Evolutionary Medicine

Adaptive Lag

* Deviations from the human environment of evolutionary adaptedness (EEA) are often thought to be detrimental to health because of the mismatch between our modern environment and that which our genes have adapted to for much human evolution (Eaton et al. 1988).
* Adaptive lag is inevitable because genes cannot respond instantaneously to environmental changes.
* However, remarkable growth in human population size and longevity seem to indicate that a major proportion of human characteristics remain adaptive even in modern constructed environments.

Non-genomic “adaptations”

* Cultural Adaptation/Behavioral Responses
  + Conventional wisdom: Environments are the source of selection, so organisms must adapt to their environment, not vice versa.
  + Niche construction perspective: Organisms drive environmental change and organism-modified environment subsequently select organisms (Lewontin 1982, 1983; Odling-Smee et al. 2003)
    - Humans are able to alter their environment to suit themselves and buffer adaptive lag through cultural niche construction (Laland and Brown 2006).
  + Cultural responses to modified selection pressures typically occur more rapidly than genetic responses do.
    - Despite drastic differences between the EEA and our modern environments, the last 4 of the roughly 8000 human generations that ever lived have experienced a remarkable increase in longevity (Burger et al. 2012).
    - Throughout most of human history, the world population remained fairly stable, but in the last 200 years, the population grew from about 1 billion in 1800 to 7 billion in 2011 (Bloom 2011).
* Physiological Acclimation and Acclimatization – reversible reactions to stimuli at any time; individual level
* Developmental plasticity – Genes can generate a range of possible phenotypes contingent on environmental experience during development
  + Developmental programming (1991) or induction (Bateson 2001) – an environmentally induced, durable biological change in the structure or function of a tissue, organ, or biological system

Intergenerational Epigenetics

* Nutritional, hormonal, and other aspects of prenatal and infant environments have effects on physiology and metabolism that persist into adult life (Barker 1994).
  + Thrifty genotype hypothesis (Neel 1962, 1999) – high rates of diabetes among some populations might trace to stressful intrauterine environments rather than to susceptibility alleles. This hypothesis fits under more conventional genetic adaptation.
* Thrifty phenotype hypothesis – Prenatal undernutrition induces insulin resistance, a shift in circulation to protect the brain, and a nutrient-conserving reduction in organ growth. In other words, the brain must be protected from short-term nutritional shortages. These adjustments enhance immediate fetal survival but subsequently increase the risk of adverse health later in life. (Hales and Barker 1992)
  + The Forecast Model – fetal adjustments to prenatal nutrition are not merely designed to improve immediate survival, but also are initiated in anticipation of nutritional conditions during childhood (Bateson 2001).
  + Predictive Adaptive Response – using prenatal cues, the fetus adjusts its physiology to be appropriate for its predicted mature environmental range (Gluckman and Hanson 2004).
    - The resulting mismatch between expected and experienced adult environmental conditions elevates risk for disease.
    - Fetal metabolic responses to undernutrition are presumed to have evolved to confer benefits primarily during adulthood.
    - However, selection late in life is minimal! (Jones 2005; Kuzawa 2005; Wells 2007)
    - The human lifespan is long, so transient environmental fluctuations, which are partially stochastic, cannot be good cues for conditions later in life. Predictive ability decays with time.
  + Wells (2003, 2007, 2011) – Thrifty phenotypes are induced to match the level of likely provisioning after weaning, as reflected in the mother’s life course and pregnancy nutritional exposures.
    - The tradeoff between offspring nutritional demand and maternal capacity to supply represents a multigenerational tracking of ecological quality and maternal provision.
    - Wells’ model links offspring phenotype to maternal characteristics (manipulation of provisioning), rather than forward-looking predictions based on environmental cues.
    - Wells’ model assumes that the focal point of selection on metabolism to be weaning. However, nutritional mortality during the juvenile period is low, so metabolic selection is probably stronger in the prenatal or infancy period. Adult disease is more likely a pleotropic side effect of an adjustment in metabolic priorities that improve fetal or infant survival. (Kuzawa and Quinn 2009)
  + Phenotypic Inertia – Maternal phenotype could provide integrated information that records a mother’s lifelong cumulative experiences and might have long-term predictive value, even in stochastic environments. (Kuzawa 2005)
    - Slow responsiveness of transgenerational nutritional cues may reflect a lingering effect of a woman’s nutritional history on nutrient transfer to offspring (Wells 2003, Kuzawa 2005).
    - This concept can be extended to the hypothalamic-pituitary-adrenal axis, which regulates the stress hormone cortisol (Belsky 2008).
    - Offspring phenotypes that are calibrated for future function (e.g. reproduction) will be more strongly predicted by long-term maternal or matrilineal experience than by acute maternal experiences during pregnancy (Kuzawa and Quinn 2009).

Distinguishing impairment/pathology from adaptive function

* Acute ecological stress during gestation may permanently modify offspring biology as a result of incomplete buffering

Coevolution with pathogens: Pathogens have shorter generation times, so natural selection makes them evolve faster than humans (Ewald 1994).

* Evolution of virulence: Tradeoff between pathogen exploitation of the host and reliance on host for transmission. Death is nearly always costly to both parasite and host (Ewald 1994).
* Conventional wisdom: Pathogens should evolve toward benign mutualism with their host. Harmful diseases are thought to be exhibiting maladaptation.
* Adaptive severity hypothesis: The greater the cycling in humans, the more sever the disease is in humans (Ewald 1983).
* Vector-borne pathogens are more virulent than directly transmitted pathogens.