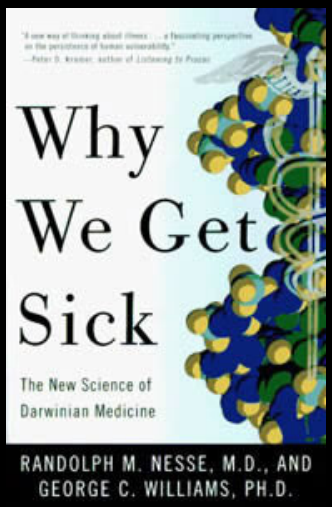
What is evolutionary medicine?

- Application of insights from evolutionary theory to biomedicine
- Relatively new field
- Nesse & Williams (1994) *Why We Get Sick*



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Why do we get sick?

- Two levels of explanation:
  - Proximate (mechanistic)
  - Ultimate (evolutionary)
- Biomedicine mostly focuses on proximate explanations, but… nothing in biology makes sense except in the light of evolution (Dobzhansky, 1973)
- Or… medicine without evolution is like engineering without physics (Nesse, 2016)

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Tinbergen's four questions

The Four Areas of Biology		Two Different Objects of Explanation	
		Developmental/Historical Explanation of current form in terms of a sequence	**Single Form** Explanation of one form of a species
Two Different Kinds of Questions	**Proximate** Explains how organisms work by describing their structures and mechanisms and their ontogeny	**Ontogeny** Description of an organism's development, from DNA code to the forms of different life stages ***Developmental explanations*** for sequential changes in individuals across the lifespan	**Mechanism** Description of an organism's structure and how its mechanisms work ***Mechanistic explanations*** for ***what*** an organism's structures are like and ***how*** they work
	Evolutionary Explains why organisms are the way they are by describing how selection shaped current forms and their phylogeny	**Phylogeny** Description of the history of a species as reconstructed from its fossil precursors and DNA evidence ***Phylogenetic explanations*** for sequential changes in a species across time	**Adaptation** Explanation for the characteristics of a species based on how they give a selective advantage ***Evolutionary explanations*** for ***why*** an organism is the way it is.

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Five Kinds of Objects of Explanation	Two Kinds of Evolutionary Questions	
	PHYLOGENY *(Macroevolution: History & relationships)*	**ADAPTIVE SIGNFICANCE** *(Macroevolution: Selection and Drift)*
Human trait	**Phylogeny of traits** Lactase persistence, Ethanol sensitivity, Blood types, HLA types Skin color, Malaria resistance	**Adaptive significance of traits** Aging, Bilirubin Narrow birth canal, Fever, Cough, Anxiety Stress response
Human gene	**Tracing the phylogeny of alleles that cause disease** Sickle cell disease Cystic fibrosis, ApoE Asthma vulnerability alleles	**Possible adaptive significance of alleles that cause disease** Sickle cell disease Cystic fibrosis, ApoE Asthma vulnerability alleles
	Population genetics, Evolutionary genetics, Signals of selection	
Pathogen trait	**Evolutionary history of pathogen traits** Virulence, Antibiotic resistance, Ability to survive outside the body, Biofilm formation	**Possible adaptive significance of pathogen traits** Virulence, Antibiotic resistance, Ability to survive outside the body, Biofilm formation
Pathogen gene	**Tracing the phylogeny of pathogen alleles** Tracing and predicting influenza subtypes, Source of food poisoning, HIV evolution	**Possible adaptive significance of pathogen alleles** Alleles that influence virulence, Antibiotic resistance, Biofilm formation, Spore formation
Cell lines	**Cancer**	**Immune system cells**

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From levels to a continuum

- Bergman & Beehner (2021): temporal timescale across generations

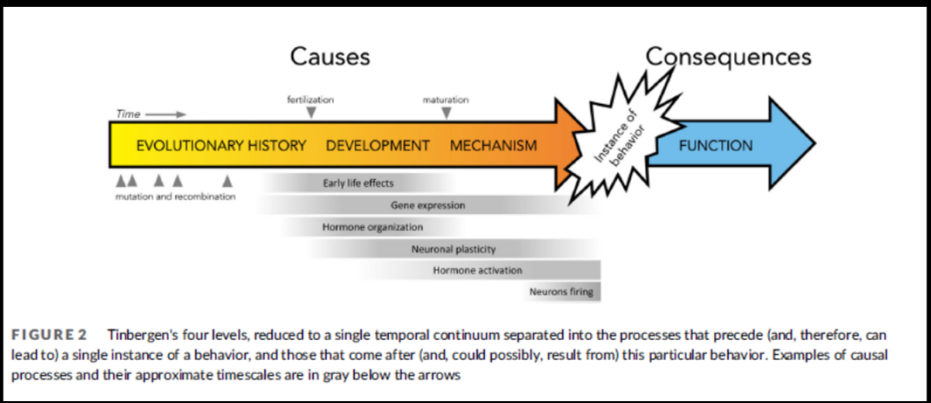

FIGURE 2 Tinbergen's four levels, reduced to a single temporal continuum separated into the processes that precede (and, therefore, can lead to) a single instance of a behavior, and those that come after (and, could possibly, result from) this particular behavior. Examples of causal processes and their approximate timescales are in gray below the arrows

