The Imperative to Vaccinate

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The Disease Legacy of Civilization

Human beings are almost certainly the most diseased species on earth. By one accounting, there are at least 1400 human pathogens, including bacteria, fungi, prions, protozoa, viruses, and worms, and of these, 100-150 appear capable of causing human epidemics.[1,2] Even this is likely to be an underestimate, as new and sensitive sequencing techniques continue to uncover new viruses at a steady rate.[3] We human beings are remarkable in many ways, but why are we remarkable for playing host to so many infectious agents? Why is it that we must maintain high levels of vaccine coverage to prevent infectious agents from sickening or even killing large swaths of the population? The answers lie in the story of human disease epidemics, and it begins with human cultural and technological ascendance and what we now understand to be its inevitable consequences for pestilence and death. It is about our ingenuity, which has caused the retreat of many infectious diseases, but highlights a central tension in human existence—immediate self-interest vs long-term collective welfare.[4] The concept is not just academic; there are real-world implications that we can resolve with an understanding of human disease ecology. The notion is that we are not only culturally connected or genetically connected through a common ancestry. Rather, there is another fundamental concept that is, perhaps, not widely accepted or even understood. We are biologically connected, in the present, through our exchange of infectious agents and our common susceptibility to disease.

To understand modern human disease prevalence, we have only to look to the most basic principles of epidemiology. A simplified version is that diffuse or small host populations cannot sustain an acutely infectious agent, meaning one in which infection is followed by clearance and long-term immunity. As the number of people with immunity increases, the density of susceptible hosts decreases, and with the corresponding decline in transmission, the infectious agent is not maintained in the population.[5] This principle described our preagricultural ancestors—a few thousand individuals congregated in groups but spread out over an enormous area.

Small or low-density populations can only sustain a certain type of infectious agent, one that persists, usually for the life of the host.[6,7] Once infected with herpes viruses, such as herpes simplex virus, cytomegalovirus, or Epstein–Barr virus, we are infected for life, and such viruses have infected us since even before we became human beings.[8-11] To some extent, this was the primordial state of disease in diffuse bands of preagricultural hunter–gathers: persistent viruses, bacteria (eg, *Mycobacterium tuberculosis*), intestinal protozoa, worms, and fleas. Our Paleolithic ancestors were not disease-free, but they almost certainly did not experience periodic and devastating epidemics.[12,13]

Conversely, large populations that live at high density, such as modern human beings, can sustain a much greater diversity of infectious agents, including those that the immune system is able to clear. Transmission from person to person is rapid enough and continuous, such that there is little selective pressure for persistence. Large and dense urban populations can maintain acutely infectious agents indefinitely due to a constant source of newly susceptible hosts in the form of immigration or births. These agents often share an ability to be transmitted by casual contact such as respiratory droplets produced by a cough or a sneeze, and as evidence of the success of this pathogen strategy, there are more than 200 different viruses from at least 6 different virus families (adenovirus, coronaviruses, influenza virus, parainfluenza virus, respiratory syncytial virus, and rhinovirus) that cause "cold" symptoms: sneezing, coughing, and runny nose.[14]

The dawn of agriculture and the domestication of animals, especially herd animals, allowed the emergence of permanent human settlements and the growth of large situated communities.[15] The world's population increased approximately 1000-fold from the beginning of the agricultural revolution to the end of the 19th century, and most importantly, settlements eventually grew into a huge massing of humanity. Simultaneously, we domesticated animals and ourselves, and we sampled all of the viruses and bacteria existing in cows, horses, pigs, sheep, goats, and birds. Those that could replicate in human beings and spread from person to person by respiratory propulsion (or other means, such as fecal–oral) became established evermore in the human population. This is the answer to why we are the most diseased species on earth. We are the only species to so profoundly and rapidly change the way in which we interact with each other and other animals; in other words, we invented for ourselves an entirely new ecosystem. So, in addition to the endless parade of cold viruses that circulate among us, we acquired a great many deadly infectious agents, such as those that cause diphtheria, influenza, measles, meningitis, mumps, plague, rubella, smallpox, typhus, whooping cough, and others. Each disease has its own history and severity, but all rely on large, high-density populations for continued propagation.

