# 1 · *Introduction*

Infectious diseases are illnesses due to pathogens that can be spread from an infected person, animal or contaminated inanimate object.[1] These pathogens may be bacteria, viruses, fungi or parasites. Parasites are helminths (worms), arthropods (insects) and single-celled protozoa that live on or in another organism, are dependent upon that host, and feed at its expense during the whole or part of their lives.[2] Therefore, parasites tend to have a long-term relationship with the person that they infect.[3] Some species of parasites have been infecting humans and their hominin ancestors throughout our evolution, starting in Africa millions of years ago. Others have evolved to live in other mammals, but jumped to infect humans when our ancestors migrated across the planet and their lifestyle resulted in exposure to these new organisms.

The aim of this book is to explore how these parasites have affected humans across the world over the millennia, and assess the ways in which they have impacted the health of those living in past civilizations. I have been fascinated by this topic since reading the first book on parasites in early medicine and science published by Reinhard Hoeppli in 1959, and more recent edited works have contributed further to the topic.[4] Could the types of parasites present contribute to our understanding of complex questions such as why some civilizations lasted much longer than others before they collapsed, why some empires were small and others covered vast geographical areas, or why some relied upon a continuous supply of slaves brought from other regions to maintain their productivity?[5]

[1] Van Seventer and Hochberg (2017).
[2] Garcia (2016, p. 1316); Gunn and Pitt (2012, p. 7); Mahmud et al. (2017, p. 1).
[3] Ledger and Mitchell (2022b).
[4] Hoeppli (1959); Ferreira et al. (2014); Mitchell (2015a).
[5] Cascardo et al. (2017).

## What is a Civilization?

If we are to explore parasites in past civilizations, we should consider what a civilization is. Most researchers interested in the concept of civilizations and their formation agree that for a society to be regarded as a civilization, it should show signs of increasing complexity over those that preceded it.[6] However, the idea of drawing a line between simpler and more complex societies is not an easy one. It has been proposed that an early civilization is one where it was not just kinship that governed social relations, but rather a hierarchy of social divisions that were unequal in wealth, power and social prestige.[7] From one perspective it could be argued that a system for comparing how complex past societies were is a helpful one to enable us to understand them better. From another perspective some might propose that people today attempting to decide that one past society was civilized while another was not merely indicates colonial-style views where we are just scoring past societies using criteria that we regard as important today, when those in the past may have held very different views as to what made a civilized society. With this in mind, the remit of this book will include not only societies that everyone would regard as a past civilization, but also those cultures, tribes, and peoples who help us to understand the evolution and formation of those subsequent civilizations.

## The Impact of Parasites Upon Health

In order to understand the impact of parasites on the health of past civilizations, we need to think about what we mean by health. This term is actually quite a complex one to define, and different people will hold contrasting views as to what health really is. The World Health Organization defines health as a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.[8] Therefore, it would be ideal if we could evaluate how each parasite might affect its ancient hosts with regards to physical effects, mental effects, and social effects. While this will be quite a challenge even for time periods for which textual evidence survives, for prehistoric time periods this becomes considerably harder.

There are two ways we can consider the impact of diseases upon past populations. The first is to consider parasite infection from the

[6] Wengrow (2010). [7] Trigger (2003, p. 44). [8] World Health Organization (2020, p. 1).

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perspective of the infected person and the past population in which they lived. For this to be possible, people from past societies need to have written such information down in texts that have survived for us to read today. From this viewpoint we can appreciate that some types of parasite may have been appreciated as illness due to the presence of unpleasant symptoms with which a proportion of them would have suffered. These are also more likely to have been conditions that doctors in the past recognized and tried to treat. Such records may also describe examples of stigma or other social consequences of past illness. However, many other parasites may not have been identified at all by early civilizations due to the due to their small size, or more subtle nature of their effects such as stunted growth and reduced IQ in children, or reduced exercise tolerance in adults. Furthermore, it can be complex and challenging to interpret past textual descriptions of disease, and doing so requires an in-depth understanding of the literature and medical beliefs of the time.[9]

The second approach is to consider the effects that parasites have in infected people today. We can then infer that people in the past may well have experienced similar effects when infected by the same parasite. This allows us to ask the modern patient what unpleasant feelings the disease causes (their symptoms), but also to use laboratory tests and clinical imaging to better understand the pathological processes that result from such infections (the biological consequences). Using this approach, the effect of parasites can be thought of in a number of ways.[10]

Many ectoparasites and biting insects that temporarily feed off humans may themselves cause itching at the site of their bite, but their ability to spread other diseases as they feed may have huge effects upon mortality and morbidity in past populations. Good examples of this type of effect upon health include fleas spreading bubonic plague, body lice spreading epidemic typhus, mosquitos spreading malaria, Tsetse flies spreading sleeping sickness, and triatome bugs spreading Chagas' disease.[11] As these diseases can all cause death, their presence may have resulted in a significant decrease in the total population of an ancient civilization compared with those where the parasite or biting insect was not endemic.