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Applications for medicine & public health

- Generating new research questions that can shed light on:
  - Pathogen phylogenies (vaccines, origins of disease…)
  - Gene + environment interactions
  - Evolutionary genetics (some genetic conditions potentially result of selection)
  - Aging
  - Infectious disease & adaptations to disease

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Why are we vulnerable to disease?

1. Natural selection is constrained
   - Can't start from scratch
2. Natural selection is usually slow
   - Host-pathogen arms race
   - Mismatch with modern environment
3. Selection is all about reproduction, not health or longevity ("healthspan")
4. Many symptoms are evolved defenses
   - fever, cough, vomiting, anxiety, depression…

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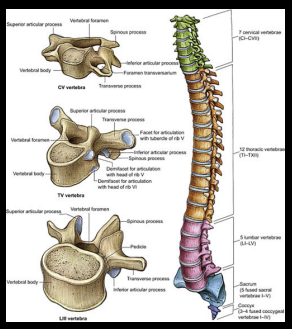
1. Constraints for natural selection

- Natural selection only operates on variation that is present–can't redesign something
- E.g. lower back pain associated with bipedalism



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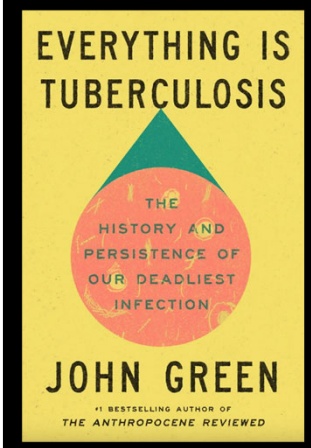
2. Host-pathogen arms race



- Drug-resistant pathogens might be biggest public health risk by 2050
  - Death toll could increase 70%
- Pathogens evolve faster than hosts: need new approaches that don't create a selective pressure for defense evasion!
- Availability of treatments

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2. Mismatch with modern environments

- Cultural and economic transitions associated with increases in non-communicable "diseases of civilization"
  - Health and well-being reflect social, cultural, political and economic dynamics
  - Developmental plasticity and developmental origins of health and disease (DOHaD): ancient vs modern environments

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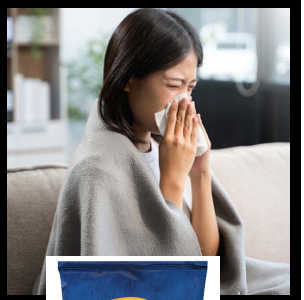
Mismatch: hygiene hypothesis

- Many people today live in much more sanitary conditions (lower parasite loads, fewer infections)
- Could autoimmune and allergic diseases result from an immune system that doesn't have enough to do?



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Mismatch: APOE-4

- Gene variant that increases risk of dementia and cardiovascular disease up to 4x; worse cognitive aging in carriers
- high frequency of APOE-4 in tropical populations (e.g. Tsimane): associated with better cognitive performance!
- Key difference: in environments with high parasite load

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3. Selection is about differential reproductive success

- … not health or well-being!
- Genes associated with benefits early in life will be selected for even if bad later, or if it doesn't work out for all individuals
- Negative effects that occur after one has reproduced are hidden from selection
- Evolutionary trade-offs between growth, maintenance, and reproduction

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Remember APOE-4?

- APOE-4 in the Tsimane is also associated with higher fecundity!
- Women who have at least one copy of the APOE-4 gene have higher fertility levels and shorter inter-birth intervals
  - Natural fertility population, ergo, higher reproductive success compared to those with no copies of the gene: will be selected for no matter what it does to the individual later

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4. Symptoms: evolved responses?

