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Pathogens and Parasites

It is a shitty world out there. Many hundreds of millions of people will fall ill this year from infectious intestinal pathogens passed in human feces. Just how many hundreds of thousands will die can only be reckoned roughly. Consider cholera. The World Health Organization estimates that most cholera outbreaks are not detected by public health agencies and that the officially reported cases of cholera probably represent 5 to 10 percent of the actual number of cases worldwide. Their experts guess at 2.8 million cases of cholera every year and an estimated 91,000 deaths, of which approximately half occur in children under the age of five years.[1] Typhoid fever probably afflicts annually more than 20 million, of which about a quarter of a million die.[2] Shigella infections take the lives of more than 200,00.[3] Each year, children suffer around 1.7 billion bouts of diarrheal disease from mostly undetermined causes.[4] From these bouts,

[1] Mohammed Ali, Anna Lena Lopez, Young Ae You, Young Eun Kim, Binod Sah, Brian Maskery, and John Clemens, "The Global Burden of Cholera," *Bulletin of the World Health Organization*, vol. 90 (2012), 209, 214.

[2] www.who.int/immunization/diseases/typhoid/en/.

[3] Ibrahim A. Khalil, Christopher Troeger, Brigette F. Blacker, Puja C. Rao, Alexandria Brown, Deborah E. Atherly, Thomas G. Brewer et al. "Morbidity and Mortality due to Shigella and Enterotoxigenic Escherichia coli Diarrhoea: the Global Burden of Disease Study 1990–2016," *Lancet Infectious Diseases*, vol. 18, no. 11 (2018), 1229–40.

[4] The burden of novel pathogenic agents that have yet to be discovered is high. Case studies of diarrheal illness in young children from low-income countries have determined that in fewer than 50 percent of the cases could researchers find any known pathogenic agents. Mihai Pop, Alan W. Walker, Joseph Paulson, Brianna Lindsay, Martin Antonio, M. Anowar Hossain, Joseph Oundo et al., "Diarrhea in Young Children from Low-Income Countries Leads to Large-Scale Alterations in Intestinal

more than a half a million children under five years of age die.[5] The number of deaths is appallingly high, yet it represents a major decline from just a generation ago, when the annual diarrheal death toll was estimated at more than 3 million.[6]

The pathogens that cause these illnesses and deaths are passed in human waste. When microscopically tiny particles of fecal matter contaminate hands, serving vessels, bowls, plates, tableware, liquids, or foods, the pathogenic agents – whether viruses, bacteria, or protozoa – travel to our intestines through the digestive tract. There, they disrupt the functioning of our guts, the incredibly complex universe known as the human microbiome. Another set of infections is caused by parasitic intestinal worms. In small numbers, some worms seem to contribute to the well-functioning of our immune systems, but in larger numbers, the same worms cause illness and, in rare cases, death. We can also become sick from contact with the fecal matter of wild or domesticated animals, but these infections are a relatively minor part of the story. Human beings transmit to each other the major infections that wreak illness and death. We are our own worst enemies.

INTESTINAL VIRUSES, PROTOZOA, AND BACTERIA

Five intestinal viruses are particularly dangerous to human health: poliovirus, hepatitis A, hepatitis E, rotavirus, and norovirus. They are passed virtually exclusively by human beings to other human beings, and their range has been global. Immunization campaigns against poliovirus, which can cause muscular paralysis and, in rare cases, death, have been highly successful and have reduced the number of new poliovirus infections to twenty-two in 2017. Hepatitis A and hepatitis E attack the liver and remain global menaces. There are effective vaccines against both, but

Microbiota Composition," *Genome Biology*, vol. 15, no. 6 (2014), R76. http://genomebiology.com/2014/15/6/R76.

For estimates of the impacts of the known intestinal pathogens, see Christopher Troeger, Mohammad Forouzanfar, Puja C. Rao, Ibrahim Khalil, Alexandria Brown, Robert C. Reiner Jr, Nancy Fullman et al., "Estimates of Global, Regional, and National Morbidity, Mortality, and Aetiologies of Diarrhoeal Diseases: A Systematic Analysis for the Global Burden of Disease Study 2015," *Lancet Infectious Diseases*, vol. 17, no. 9 (2017), 909–48.

[5] www.who.int/mediacentre/factsheets/fs330/en/.

[6] C. Bern, J. Martines, I. de Zoysa, and R. I. Glass, "The Magnitude of the Global Problem of Diarrhoeal Disease: A Ten-Year Update," *Bulletin of the World Health Organization*, vol. 70, no. 6 (1992), 705–14.

the public health systems are too weak in many countries to allow for population-level coverage. There are thought to be about 114 million infections of hepatitis A and 20 million infections of hepatitis E every year, although most cases are asymptomatic. More than 1 percent of those annually infected with hepatitis A (about 1.4 million people) and more than 15 percent of those afflicted with hepatitis E (about 3.3 million people) experience the characteristic symptoms of dark urine, jaundice, and extreme weakness. Those who recover from hepatitis A are immune to reinfection. There are multiple genotypes of hepatitis E, however, and the extent to which survivors enjoy any degree of protective immunity has not been determined. A high percentage of the population in the Global North is potentially susceptible because of the low levels of endemic transmission. In the Global South, virtually all adolescents and adults have been exposed to hepatitis A, and new cases are found almost exclusively among the young.[7] Hepatitis E affects a broader spectrum of the population and is a particular threat to adults with compromised immune systems.[8]