Certain intestinal helminths may contribute to malnutrition either by consuming energy and proteins from the diet before the human host can absorb them, or by impairing the ability of the gut to absorb the nutrients present. This becomes particularly problematic for children who need

[9] Mitchell (2011a, 2017b). [10] Garcia (2016); Gunn and Pitt (2012); Mahmud et al. (2017).
[11] Amanzougaghene et al. (2020); Bain (2004); Leulmi et al. (2014); Thongsripong et al. (2021).

calories and proteins to grow, especially if they have a high burden of worms. In this way, children with recurrent episodes of diarrhoea or those infected with geohelminths such as roundworm and whipworm may develop stunted growth and reduced IQ as a result.[12] Because these effects are gradual and long-term, the link may never be noticed by past societies.

A range of parasites cause anaemia, where red blood cell numbers or haemoglobin concentration are lower than normal and insufficient for the individual's physiological needs.[13] Anaemia may be caused by the destruction of red blood cells by the parasites themselves (such as in malaria), or by the parasites triggering the loss of blood into the intestines or bladder (such as in hookworm or schistosomiasis).[14] Chronic anaemia leads to impaired exercise tolerance, so that the amount of physical work a person can achieve in a day is reduced. When multiplied up amongst an entire population, this can have major consequences for the productivity of an ancient civilization.

Some parasites cause chronic inflammation in tissues that over many years can trigger the formation of cancers in certain organs. In past societies when there was no effective treatment for cancer, this will lead to a period of ill health followed by premature death of some of those with the parasite. Examples of cancers cause by parasites include bladder cancer due to the urinary blood fluke (*Schistosoma haematobium*) in the Middle East and Africa, and cancer of the bile ducts of the liver (cholangiocarcinoma) by both Chinese liver fluke (*Clonorchis sinensis*) and South-East Asian liver fluke (*Opisthorchis viverrine*).[15]

Certain parasites can lead to disfiguration of the face or skin, blindness, or unusual behaviour as part of the disease process. This has the potential to result in stigma against people with infection in those societies, which can lead to impaired mental health.[16] It is possible that in past societies if the infection was so common that everyone has lesions, then they may become normalized and stigma disappear. However, others from different regions who meet infected people may still potentially regard the lesions as unpleasant, and so lead to stigma. A good example of a parasite infection that can lead to potentially stigmatizing lesions is mucocutaneous leishmaniasis. The leishmania protozoa that cause this condition

[12] Brooker (2010); Crompton and Nesheim (2002); Joseph et al. (2014).
[13] Chaparro and Suchdev (2019).
[14] Chami et al. (2015); White (2018).
[15] De Martel et al. (2012); Dheilly et al. (2019).
[16] Bennis et al. (2018); Bailey et al. (2019); Vlassoff et al. (2000).

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are spread by sand fly bites. These bite sites form ulceration and unpleasant scarring, but can progress to satellite lesions, with the most disfiguring form being destruction of the nose and face. This is a particular problem in regions of Central and South America.[17]

The World Health Organization uses statistical approaches to quantify the global burden of disease, known as disability-adjusted life years (DALYs) and healthy life expectancy (HALE).[18] These techniques factor in the degree to which a disease causes impaired health or disability, the number of years lived with disability (YLD), and the number of years of life lost (YLL) due to premature death.[19] One DALY represents the equivalent of one year of full health lost. While it has been argued that they underestimate the health consequences of many parasites compared with other diseases,[20] they are, at least, a widely used comparator which can be employed as a starting point from which to investigate the effects of disease. The six parasitic worms with the highest values for DALYs are hookworm due to anaemia, schistosomiasis due to anaemia and bladder cancer, lymphatic filariasis due to limb swelling, food-borne trematodes, and then roundworm and whipworm due to anaemia, stunted growth and reduced intelligence in children.[21] Among foodborne parasitic diseases, the parasites with the highest impact upon DALYs are pork tapeworm causing cysticercosis, *Paragonimus* sp. fluke causing lung disease, roundworm causing malnutrition, toxoplasmosis causing chronic malaise and stillbirths, and Chinese liver fluke causing liver disease and cancer.[22]