MMR	Measles, mumps, rubella
VICP	Vaccine Injury Compensation Program

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These newly acquired infectious agents not only caused severe or deadly disease, they shaped the population. Many are known as childhood diseases because they infect susceptible children who either recover from the disease and retain immunity or die. In a population in which a disease like measles existed, everyone contracted the virus exactly once, such that almost all surviving adults were immune. What does the world look like in the face of measles? From 1956 to 1960, before the availability of a vaccine, an average of 542 000 cases of measles were reported each year in the US, along with an average of 450 measles-related deaths, 4000 encephalitis cases (often with permanent brain damage), and 150 000 respiratory complications. The measles vaccine was licensed in 1963 and the measles, mumps, rubella (MMR) vaccine was licensed in 1971. For the years between 1987 and 2000, the number dropped to 28 730 cases of measles in children younger than 5 years of age; 97 died, 43 contracted encephalitis, and 2480 contracted pneumonia. Since 1997, there has been less than 1 case per million population in the US.[16] The global burden of measles in 1999 was an estimated 873 000 deaths that were reduced through a world-wide vaccination campaign to an estimated 164 000 deaths in 2008.[17]

Those who survive measles without lasting effects still have 2 worries. One is that measles infection depresses the immune system for up to 2 years, making children more susceptible to other infections,[18] and a second is the possibility of developing subacute sclerosing panencephalitis, a usually fatal neurologic degenerative disease caused by reactivation of latent measles virus. The assessed risk is on the order of 1 in 10 000 measles cases and as much as 10-fold greater for children who contract measles before the age of 12 months.[19] For children who are immunocompromised, such as those being treated for leukemia, an actual measles infection is severe, extended, and often fatal.[20]

Although measles is possibly the world's most infectious human virus, it was not the most devastating of the childhood infectious diseases. The smallpox death toll for just the 20th century has been estimated at upwards of 300 million people, similar to the entire population of the present-day US.[21] Smallpox caused more deaths than all the wars in history. For centuries before vaccination, most urban families could count on losing multiple children to smallpox, diphtheria, scarlet fever, or whooping cough. With widespread vaccination, combined with targeted vaccination to insulate the last few cases, smallpox was eliminated as an infectious disease on earth.

Connected by Infectious Disease

Smallpox eradication was our first and thus far only complete victory over a human disease–causing agent, made possible by universal, global vaccination, and intensive surveillance. After tortuous millennia of epidemic disease and hundreds of millions dead, who would argue that this was not a most wonderful gift given by humankind to itself? But that gift was not without cost, and the cost was a tincture of personal independence and the acknowledgement that each of us is inextricably tied to the entire human community. It took the idea of community out of the realm of philosophy and placed it as a fundamental property of life. Smallpox eradication itself was a physical enactment of the tension between personal freedom and the authority of society. In *On Liberty*, in Chapter IV, John Stuart Mill asks, "What then is the rightful limit to the sovereignty of the individual over himself? Where does the authority of society begin? How much of human life should be assigned to individuality, and how much to society?"

Mill's inquiries can be answered by biology, but first consider the concept of community protection (often referred to as "herd immunity"). As the density of susceptible (unvaccinated or disease naïve) hosts declines, so does the incidence of disease. Below a certain threshold, the incidence of disease (frequency of new infections), even in unimmunized people, approaches zero. This is community protection, and it follows directly from basic epidemiology. Vaccination effectively reduces the number and density of the disease-susceptible people, making acutely infectious agents unsustainable in the population.[22] Conversely, because vaccine protection is sometimes imperfect, a vaccinated individual living within a disease-susceptible population is at substantial risk. The risk of disease for any individual is thus most importantly dependent on the collective immunity of the population, especially those most susceptible to infection, usually the youngest children and oldest adults.

In this regard, disease ecology does not equivocate; in the world as it exists today, our health and our very being depend on the immune status of the rest of humanity. The rightful limit to the sovereignty of the individual over him or herself stops at the boundary of disease immunity. As long as one case of smallpox could be found on earth, billions were at risk. Even without considering the imperative of contagious disease, Mill came to the same conclusion, "As soon as any part of a person's conduct affects prejudicially the interests of others, society has jurisdiction over it. . .." Two centuries before *On Liberty* and before the Enlightenment, this was expressed after a fashion in John Donne's Meditation XVII, "Now this bell tolling softly for another, says to me, Thou must die," written while he was convalescing from a near-fatal disease, possibly typhus. Although this meditation was ostensibly concerned with God as the author of every person and every death, we might equally apply it in a way that Donne could not—we are each of a network, a medium for disease that transcends us as individuals. The death of one of us portends many more. We can rage against this injustice, but it is literally a fact of life. In this context, the famous line from Meditation is relevant, "No man is an island, entire of itself."

Who Does Not Vaccinate and Why?

Community protection is a fundamental concept with no strict definition. The threshold is sharp but varies with each infectious agent. It protects vaccinated and unvaccinated people alike. It is the most powerful force in disease prevention but exists only in the immunity status of the entire population network. Considering the difficulty of this concept, it is no wonder that as a society and as a people we do not have a consensus

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