By contrast, until the first decade of the twenty-first century, rotavirus infections were nearly universal. Before the rollout of a vaccine in 2006, rotavirus infected virtually all children in the United States before their fifth birthday. Rotavirus continues to infect unvaccinated children around the world and kills 200,000 each year. Rotavirus transmission is principally via fomites, that is, surfaces on which we inadvertently deposit invisibly small viral particles from fecal matter, which are then inadvertently picked up by others. In the developed world, children's toys, doorknobs, and shared tableware are the usual culprits.[9] Norovirus is also a very bad actor, and because there is no vaccine, its prevalence is roughly equivalent to rotavirus earlier in the century. It is responsible for about 20 percent of all cases of diarrhea and vomiting in the United States. Indeed, norovirus is the leading cause of severe gastroenteritis worldwide.

[7] K. H. Jacobsen and S. T. Wiersma, "Hepatitis A Seroprevalence by Age and World Region, 1990 and 2005," *Vaccine*, vol. 28, no. 41 (2010), 6653–7. doi:10.1016/j.vaccine.2010.08.037.

[8] Lisa J. Krain, Kenrad E. Nelson, and Alain B. Labrique, "Host Immune Status and Response to Hepatitis E Virus Infection," *Clinical Microbiology Reviews*, vol. 27, no. 1 (2014), 139–65.

[9] Jacqueline E. Tate, Anthony H. Burton, Cynthia Boschi-Pinto, Umesh D. Parashar, World Health Organization–Coordinated Global Rotavirus Surveillance Network, Mary Agocs, Fatima Serhan et al., "Global, Regional, and National Estimates of Rotavirus Mortality in Children < 5 Years of Age, 2000–2013," *Clinical Infectious Diseases*, vol. 62, suppl. 2 (2016), S96–105.

It spreads when we ingest food and water contaminated with microscopically small specs of fecal matter.[10]

There are two major protozoa that infect the human intestinal tract: *Giardia lamblia* and *Entamoeba histolytica*.[11] These infections are infrequent in the developed world. They are introduced to humans via contamination from the feces and urine of other animals, such as dogs, cats, birds, sheep, deer, beaver, and cattle.[12] Hikers in remote areas who drink from streams and rivers are particularly at risk. Both protozoal intestinal infections produce diarrhea (and in the case of *Giardia lamblia*, sometimes severe constipation), but they are generally cleared within a matter of days or, at most, weeks. In the rural areas of the less developed world, these protozoal intestinal infections are common. The rural water supplies are frequently contaminated because human beings get their water from the same sources as do domesticated and wild animals. In many regions, the chains of infection are nearly continuous. Giardiasis is the most common cause of parasitic diarrhea in the world, although it does not kill. Amoebiasis from *Entamoeba histolytica* (also known as amoebic dysentery), however, is also widely distributed and causes about 50 million cases of diarrhea per year and kills about 100,000 people. It can be particularly destructive to the intestinal walls and open the gates to other infectious diseases.

Bacterial intestinal infections have been among the deadliest scourges of humankind. Two infections have killed large numbers of adults: typhoid fever (*Salmonella typhi* and *Salmonella paratyphi*) and cholera (*Vibrio cholerae*). Typhoid fever could exact a toll on the order of a 10–30 percent case fatality rate. It typically involved the passage of the bacteria from the intestine into the blood, producing sepsis. Cholera was even deadlier, with a case fatality rate that could reach 50 percent. Untreated cholera typically killed via severe diarrhea, which led to fatal dehydration.[13] A large number of additional pathogens could kill infants

[10] Sharia M. Ahmed, Aron J. Hall, Anne E. Robinson, Linda Verhoef, Prasanna Premkumar, Umesh D. Parashar, Marion Koopmans, and Benjamin A. Lopman, "Global Prevalence of Norovirus in Cases of Gastroenteritis: A Systematic Review and Meta-analysis," *Lancet Infectious Diseases*, vol. 14, no. 8 (2014), 725–30.

[11] Protozoa are similar to bacteria in that they are single celled, but they behave more like animals in that they typically have a sexual stage to their reproduction, whereas bacteria reproduce asexually.

[12] In the system of classification proposed by Thomas Cavalier-Smith, *G. lamblia* would be considered a member of the Archaea kingdom, rather than the Protozoa.

[13] The poor were particularly susceptible to infection by cholera and typhoid because many suffered from undernutrition, which is accompanied by low gastric acid activity in the

and young children whose immune systems were not fully developed. Even common, run-of-the-mill *E. coli* infections could pull into the grave infants and small children who were already weakened by malnutrition and/or other infections. They robbed the body of fluids and nutrients, causing severe diarrhea, dehydration, and, ultimately, death.