One recent study estimated DALYs for people living in medieval Britain to see which diseases probably had the greatest impact upon health.[23] Prior to the analysis it was suspected that bubonic plague, spread by the bite of fleas, may have been the most significant disease. However, plague actually came out 11th in the list of diseases, due to the intermittent, episodic nature of plague outbreaks. The bulk of top 10 diseases that resulted in the worst values for DALYs were infectious bacterial, viral, and parasitic diseases that were an ever-present health risk, especially to young children. Among parasites, protozoal diseases such as malaria and dysentery have particularly high values for DALYS due to their ability to kill young children.

[17] Burza et al. (2018).
[18] World Health Organization (2021, p. 16); GBD 2013 DALYS and HALE Collaborators (2015).
[19] Mathers (2017). [20] Payne et al. (2009). [21] King (2015). [22] Torgerson et al. (2015).
[23] Robb et al. (2021).

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## Where We Can Find Ancient Parasites

Evidence for parasites may be preserved in a range of archaeological contexts. Intestinal parasites frequently release their eggs into the faeces, and so the best place to find them is to look for ancient faeces. Once past civilizations had developed latrines, these act as an ideal source of concentrated faecal material.[24] Prior to the development of latrines, sometimes pieces of faeces can be preserved, and these are known as coprolites. They may be dried, mineralized, or preserved wet in anoxic environments that prevent the normal decomposition process.[25] Bile acids and sterols can be analysed to determine if the coprolites were from humans or different animals.[26] In prehistoric societies that built houses over water, the faeces and urine may become mixed with the sediment on the floor of the lake and preserved around the margins of the wooden dwellings. Sampling this sediment can recover the eggs originally deposited in the faeces and urine of the inhabitants.[27] Some past societies made portable toilets out of clay, known as chamber pots, and the eggs of intestinal parasites may survive in the mineralized concretions to be found at their base.[28] When a person dies and their body is buried, the intestines decompose and become mixed into the soil of the pelvic area. Therefore, sampling sediment from the sacral and pelvic region of human skeletons at the time of their excavation can result in the recovery of the eggs of the intestinal parasites that were originally present during life.[29] Sieving the sediment from the region of a burial may also enable recovery of ectoparasites such as fleas and body lice.[30]

When environmental conditions prevent decomposition of the body after death, then a range of soft tissue may be preserved. These are known as mummies. Some mummies are naturally preserved, such as the frozen Bronze Age Ice Man from the Alps in Italy, the bog bodies of northern Europe preserved in the acid peat bogs, the dried mummies in monastery crypts of renaissance Sicily, or the high-altitude mummies of the Andes.[31] However, some societies actively mummified bodies by removing soft tissue organs from the chest, abdomen, and head, and packing the cavities with preservative materials. The most famous ancient civilization for doing this was that of Ancient Egypt.[32] The survival of mummified tissues allows us to look for preserved mature parasites that

[24] Smith (2013). [25] Bryant and Dean (2006); Shillito et al. (2020); Yang et al. (2022).
[26] Ledger et al. (2019a); Mitchell et al. (2022).
[27] Dommelier et al. (1998); Ledger et al. (2019b); Maicher et al. (2019).
[28] Rabinow et al. (2022). [29] Mitchell (2017c); Le Bailly et al. (2006); Reinhard et al. (1992).
[30] Raoult et al. (2006). [31] Lynnerup (2007). [32] David and Tapp (1984).

normally live in those surviving tissues, and also to detect proteins and DNA from parasites that would have spread around the body during life. Head lice and body lice may also be preserved adherent to the hairs on the mummies' skin, while fleas may be in their clothes.[33]

## How We Can Detect Ancient Parasites

The various types of evidence for parasites require quite different laboratory techniques to identify them. The eggs of most intestinal parasitic worms have evolved to be tough and robust to prevent their being digested in the human intestines. For this reason they may survive in a recognizable form in archaeological material for thousands of years, if not consumed by fungi and insects in the environment.[34] However, the eggs of some helminths, such as pinworm and hookworm, are fragile and only survive in environments ideal for the preservation of organic material.[35]

A number of techniques have been found by different teams to be effective for concentrating helminth eggs from archaeological sediment and coprolites, including the use of sedimentation, flotation, and micro-sieves. The eggs can then be viewed using light microscopy at ×400 or ×600 magnification.[36] While some species of parasite can be accurately identified by the shape, size, colour, and special characteristics of their eggs, for others it may only be possible to allocate the genus and not the species if several related helminths produce eggs of similar appearance.