- Many "classic" symptoms of disease are in fact evolved responses/defenses!
  - Coughing, sneezing, vomiting, diarrhea: ejecting toxins/pathogens from the body
  - Anxiety, depression: avoidance of behaviors associated with negative outcomes
  - Need to recognize difference between "normal" responses from maladaptive ones (e.g. excessive cough suppression post-surgery can lead to pneumonia)

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Smoke detector principle

- Protective responses often give rise to false alarms and apparently excessive responses: frequent annoyances that are necessary to avoid possible catastrophes
  - Maladaptive if triggered too often, too high a degree
- Anxiety, inflammation, pain, vomiting, anxiety, cough and diarrhea are protective responses whose costs tend to be small relative to possible catastrophic costs of failing to respond

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The spandrels of San Marco

- Gould & Lewontin (1979) – danger of confusing *function* with *adaptation*

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Pitfalls of evolutionary medicine

- As with all evolutionary approaches, risk of over-interpreting phenomena as resulting from natural selection ("adaptationism")
- A lot of traits evolve by genetic drift—should be the null hypothesis
- Hard evidence for selection can only come from population genetics
  - Selection acts on individuals, but it's the population that evolves

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"Just so stories"

- Current utility is not necessarily the reason *why* a feature evolved
- Correlation is not causation!
- "just so stories" – speculative, cannot be (or are not being) tested
  - Common issue in studies of human behavior (e.g., evolutionary psychology) or morphology (e.g., paleoanthropology)
  - Ethical and practical limitations

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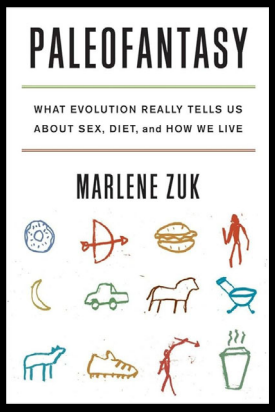
Paleofantasy

- No organism is, or ever was, perfectly adapted!
- Humans never had a singular "ancestral" environment or diet
- Evolution can act quickly in face of strong positive (e.g., lactase persistence) or negative selective pressures (e.g., malaria)



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Beyond adaptationism or paleofantasies

- In absence of genetic data, you cannot really test which evolutionary forces are acting on the trait
  - You can observe, measure, compare, etc, but you cannot know which evolutionary force is driving it—and that's OK!
  - Documenting patterns is still helpful
  - Proof-of-concept approaches using models and simulations
  - Practical, tangible benefits still exist!

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Evo med applications

- Generating new research questions
- Better understanding of proximate and ultimate explanations of disease
- Better therapeutics
- Informing clinical approaches with the goal of improving patient outcomes
- Reducing or eliminating social stigma
- Informing public health interventions

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Evo med applications

	Disease causation	Disease prevention	Biomedical innovation
Role and opportunity	Better understand the etiology of diseases Forecast future disease burdens	Inform public health policy and disease prevention efforts	Accelerate transformational therapeutic innovation
Examples	Evolutionary and developmental mismatches, e.g. • obesity, type 2 diabetes, cardiovascular disease • allergy • microbiome change • mental health Infectious disease epidemiology, e.g. • evolution in virulence and transmissibility (including COVID-19/SARS-CoV-2 and future pandemics) Life history trait evolution • growth, reproduction, and survivorship dynamics Human behavior, e.g. • inclusive fitness vs survival trade-offs		Cancer, e.g., targeting cancer resistance evolution • adaptive approaches • extinction approaches Infectious diseases, e.g., targeting antimicrobial resistance evolution • anti-antibiotics • phage therapy

https://doi.org/10.3389/fsci.2023.997136

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One Health approach

- Formalization of the concept that human, animal and environmental health are all interconnected
  - From the CDC: a collaborative, multi-sectoral, and transdisciplinary approach – working at the local, regional, national, and global levels – with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment

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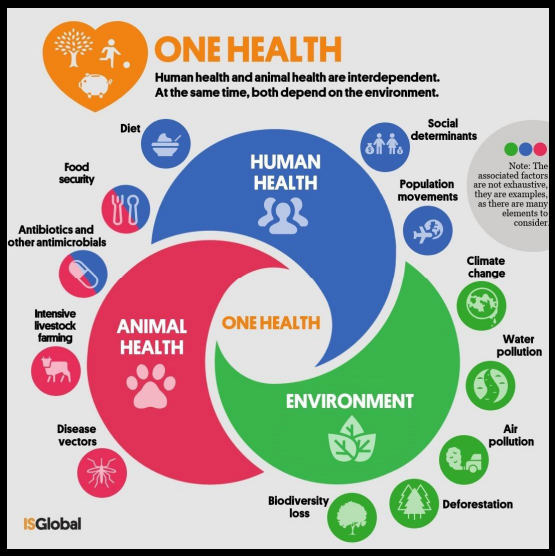
One Health triad



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