Today, typhoid fever, cholera, and amoebic dysentery are rare in communities that disinfect their water supplies with chlorine or ozone and maintain the physical integrity of the water delivery systems, from the reservoir to the tap. Even with this broad public health success, occasionally some bacterial pathogens, such as variants of *Escherichia coli, S. enterica,* and *Campylobacter,* enter the food supply and cause outbreaks of diarrheal disease and vomiting. But these are generally small-scale events that are easily contained, unless the local water supply system has become contaminated. For those who fall ill, the results are highly unpleasant but only temporarily debilitating, except in the case of the elderly and those with compromised immune systems, who are at greater risk for more serious consequences. The relative infrequency of bacterial infections is a positive reflection of our safe water treatment systems and our relatively high nutritional status. If bacterial pathogens are introduced only occasionally and the host's immune system is competent, the host is able to clear the infection and, generally, to kill or expel the pathogen. In the developed world, the risk of death from a bacterial pathogen is very low.

INTESTINAL WORMS

The final group of unwelcome visitors to the human intestinal tract comprises intestinal worms known as helminths. Some of the worms attach themselves to the linings of the human intestines and draw their nourishment by sucking blood from their hosts. Most live from nutrients available in the intestinal tract. Some helminths, such as tapeworms and pinworms, are of minor public health significance. They spread via infinitesimally small eggs passed in human feces. The tapeworm eggs are ingested by cattle (*Taenia saginata*) or pigs (*T. solium* and *T. asiatica*),

stomach. This is one of the first lines of biological defense against *V. cholerae*, and normal gastric acid activity reduces the chances of the bacteria surviving its journey through the stomach to the small intestine. On the role of poverty and undernutrition in explaining the higher historical vulnerability of people of African descent in the Caribbean to cholera, see Kenneth F. Kiple, "Cholera and Race in the Caribbean," *Journal of Latin American Studies*, vol. 17, no. 1 (1985), 157–77.

where they develop into larvae, known as cysticerci, in the musculature of the animals and then are transferred to human beings who eat undercooked beef or pork, in which the taenia larvae survive. Once ingested, the cysticerci develop into adult tapeworms in the human intestine.[14] The pinworms (*Enterobius vermicularis* and *E. gregorii*) do not have a nonhuman host. They release tiny eggs that are deposited in tiny folds in the human anus, which becomes irritated and demands to be scratched. Sufferers from pinworm can then inadvertently transfer the eggs from hand to mouth, and once ingested, the cycle continues. It is also possible to transmit pinworm eggs via fomites – clothing, utensils, furniture, or other surfaces on which pathogens and parasites can survive – and a small proportion of the tiny eggs may become airborne and make their way to a human mouth and be inadvertently swallowed. They are remarkably common even in the developed world. An estimated 20 percent of the people in the United States will acquire a pinworm infection at some point in life.[15]

Far and away, however, the biggest intestinal worm challenges in global health are from a category known as soil-transmitted helminths (S-THs). A major difference is that the tiny eggs of the soil-transmitted helminths, after being passed through human feces, must mature in the soil. The three major S-THs are roundworms, whipworms, and hookworms. They are far and away most common of all the intestinal worms, and today they have a global distribution centered on the tropics and subtropics. The roundworms live from nutrients in the intestines. The hookworms and whipworms attach themselves to the human intestinal walls, where they grow to maturity, feeding upon human blood.

Researchers agree that roundworms, whipworms, and hookworms produce a large, global burden of disease. The difficulties in estimating the extent of the disease burdens are very considerable, because the data are not comprehensive or fully reliable. What seems clear, however, is that the likely total number of global deaths caused by complications from soil-transmitted helminths would be relatively small in comparison to the mortality caused by bacterial, protozoal, and viral infections.[16]

[14] It is also possible for human beings inadvertently to ingest *Taenia* eggs and host the development of the larvae in human tissues, such as the lung, liver, or brain.

[15] Edy Stermer, Igor Sukhotnic, and Ron Shaoul, "Pruritus Ani: An Approach to an Itching Condition," *Journal of Pediatric Gastroenterology and Nutrition*, vol. 48, no. 5 (2009), 513–16.

[16] Simon Brooker, "Estimating the Global Distribution and Disease Burden of Intestinal Nematode Infections: Adding Up the Numbers – A Review," *International Journal of Parasitology*, vol. 40, no. 10 (2010), 1137–44.

Somewhat paradoxically, it is more than likely that very light infections with these same worms have done us some good. There is evidence, for example, that populations with helminthic infections are less likely to suffer from allergic and autoimmune diseases. How can this be explained? According to the "hygiene hypothesis," because *Homo sapiens* co-evolved with intestinal worms until very recently, it seems likely that they have played a symbiotic role in our intestinal systems. The influence of helminths on the human immune system is under active investigation.

Roundworm (*Ascaris lumbricöides*) is the most widely distributed helminth in the world. It also afflicts the largest number of people, on the order of 1 billion. Adult worms live in the small intestine. The males grow to fifteen to thirty centimeters and the females to twenty to thirty-five centimeters. They are prolific. Each female can release up to 200,000 eggs per day, and both fertilized and unfertilized eggs are passed in feces. Where humans with roundworms defecate outdoors, the fertilized eggs – if the soil, moisture, and temperature conditions are suitable – develop in eighteen days to several weeks. Thereafter, they may be picked up by children playing outdoors or adults working on the land, and some eggs may become windborne and can be inadvertently ingested through the simple act of breathing, as well as via the fecal–oral route. When the mature eggs are ingested, they pass into the intestine, where they develop into larvae. They make their way from the intestine via the blood or lymphatic system to the lungs, from which they are then coughed up into the mouth and swallowed. They mature in the small intestine, attach themselves to the linings, and live on for one or two years. The cycle of infection must be ongoing for infections to be chronic. Most infections are relatively light, and many such sufferers do not experience any symptoms of infection. Heavy infections, on the other hand, can cause severe problems, including intestinal blockage.

