Evolutionary Medicine\_Annotated Bibliography

**Gluckman and Hanson 2004**

Developmental Origins in Disease:

Being born small

* Very little genetic component: mostly reflection of quality of intrauterine environment
* Significant relationship between birth size and diabetes/hypertension risk

🡪Doesn’t imply causal role of birth weight. Reflects sensitivity of fetal growth to adverse influences

🡪 “maternal constraint” – may limit birth size

Nutrition and future risk

* Pan-undernutrition and Low-protein/ high fatimpact cardiovascular and metabolic functions
* Undernutrition suppresses placental 11-Beta-hydroxysteriod dehydrogenase type 2, which inactivates cortisol and exposes fetus to excessive maternal steroid

Predictive Adaptive Response

* Future adaptive value: developmental plasticity to set post-natal phenotype to be better fit for expected environment.
* “Maternal Effects”: experiences in one generation effects multiple future gens
  + 🡪 transgen passage of epi change? Or effect on reptro tract of F1 gen
* “Thrifty genotype”- populations have been selected for alleles favoring insulin resistance (confer advantage in poor food/ high energy expenditure environment, reduces glucose uptake and limits body growth)
* “Thrifty phenotype” – fetus becomes growth retarded in response to adverse environmental conditions in utero

Developmental origins of the metabolic syndrome

* Adverse embryonic and fetal envt induce structural and functional abnormalities in the pancreatic islet cells and lead to permanent changes in insulin sensitivity.
* Homeostatic response vs. Predictive Adaptive Response: immediate survival advantage (trade-offs) vs. induced expectation of future adaptive advantages (not nec. Immediate)

Biological basis

* Epigenetic changes in gene expression (methylation)
* Altered tissue differentiation (i.e. adult nephron numbers are reduced in humans born small, and later develop hypertension.)

🡪May be biological tradeoff to conserve energy in response to deprivation during crucial development period, having immediate, but not longterm adaptive value.

* Non-adaptive, developmental disruption in cell differentiation (i.e. B-cell apoptosis increased in rats whose moms were fed low-protein diet, perhaps bc of increased sensitiviety to cytokines)
* Altered homeostatic processes: low protein diet in rat moms led to altered ratio of periportal to perivenous hepatocytes…

Evolutionary Perspective

* Without PARs, models suggest transient enviro change could drive gene pool to extinction.
* Selection favored PARs that allowed the indiv survival to reproduction.
* In early hominids, life expectancy was short and post-natal enviro was likely restricted, there wouldn’t have been selection against insulin-resistant phenotype. Only now, in modern enviro, do we see deleterious effects.

Patterns of Disease

* Enviro mismatch- fetus expecting resource deprivation, but being born into abundance increases risk of obesity, central adiposity, insulin resistance.
* Importance of Nutritional Transition (4-5)

Transgeneration Effects

* Women whose mom’s experienced famine in 1st trimester (and thus were born smaller), also had children who were smaller. Epigenetic?

**Stearns 2012 Evolutionary Medicine: it’s scope, interest and potential**

Stearns, S. C. (2012). Evolutionary medicine: its scope, interest and potential. *Proceedings. Biological Sciences / The Royal Society*, *279*(1746), 4305–21. doi:10.1098/rspb.2012.1326

Issues

* Medically significant genetic variation (i.e. lactose and alcohol-intolerance, lack of drug metabolization, variation for disease resistance
* Mismatches to modernity

1. the Old Friends/Hygeine Hypothesis
2. Contraception and breast cancer (# of cell divisions has increased in non-natural fertility populations- increasing risk of breast cancer

* Reproductive Medicine:
  + 3 hypotheses on evol of menopause
    - Mother Hyp (Williams): if probability of mother dying in childbirth or child dying in infancy increases w age, selection (at some point) should favor mothers who stop reproducing to ensure survival of their last child
    - Grandmother Hyp (Hawkes et al): help daughters rear infants
    - By-product of some function of oocytic atresia
  + Conflicts, parent-of-origin imprinting and maternal investment.
    - Hamilton: kin selection-genes can be selected to increase representation in future generations by influencing behavior of relatives.
    - Trivers: selection favors offspring behavior to increase maternal investment at expense of future sibs.
    - Moore and Haig: mat/pat conflict, mediated by parent-of-origin imprinting. Silencing of genes in parental germ line of genes expressed in the foetus and offspring; different genes are imprinted in father and mother. Father silences genes that would express the mother’s interests..
  + Quality control of gametes and concepti
* Degenerative Disease
  + The evolution of ageing
    - ANTAGONISTIC PLEIOTROPY! Selection lessens as we age- mutations that improved fitness early in life would be selected for, regardless of costs later in life. “reproduction-survival trade-off” ageing and lifespan are “bi-products” of selection for repro success
  + Cancer as an evolutionary process
    - Why do humans have more? (1) live longer (2) not yet adapted to new risk factors (smoking, alcohol, high-calorie) (3) by product of unusual reproductive cycling.
  + Pathogens in Degenerative Disease
    - Insertions and transpositions of retroviruses in the genome that cause genetic change and instability – increase cancer risk
* Pathogen Evolution
  + Virulence (increase in host morbidity and mortality caused by pathogen)
    - Vertically vs. horizontally transmitted viruses: selection pressures are different. Selection for avirulence when parasite is transmitted from parent-offspring
      * i.e. myxomatosis- virus used to control rabbit population, over the course of decade, evolved intermediate virulence (uses hosts resources, but not enough to kill host before it’s transmitted)
    - Evolution of antibiotic resistance
      * Doesn’t arise from de novo mutations, but instead from horizontal transfer of resistant genes. (via plasmids, viruses, direct uptake of DNA released by dead bacterial cells)
    - Evading and suppressing immune system
    - Host tolerance
      * Defensive device- as it leads to longer lives, given decreased selection on evasion and suppression in pathogens
    - Emerging disease
  + Evolution of complex parasite life-cycles
    - Upward incorporation: Infected host (containing parasite) is consumed by a predator --> if parasite survives and flourishes in new host (is able to use new hosts resources), there is evolution toward host higher up in the trophic chain, which adds is added to the life cycle of the parasite. The initial host may become the intermediate host in the future life cycles of the parasite (the parasite might use this intermediary as a place to grow and mature, but not reproduce)
    - Downward incorporation: newer host (lower in the trophic chain) is added to the parasites life cycle; new host is added by virtue of it’s usefulness to be found by main (OG) host.
  + Comparative medicine: insights from other species

