Human Health and Disease Outline

1. Human Disease, Immune Responses, Fitness
   1. Human Diseases
      1. General
      2. Different impacts/risks for humans as compared to primates, other mammals
   2. Human Immune System
      1. Adaptations different from other mammals related to what aspects of human behavior/evolution/ecology
   3. Human/Pathogen Co-evolution and Arms Race
      1. Red Queen
         1. Pathogens have typically large population sizes and rapid reproduction and mutation rates
         2. Any counter strategy by host (immune response, treatment) will be further countered by a reciprocal evolutionary change in pathogen (and likely at a much faster rate)
      2. Evidence
   4. Immune and Growth/Fitness trade-offs
      1. Immune vs. Growth
      2. Immune vs. Reproduction
      3. Resistance vs. Tolerance
         1. Evidence for
         2. Evidence against: Nigerian children under 8 contribute most to parasite transmission (must harbor heaviest infections??) and also experience highest virulence (Mackinnon 2008). Does this support Kuris’ idea—that resistance and tolerance can’t be separated (if your risk of infection is high, you should also evolve responses that reduce pathology)
2. Evolutionary perspectives on human health and disease
   1. Evolutionary Medicine
      1. Pathogens can grow, reproduce, and mutate at rates that far exceed human reproductive rates or technological development; moreover human vaccines and antibiotics have placed enhanced selective pressures on the rapid evolution of resistant strains. *Nowhere is an evolutionary perspective more indispensible than in the development of effective and sustainable treatments of microparasitic diseases* (Williams 2009)
      2. Life-History trade-offs in virulence (reviewed Williams 2009)
         1. Tradeoff model assumes functional relationships between different traits (transmission, virulence, infection duration) constrain mutual evolution
         2. Pathogen fitness determined by transmission, infection duration and virulence—traits that are mutually dependent on the rate at which pathogens can exploit hosts. Alterations in the tradeoff structure (e.g. vaccines) induce novel selective pressures on exploitation strategies that in turn alter pathogen traits (Ebert and Bull 2003). So, when a virus (say influenza) is targeted by a vaccine, the number of potential hosts diminishes, placing selective pressure on the vaccine to perhaps develop more virulence, which alters host behavior (like sneezing coughing) to increase the likelihood of transmission. But that scenario is incomplete because what is the existing pre-vaccine trade-off and post-vaccine trade-off. Have to check but trade-offs likelty to be
            1. Rapid transmission favors high virulence—trade-off is killing the host, success in new host not guaranteed; pathogens can ONLY rapidly exploit host, can’t exploit host for a long period of time
            2. Infection duration—long dormancy or infection favors low transmission and low virulence?; pathogens can exploit one host for a long period of time (e.g. parasites); trade-off is diminished reproduction???
            3. Classic example: Myxoma system
            4. To date little empirical support, but may be relevant to HIV and malaria
         3. Vaccine-driven virulence evolution (reviewed in Williams 2009, see Gandon et al.)
            1. Infection-blocking and transmission-blocking treatments are non-selective
            2. Antitoxins and growth-suppressing treatments (which diminish infection-induced mortality—diminish virulence-- and reduce pathogen exploitation), however, select for increased exploitation and therefore greater virulence
            3. Enhanced immune clearance can also select for increased virulence (Porco 2005)
            4. However, above models assume homogenous populations; extremely susceptible and vulnerable hosts select for less-intense exploitation (you don’t want to kill your host before transmission can occur)—so targeting these populations selects for decreased virulence.
            5. Pathogens may evolve resistance, virulence, or both to vaccines (Table 1 in Williams 2009). Resistance develops in response to growth-suprresion??
         4. Immune evasion/escape (frequencies of different strains with different antigen profiles lead to temporal evolution) vs. game theoretical/life-history models (single variant vs. wild type mutant competing for eventual dominance)
      3. Source-sink dynamics (reviewed in Williams 2009)
         1. Environment consists of multiple connected dynamics which provide conditions conducive (sources) and not conducive (sinks) to population persistence; both conditions s are selective
            1. Adaptation to sink environments occurs with high migration rates and limited environmental harshness (?)
            2. Pathogen treatment strategies that reduce transmission produce sink environments among host population (pathogens are now operating at a demographic deficit with fewer potential hosts)
            3. May factor in evolution of antibiotic resistance and seasonal epidemics
      4. Applications (see Williams 2009 for review of medical applications—predictive modeling and targeted gene therapies—in vaccine development strategies based on evolutionary ecological principles that recognize need to gain a leg in arms race with multiple facets)
   2. Ecological Immunology
      1. Nutrition and Immune Function
      2. Ecological risks and local adaptations
      3. Seasonal risks and adaptations
3. History of Human Health and Disease
   1. Parasites
   2. Bacteria
   3. Viruses
   4. Old/World New World
   5. Modern Medicine, the war on pathogens, emerging resistance
      1. Antibiotics and vaccination programs after WWII led many to believe war against pathogens had been won. Yet today, developing and developed countries are plagued by novel (HIV/AIDS, Hepatisis C, SARS, foot-and-mouth disease, avian influenza) and re-emerging (malaria, cholera, tuberculosis) pathogens (Williams 2009), while long-standing parasitic diseases continue to cause significant morbidity and mortality in developing nations
      2. The causes of this recent epidemiological shift include environmental, social, and ecological factors (Williams 2009)
         1. Anthropogenic disturbance increases zoonotic transmission
         2. Increased disease susceptibility due to aging populations, emergence of concomitant innunosuprresive factors, increased urban populations (high-density)
         3. Widespreasd use of accines, antibiotics, and chemical therapies/eradication schemes by both medical and agribuisness has placed heavy selective pressure on viruses and bacteria, driving their evolution and giving rise to resistant srains
   6. Modern evidence of immune adaptations
      1. Malaria
      2. HIV
      3. Other STDs
   7. Diseases of Modernity
      1. Hygiene Hypothesis
      2. Chronic vs. Acute Disease