Whipworm (*Trichuris trichiura*) infects perhaps three-quarters of a billion people. The worms live in the large intestine and produce eggs that are passed in feces. If the soil conditions are propitious, the eggs mature in fifteen to thirty days. They then become infective. These eggs, once ingested via the fecal–oral route, hatch in the small intestine and release larvae that attach themselves to the colon. They live for about one year. The adult female worm produces 3,000 to 20,000 eggs per day, which are passed in feces. Those with light infections may suffer no symptoms, while those with heavier infections may experience pain when passing stool and may even suffer rectal prolapse, when the lower part of the large intestine protrudes from the anus.

Hookworm (*Necator americanus* and *Ancylostoma duodenale*) infects about 500,000 to 600,000 people. Hookworms live in the small intestine, and the females produce eggs that are passed in feces. The eggs hatch quickly and turn into infective larvae – in six to twelve days under favorable conditions – and, unlike the other soil-transmitted helminths, the hookworm larvae live in the soil for three to four weeks. The larvae attach themselves to human skin – often the bare feet or hands of children or agricultural workers – and burrow under the skin, causing a rash. The larvae then enter the bloodstream and make their way to the heart and lungs, after which they ascend the pharynx and are swallowed. Most hookworms have a life-span of about one or two years, although some are much longer lived. *Ancylostoma duodenale* can become dormant in muscle tissue or in the intestine and may be able to be transmitted by an oral route or through breastfeeding.[17]

DETERMINANTS OF DISEASE TRANSMISSION

The transmission of infectious intestinal pathogens is influenced by a large number of variables. Different societies have held different views about the appropriate means to dispose of human waste and whether or not to use excrement as a soil fertilizer, and different practices in different contexts have had epidemiological importance. Public health researchers have worked to establish firm relationships between "improved" systems of excreta disposal and better health, but they have found this difficult to do, because the relationships are complex and grounded in local ecological and cultural circumstances. Few universal rules apply.

The issue of sanitation – in the broadest sense, a range of behaviors that protect against the transmission of intestinal pathogens – is now recognized to be more complex than the "safe" disposal of human waste by modern sewerage and access to potable water. It is now clear that a range of hygienic practices can have a determinative effect. Some of our most basic and ancient practices, such as cooking food, not only make some foodstuffs more palatable and easy to digest but can kill viruses, bacteria, protozoa, and helminth eggs. Boiling drinking liquids can likewise

[17] The basic information about the biology and epidemiology of roundworm (*A. lumbricöides*), whipworm (*T. trichiura*), and hookworm (*N. americanus* and *A. duodenale*) was drawn from the website of the US Centers for Disease Control and Prevention: www.cdc.gov/parasites/ascariasis, www.cdc.gov/parasites/whipworm, and www.cdc.gov/parasites/hookworm.

dramatically reduce their pathogenic potential. Thus, access to energy supplies, such as firewood, dung cakes, and charcoal, has an enormous public health significance. Shortages of fuel can set off disease outbreaks, as can natural disasters that displace families from their energy resources. The use of soap to cleanse the hands after defecation or after cleaning up an infant's stool has been shown to sharply reduce the transmission of intestinal pathogens. Some of our basic understandings of the threats to children from infectious intestinal diseases are being reshaped by ethnographic research.

The transmission of intestinal pathogens is not, however, exclusively a function of access to "improved" sanitation, potable water, energy resources, or soap. Three basic biophysical factors set the parameters for some disease transmission processes. The first is temperature. Roundworm, whipworm, and hookworm eggs, for example, cannot survive when they are released in extremely cold temperatures, and for this reason, those who live in the Arctic regions do not suffer from these intestinal worms. Yet, extremely cold temperatures can militate against the washing of hands, and this enhances the possibilities for fecal–oral transmission of bacterial and viral pathogens. Extreme cold precludes the keeping of livestock and fowl and thus eliminates some sources of potential infection. Yet reliance upon hunting and fishing carries its own risks. Researchers have documented in the Arctic wide outbreaks of trichinosis, a helminthic infection with an enteric phase that causes prolonged diarrhea, and traced it to undercooked walrus meat. Communities in the Arctic also suffer occasional cases of diphyllobothriasis (fish tapeworm) from the consumption of undercooked fish and occasional cases of echinococcosis (tapeworms acquired from contact with dogs, reindeer, and elk).[18] At the other end of the temperature spectrum, a lengthy hot season is generally conducive to the survival and rapid maturation of the soil-transmitted helminth eggs and for the survival of bacterial and viral pathogens on fomites. There are decidedly greater risks to living in the tropics and subtropics.