The cysts and oocysts of intestinal protozoa that cause dysentery are fragile and often do not survive well in archaeological samples. One effective approach can be to employ special stains that highlight the protozoa on microscopy, such as immunofluorescence.[37] Another helpful technique is enzyme-linked immunosorbent assay (ELISA). This method uses antibodies made to bind to proteins that are unique to a particular species of organism. The process of binding changes the colour of the ELISA test well, which can be detected by passing light of a specific wavelength across the ELISA plate in an ELISA reader. This allows detection of protozoal cysts even when they have been distorted or damaged so as not to be recognizable on microscopy.[38]

[33] Arriaza et al. (2013). [34] Morrow et al. (2016). [35] Reinhard et al. (2019).
[36] Anastasiou and Mitchell (2013a); Dufour and Le Bailly (2013); Fugassa et al. (2006); Warnock and Reinhard (1992).
[37] Faulkner et al. (1989); Le Bailly et al. (2008).
[38] Gonçalves et al. (2002, 2004); Le Bailly and Bouchet (2006).

Ancient DNA (aDNA) analysis detects the genetic material of past organisms, often allowing identification down to species level. Unlike the genetic material of modern organisms, aDNA is typically fragmented and survives in short segments.[39] Genetic research using polymerase chain reaction (PCR) and either the earlier Sanger sequencing or more recent next-generation sequencing would use a primer to target a specific section of the DNA unique to that species, and analysis would give either a positive or negative result.[40] However, a negative result might indicate the absence of the organisms, or merely that the DNA from that section of the genome had not survived well enough for detection. In other words, there is potential for false negatives, where scientists would not be able to detect species that were actually present in their samples. Furthermore, species of parasite will only be identified if the lab specifically tests for them. This means that species not thought likely to be present, and so not targeted for testing, could be missed. Different environments will affect whether parasite eggs or aDNA survive better, so that some studies have shown species visible on microscopy but not picked up with aDNA analysis, and similarly other species noted on aDNA but not visible on microscopy.[41]

Recently, a further advance in aDNA analysis has been developed, known as metagenomics. This uses an approach where all the DNA fragments in the sample are amplified and sequenced, and computational analysis separates out the irrelevant data and then compares relevant data to databases of known organisms.[42] When searching for ancient parasites, this means separating out the data for the DNA of humans, farm animals, environmental soil organisms, and just looking for sequences that match known parasites.[43] Some genetic sequences are shared by many different organisms, but where sequences are unique to a particular species of parasite then an identification can be made.[44] One key limitation of this approach is that data analysis will only highlight organisms whose genome is known and uploaded to the reference database used. Many parasites that we know exist have yet to have their whole genome sequenced, and so may not be detected using metagenomics.

[39] Wood (2018). [40] Côté et al. (2016); Flammer et al. (2020).
[41] Maicher et al. (2017); Flammer et al. (2018). [42] Spyrou et al. (2019).
[43] Sabin et al. (2020). [44] Anastasiou and Mitchell (2013b); Côté and Le Bailly (2018).

## Structure of the Book

Each chapter will begin with a summary of what we know about the peoples, cultures, and civilizations covered there. This will provide the context for who lived in the region, how cultures rose and fell, and the way in which people lived their lives. Evidence for parasites affecting those populations will then be discussed and interpreted. Where sufficient data exist we may be able to estimate how common key parasite diseases were. When integrated with modern understanding of the symptoms and consequences of infection, a well-rounded view of the effects of parasitism in each society should be achieved.

At the end of the book, the conclusion chapter will be where we compare and contrast parasitism in different past civilizations. This will allow us to clearly see the dominant types of parasite in different regions of the world through the millennia. There we can highlight which civilizations experienced the greatest burden of ill health from parasites. This will be determined based upon the way in which different parasite species cause disease or death, and how common infection was among the people. Once we know which past civilizations were hardest hit by parasite infection, we will have achieved a clearer understanding of the process by which infectious diseases may have affected how those civilizations arose, flourished, and later collapsed and faded into memory.