Barrett, R., Kuzawa, C. W., McDade, T., & Armelagos, G. J. (1998). EMERGING AND RE-EMERGING INFECTIOUS DISEASES: The Third Epidemiologic Transition. *Annual Review of Anthropology*, *27*(1), 247–271. doi:10.1146/annurev.anthro.27.1.247

Trotter et al 2010: Linking ecological immulology and evolutionary medicint: the case for apolipoprotein **Evolutionary Medicine**: seeks to understand whether and to what extent aspects of disease are adaptations for coping with infections or injuries, or the consequence of mismatches between modern and ancestral environments.

**Ecological Immunology**: focuses on how organisms balance investments in immune defenses against other traits (e.g. cognitive and reproductive functions) to maximize fitness.

Organisms evolve optimal (not maximal) immunity- selected to maximize reproductive fitness, not longevity

Argument: ApoE allelic variants and their associations with disease represent the outcome of previous selection (i.e. genetic accommodation) for particular plastic phenotypic responses in ancestral environments that are often non-adaptive in modern environments.

* ApoE allelic variation and immune function
  + apoE variants differentially balance investments in immune function vs. other traits (apoE is great route for infection and a way for hosts to convey information to lymphoid tissues abt availability of lipids and cholesterol.
  + Carriers of apoE4 have a more inflammatory phenotype (more IL-8 and TNF-alpha)
* Carriers of Apo2 are longer-lived (under-representation of apo4 in elderly)
* So why apoE 4 and not apoE2 or apoE3, which seem less costly (cause less of an inflammatory response)?
  + apoE4 may have been favorable in population with short life expectancy where individuals wouldn't live long enough to experience effects of collateral damage.
  + Reproductive: apoE4 has a role in mediating tradeoffs among competing traits (greater reprod success of apoE4 carriers in their environment of evolutionary adaptedness)
  + Cognitive: apoE4 in young carriers associated with increased cognitive ability also, enhanced spatial learneing

Monaghan, P. (2008). Early growth conditions, phenotypic development and environmental change. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *363*(1497), 1635–45. doi:10.1098/rstb.2007.0011

Environmental influences on phenotypic development likely to mediated (in part) by endocrine system.

Phenotypic and environmental changes

* Reaction norms: range of phenotypes that can be produced by a single genotype in the environments in which it can survive
* Phenotypic plasticity: exhibiting alternative phenotypes to match prevailing local conditions
  + Phenotypic changes to mitigate the detrimental effects on fitness—trade-offs, which may involve selective allocation of resources to some organs rather than others when conditions are poor; beneficial effects of different life history stages (i.e. compensatory growth in stunted children usually associated with reduced lifespan)

Interaction between development and adult environments

* “Quality continuum” in environment (weather, predator, or socially imposed)
* Environmental mismatch

Predictive Adaptive Response

\*\*\*why isn’t this being more talked about? You have thrifty phenotype, but usually individuals in these environments don’t go from resource poor to healthy abundance—they usually go from resource strapped to exploited environments where they only have access to poor quality nutrients\*\*\*

**Bogin, B., & Loucky, J. (1997). Plasticity, political economy, and physical growth status of Guatemala Maya children living in the United States. *American Journal of Physical Anthropology*, *102*(1), 17–32. doi:10.1002/(SICI)1096-8644(199701)102:1<17::AID-AJPA3>3.0.CO;2-A**

Plasticity: the ability of many organisms to change their biology or behavior during ontogeny to respond to changes in the environment

Political Economy: the study of how people or groups of people living under conditions of constraint allocate scarce resources within their hierarchy of goals.

**Chubb et al. 2010. Living in intermediate hosts: evolutionary adaptations in larval helminthes**

Given the small size of helminthes, yet the greatest fitness advantage of occupying a large host, helminthes oft take advantage of intermediate hosts, during which time their larvae incubates, before being transmitted to the definitive host. The three sets of selection pressures that shape lives of helminthes in their intermediate host are:

* Growth
* Survival
* Transmission to the next host