Moisture is a second major factor. In dry deserts, such as the Sahara and the Gobi, the low humidity and near absence of rainfall combine with extreme diurnal temperature variations to kill some of the intestinal pathogens released into the environment. Feces desiccate quickly, and helminth

[18] Peter J. Hotez, "Neglected Infections of Poverty among the Indigenous Peoples of the Arctic," *PLoS Neglected Tropical Diseases*, vol. 4, no. 1 (2010), e606. doi:10.1371/journal.pntd.0000606.

eggs generally do not survive. It is possible, of course, to foul wells with human or animal waste and to transmit pathogens via the fecal–oral route, and for the populations of dry deserts, this can be a significant problem. In wet environments, high levels of moisture improve the survival of most intestinal pathogens. Rainfall runoff, if contaminated with human and animal feces, can distribute pathogenic materials widely and increase the possibilities for the transmission of disease.

Soil type is a third major biophysical determinant of intestinal pathogen transmission. Different soils have their most significant influence on the survival of helminth eggs. Hookworm eggs, for example, are able to germinate and produce larvae much more easily in sandy soils. Clayey soils are more impervious, and the survival rates of the helminth eggs are lower. As we will see in Chapter 6, the rates of hookworm infection in the US South in the early decades of the twentieth century were much higher in the coastal regions with sandy soils than in the upland regions with clayey soils.

Patterns of human lifestyle, particularly the practices of livestock keeping and herding, have also had a profound impact on the transmission of infectious intestinal disease. In societies that depend upon domesticated animals for milk, meat, hides, eggs, or furs, the close contact between animals and people increases the transmission of pathogens, such as the giardia protozoa, that have animal as well as human hosts. Whether or not the domesticated animals are held within enclosures is also epidemiologically significant. Enclosures such as barns or open-air pens concentrate the animal manure within the enclosure and ensure greater human contact with it, further enhancing the prospects for disease transmission. One of the most dangerous known practices is one of the most common: keeping free-ranging or penned chickens or other fowl close to the homestead. This is a prescription for the infection of young children who inadvertently contaminate themselves with pathogenic bacteria.

Cultural choices of where to defecate have also had epidemiological significance. A cultural preference for defecating in a stream or river, for example, principally put the communities downstream at risk. A cultural preference for defecating indoors – in the early twentieth-century United Kingdom, a usual spot for young children under the age of three or four was in the kitchen, eating room, or scullery – probably increased the contamination of foodstuffs, although the epidemiological consequences of this behavior were never quantified.[19]

[19] O. H. Peters, *Observations upon the Natural History of Epidemic Diarrhoea* (Cambridge: Cambridge University Press, 1911), 60–1.

Cultural practices of how to cleanse oneself after defecation have also been important. In Muslim societies, the religious requirement is to use the left hand to remove fecal matter and cleanse the anus with water. In Indonesia, for example, many Muslims met their obligation by defecating in waterways, which offered the immediate benefits of the submersion of feces and masking of its smell, as well as water for cleansing. In desert regions, Muslims have used sand to clean their left hands after defecation, thereby meeting the ritual requirement for ablution. These religiously sanctioned practices undoubtedly have their own deep histories that have not yet attracted the interest of cultural historians.

Across the globe, wherever human beings settled or congregated, their environments reeked. Both rural and urban life were permeated with the odors of urine and excrement. At night, to protect themselves from molestation by animals or other humans, many people relieved themselves nearby their homesteads or availed themselves of vessels within the homestead. By day, people relieved themselves on beaches and riverbanks; in fields, rivers, streams, forests, and grasslands; near schools, temples, and churches; in side yards, courtyards, barnyards, basement and outdoor cesspits, and privy vaults. Stench was pervasive. Daily encounters with one's own and others' shit and ammonia-reeking piss were inescapable, part and parcel of the lived world. (It is a measure of our distance from these experiences that in the "modern" Anglophone world, we have relegated the common nouns *shit* and *piss* to the realm of cusswords.) In environments permeated with bodily waste, it was hard to conceptualize feces as dangerous to health.

CHANGING PERSPECTIVES ON CHILDHOOD DIARRHEAL DISEASES

In recent years, our understandings of the causes of childhood diarrhea and malnutrition have broadened. A major shift in thinking has been brought about by the appreciation of a condition known as environmental enteropathy. It is caused by the ingestion by young children of large quantities of fecal bacteria, principally from chickens raised nearby rural dwellings. The condition is characterized by poor growth, reduced intestinal barrier function, and chronic systemic inflammation.[20]

[20] Francis M. Ngure, Jean H. Humphrey, Mduduzi N. N. Mbuya et al., "Formative Research on Hygiene Behaviors and Geophagy among Infants and Young Children and

Researchers discovered that around homesteads where chickens were raised the possibilities for the ingestion of massive loads of bacteria were unmistakable.[21] In Zimbabwe, for example, the bacterial loads ingested by young children from homestead soils were estimated to be comparable or greater than the bacterial loads ingested from untreated drinking water. And these loads paled when compared with the inadvertent direct ingestion of chicken feces, which was roughly 4,000 times greater than from either untreated drinking water or from homestead soils. This revolutionary insight helped to refocus efforts in rural areas. Previously, the water, sanitation, and hygiene interventions had focused on improved disposal of human fecal matter, point-of-use water treatment, and maternal handwashing. There had been no interventions to interrupt the ingestion of contaminated soils and animal feces.[22]

A second major shift has occurred as a result of evidence that the quantity of water available is more important than its quality. Greater water availability encourages better hygiene – and more handwashing, in particular – and reduces the incidence of diarrheal disease. This evidence has challenged a foundational assumption that

Implications of Exposure to Fecal Bacteria," *American Journal of Tropical Medicine and Hygiene*, vol. 89, no. 4 (2013), 709; Jean H. Humphrey, "Child Undernutrition, Tropical Enteropathy, Toilets, and Handwashing," *Lancet*, vol. 374 (2009), 1032–35.

[21] Noel W. Solomons, Manolo Mazariegos, Kenneth H. Brown, and Kirk Klasing, "The Underprivileged, Developing Country Child: Environmental Contamination and Growth Failure Revisited," *Nutrition Reviews*, vol. 51, no. 11 (1993), 327–28.

Interestingly, researchers' attention to the link with chicken feces was drawn by the chicken breeders' maxim: "a dirty chicken is a poorly growing chicken." Chicken breeders had found that it was cheaper to add antibiotics to chicken feed than to build sanitary housing for the birds. The parallel with infants and children growing in highly unsanitary environments was far from exact. Some children – such as those who were infected or exposed to HIV and/or acutely malnourished – might be put on a regimen of antibiotics, if they had access to medical services, but the possibility to scale up to population level dosing with antibiotics was not in the cards. Such a program would have greatly accelerated antibiotic resistance. In addition, there were concerns that antibiotic use interfered with the microbiome and had been associated with antibiotic-associated diarrhea. Ethan K. Gough, Erica E. M. Moodle, Andrew J. Prendergast, Sarasa M. A. Johnson, Jean H, Humphrey, Rebecca J. Stoltzhus et al., "The Impact of Antibiotics on Growth in Children in Low and Middle Income Countries: Systematic Review and Meta-Analysis of Randomised Controlled Trials," *British Medical Journal*, Vol. 348 (2014).

[22] Francis M. Ngure, Brianna M. Reid, Jean H. Humphrey, Mduduzi N. Mbuya, Gretel Pelto, and Rebecca J. Stoltfus, "Water, Sanitation, and Hygiene (WASH), Environmental Enteropathy, Nutrition, and Early Child Development: Making the Links," *Annals of the New York Academy of Sciences*, vol. 1308 (2014), 121–24.

poor-quality drinking water was the primary cause of diarrheal disease.[23]

A third shift has evolved in linking the category of diarrheal disease with that of malnutrition. In many cases, the relationships are entwined. Malnutrition can cause diarrheal disease, and diarrheal infections can profoundly disrupt the body's ability to absorb and utilize nutrition.[24] The whys, hows, and wherefores of these dynamics are under investigation by scientists who are exploring the universe of the human gut.

THE MICROBIOME

In recent years, biomedical scientists have launched major research projects to investigate the ecological world of the human microbiome.[25] These investigations promise to yield new understandings of our gut biota that will improve our abilities to treat intestinal infections, through improved drug uptake and better-targeted interventions. The human microbiome project will illuminate the chemical interactions between gut bacteria and the linings of our intestines; the transformational impact of diet on the microbiome; the relationship between the gut microbiome and other aspects of human health; and the roles that probiotics, fecal transplants, and microbiome vaccines can play in improving health outcomes. Some rather astonishing breakthroughs have already taken place. In 2017, for example, researchers discovered a new organ in the human body, known as the mesentery, that attaches the intestine to the wall of the abdomen, opening up the entirely new field of mesenteric science.[26] A revolution in biomedicine is in incubation.

[23] Valerie Curtis, Sandy Cairncross, and Raymond Yonli, "Domestic Hygiene and Diarrhoea – Pinpointing the Problem," *Tropical Medicine and International Health*, vol. 5, no. 1 (2000), 22–32.

[24] Jessica MacIntyre, Jennifer McTaggert, Richard L. Guerrant, and David M. Goldfarb, "Early Childhood Diarrhoeal Diseases and Cognition: Are We Missing the Rest of the Iceberg?," *Paediatrics and International Child Health*, vol. 34, no. 4 (2014), 295–307.

[25] The domain of investigation is broad, including the microbiome of the skin as well as the intestines. Most of the research, however, is focused on the gut. For an overview, see Jacques Ravel, Martin J. Blazer, Jonathan Braun, Eric Brown, Frederic D. Bushman, Eugene B. Chang, Julian Davies et al., "Human Microbiome Science: Vision for the Future, Bethesda, MD, July 24 to 26, 2013," *Microbiome*, vol. 2 (2014), 16, www.microbiomejournal.com/content/2/1/16.

[26] J. Calvin Coffey and D. Peter O'Leary, "The Mesentery: Structure, Function, and Role in Disease," *Lancet Gastroenterology & Hepatology*, vol. 1, no. 3 (2017), 238–47, https://doi.org/10.1016/S2468-1253(16)30026-7.

The research of the molecular scientists to date has resulted in new characterizations of the bacterial assemblages within our intestinal systems. One set of findings has illuminated the fact that the composition of the gut microbiota changes over the course of the human lifetime. The gut biota of the newborn infant is strongly influenced by the gut bacteria of the mother; the gut bacteria of breast-fed babies is less diverse, more stable, and more protective than that of formula-fed babies; and the child's bacterial assemblage will change dramatically over the first three years of life.[27] The intestinal biota of pregnant women is different from women who are not pregnant. The core intestinal biota of the elderly is markedly different from younger adults.[28]

The microbiome research has also illuminated the fact that different human communities possess rather different variants of a common microbiome. Researchers now think that there are three different types of enterobacteria arrays or enterotypes.[29] These arrays may be determined in part by genetic inheritance, although they are probably governed in larger measure by the kinds and quantities of foods that we eat.[30]

In one sense, the research suggests the truism that we are what we eat. There is a marked difference in the enterobacteria of those with a diet high in protein and simple sugars (in the microbiome literature sometimes referred to as the "Western diet") and those with a diet high in complex carbohydrates. The histories of the major cultigens, farming systems, and networks of international trade in foodstuffs have had a role in shaping the microbial universes that we carry around within us. As have our varying exposures to wildlife and domesticated livestock. As have our

[27] Wenguang Fan, Guicheng Huo, Xiaomin Li, Lijie Yang, Cuicui Duan, Tingting Wang, and Junliang Chen, "Diversity of the Intestinal Microbiota in Different Patterns of Feeding Infants by Illumina High-Throughput Sequencing," *World Journal of Microbiology and Biotechnology*, vol. 29, no. 12 (2013), 2365–72.

[28] Marcus J. Claesson, Siobhán Cusack, Orla O'Sullivan, Rachel Greene-Diniz, Heleen de Weerd, Edel Flannery, Julian R. Marchesi et al., "Composition, Variability, and Temporal Stability of the Intestinal Microbiota of the Elderly," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 108, Suppl. 1 (2011), 4586–91, https://doi.org/10.1073/pnas.1000097107.

[29] Manimozhiyan Arumugam, Jeroen Raes, Eric Pelletier, Denis Le Paslier, Takuji Yamada, Daniel R. Mende, Gabriel R. Fernandes et al., "Enterotypes of the Human Gut Microbiome," *Nature*, vol. 473 (2011), 174–80, https://doi.org/10.1038/nature09944.

[30] Studies in mice suggest that diet is the dominant factor in shaping gut microbiota. Huizi Tan and Paul W. O'Toole, "Impact of Diet on the Human Intestinal Microbiota," *Current Opinion in Food Science*, vol. 2 (2015), 71, https://doi.org/10.1016/j.cofs.2015.01.005.

cultural inheritances of hygienic and nonhygienic practices. In the developed world, as these inheritances are at play, our profligate use of antibiotics is altering our gut bacteria.

We typically think of genetic variation between human populations as differences in the allele frequencies of our *Homo sapiens* genes. Yet because bacteria play such a significant role in regulating our basic metabolism of food and our immune responses to pathogens, we need to broaden our perspective to include the astounding genetic and metabolic diversity that can be found in the millions of genes and myriad gene functions within our gut microbial communities.[31] We are alive as a result of the vast and complex interactions that take place between our intestinal bacteria and our body organs.

Some of these interactions – perhaps the large majority of them – are mutually symbiotic, meaning that both human beings and our bacteria draw benefits from the interactions. Some may be commensal – that is, that the bacteria draw benefits from their colonization of our intestines while we do not – although this is more a theoretical possibility than an established fact. And some are clearly parasitic – that is, the bacteria draw energy resources from us. In doing so, they may weaken us or draw forth an immune response to an infection.

This typology of ecological associations – symbiotic mutualism, commensalism, and parasitism – is a useful as a heuristic construct, but it greatly simplifies our understandings of our relationship to our gut flora. This is because our gut flora interact within the intestinal microbiome, and they probably do so with bacteria elsewhere in the body.

The sheer number of bacteria in the human gut is astounding – on the order of 100 trillion or ten times the number of human body cells. And their variety is impressive, too. There are about 500 different species of bacteria in the gut, as well as some fungi, protozoa, and archaea. The bacteria in our intestines weigh up to about two kilograms, and they make up about 30 percent of our feces. They produce vitamins. They modulate our immune responses to intestinal challenges. They are critically determinative in our ability to fight off infectious pathogens. This has come into popular appreciation through the once unthinkable and now accepted

[31] Tanya Yatsunenko, Frederico E. Ray, Mark J. Manary, Indi Trehan, Maria Gloria Dominguez-Bello, Monica Contreras, Magda Magris et al., "Human Gut Microbiome Viewed across Age and Geography," *Nature*, vol. 486, no. 7402 (2012), 222–27, https://doi.org/10.1038/nature11053.

procedure of using fecal implants to bolster the immune response to *Clostridium difficile*, a particularly nasty bacterium that can cause devastating diarrhea in the elderly and others with compromised immune systems.

Our knowledge of the mysteries of the microbiome will develop as more research discoveries are made. It seems likely that the different enterotypes exercise an influence on the immunological response of the intestinal system to pathogenic challenge, and thus help to determine just how severe is our illness when we do get sick. And it is possible that they have a significant influence on the pathogens to which we are susceptible and thus help to determine whether or not we get sick at all.

The human microbiome is also, of course, made up of a vast number of viruses, many of which are highly beneficial to us, and most of which have not been studied. In years to come, the virologists, who are lining up for the microbiological study of the human biome, will certainly come to play a significant role. The human microbiome project will continue for decades, and over time it will revolutionize our understandings of our bodies and the internal environments that nourish us. It will open up a new field of medical interventions that can use this knowledge to improve human health. Already, it is increasingly accepted that we have a second "brain" located in our intestines that sends signals to the brain in our skulls and that we make decisions – for example, about what and what not to eat and how much – in response to these gut signals, without any conscious reflection.[32]

The preliminary discovery of three different human enterotypes suggests that fundamental environmental influences such as diet help to structural the bacterial and viral environments of our guts. Because our intestinal universes are extraordinarily complex and have changed over time with our changing diets and with our species' expansion into new biomes, our guts have had to adapt to our changing gut biota. This is an epitomic example of the physical incorporation of environmental influences into our bodies to which our genes must necessarily respond. The study of these epigenetic processes will open new paths for genomic study of the influence of intestinal flora on nutrition and growth and for pathogenic challenge and response.

[32] The best popular introduction to these perspectives is Guilia Enders, *Gut: The Inside Story of Our Body's Most Underrated Organ* (Vancouver, BC: Greystone Books, 2015).

HISTORICAL EPIDEMIOLOGY AND CONTEMPORARY INTERVENTIONS

Infectious intestinal diseases are central to understanding the human past because they have played such a large role in our species' demographic history. Over millennia, they have quietly killed infants and young children and put a brake on population growth. They have also chronically sickened older children, adolescents, and adults, and in occasional epidemic outbreaks, they have scourged the populations of army encampments, refugee camps, prisons, and besieged towns. In recent centuries, infectious intestinal diseases have circulated globally as a result of the increased speed and volume of international trade and travel. Around the globe, they have afflicted populations whose water sources, excreta disposal systems, and access to energy supplies have been compromised through warfare, failed maintenance, or natural disaster.

Common infectious intestinal diseases have long been accepted as a natural part of the human condition. Most couples accepted the sad fact that they might lose children to one infectious disease or another, and the loss of children to diarrheal disease was unexceptional. It is only in the last few generations in developed countries with "improved" water supplies and excreta disposal systems that we have come to view childhood death as unnatural and exceptional.

In the twentieth century, public health investigations began to reveal the large dimensions of global childhood mortality and morbidity beyond the developed countries. There were two major lines of explanation for the high rates of childhood mortality and morbidity outside the developed countries and the falling rates within. One explanation was that decreasing childhood mortality was the result of increasing incomes and standards of living in the "modern" states. Another held that the so-called third epidemiological transition of lengthening life expectancy at birth and declining childhood mortality was principally a result of improvements in the quality of the water supply and in human waste disposal practices. Some analysts blended these understandings together, linking improvements in childhood survival either to access to more nutritious food, better clothing, and shelter made possible by improved economic circumstances or to investments in basic infrastructure made possible by improved state resources. These were useful perspectives from the domain of neoclassical development economics, but they were hardly comprehensive.

In the late twentieth century, new frames of reference were forged. Many thinkers came to understand intestinal diseases as diseases of the poor, and poverty was understood as the result of power relations between classes, ethnic groups, and state actors rather than as a "natural" condition of humanity. From this perspective, the historical power relations between colonizer and colonized; master and slave; and middle and upper classes versus lower classes were seen to be the most critical social determinants of health or illness that had left long legacies of inequality in their wakes. From this vantage point, the privileged classes could be seen to have largely allocated services to themselves; the underprivileged classes received modest services, if any. Sometimes the power differential between classes matched up closely with race or ethnicity, as, for example, throughout the European colonial world and in apartheid-era (and post-apartheid) South Africa and in the early and mid-twentieth-century US South (and in poorer US urban areas today). Virtually everywhere, power and income differentials were correlated with differential access to clean water, sanitation, and general health care. This was expressed in higher rates of childhood and adult mortality and morbidity.

This book explores the historical epidemiology of infectious intestinal disease, sanitation, and health interventions with the goal of illuminating a wide range of historical experiences with disease control. It takes the position that differing perspectives should be understood as different truths that can be usefully invoked to illuminate specific epidemiological contexts and that an exclusive insistence on any one set of perspectives can distort our broader appreciation of epidemiological processes in human history.

Depending on one's perspective, the fact that hundreds of thousands of children die every year from intestinal pathogens that are transmitted by a fecal–oral route might be seen to be a chronic problem that will improve with the passage of time if countries develop, a global public health crisis that must be prioritized in order to focus international programs and financial resources on it, or an ongoing challenge that can only be addressed by engaging local populations to find locally appropriate solutions. The fact that large numbers of children are infested by soil-transmitted worms can be seen as a minor public health problem that will ultimately be solved by economic growth, as a chronic problem that should continue to be addressed through the mass administration of deworming drugs, or as prima facie evidence of the need to end the practice of open defecation.

The assessment of differing critical perspectives is important because it is on this basis that we form our understandings of the nature of contemporary intestinal disease challenges and weigh the feasibility of proposed efforts to reduce the burden of disease. Our knowledge about the successes and failures of past interventions constitutes a foundation for planning new interventions.