Part I - Parasites, Human Hosts, and the Environment

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7

The Origin of Parasites of Humans

Luiz Fernando Ferreira • Karl Jan Reinhard • Adauto Araújo

The origin of parasites of humans is subject to interesting speculation. Paleoparasitology has contributed extensively with its data and findings of parasites in ancient material, shedding light on some questions while raising others concerning the origin and evolution of parasitic infections.

Two main routes are discussed for the origin of parasites in the human species. The first was the so-called ecological route, by which new parasites acquired from the environment began to infect humans as the latter conquered new spaces. This happened during the exploration of new territories and contact with different animal species and their parasites, in addition to free-living species potentially capable of adapting to parasitism. The second route was phylogenetic, by which various parasite species persisted in *Homo sapiens*, inherited ancestrally and originating during pre-hominid times (Ferreira, 1973). In the latter case, these parasite species are also found in phylogenetically proximate hosts, like the apes of the superfamily Hominoidea, family Hominidae, since the parasites were inherited from a common ancestor. Protozoan species that parasitize humans show greater phylogenetic affinity with those that parasitize primates as compared to those that parasitize other mammals (Hegner, 1928). Thus, phylogenetically inherited parasites include those now found in species *Homo sapiens* and shared with close primate species like gorillas, chimpanzees, bonobos, and gibbons. When *Homo sapiens* emerged as a species, some parasites were already ecologically and physiologically adapted to infect us (Ferreira, 1973).

Pinworm infection (*Enterobius vermicularis*), discussed later in this chapter, illustrates the case of parasites inherited from ancestors. However, other parasites began to infect our species through contamination of different environments that humans began to inhabit, in a dynamic adaptive process. Some parasites are unable to infect humans, or only do so partially. For example, when larvae from hookworms of canids (*Ancylostoma caninum* and *Ancylostoma braziliense*) penetrate the human skin, they are unable to complete their life cycle, remaining in the skin tissue and causing a dermatosis called cutaneous larva migrans or creeping eruption due to the itchy trail left by the larvae. The same occurs with larvae of *Toxocara canis*, which hatch from eggs ingested by the human host. Similar to infection with *Ascaris lumbricoides*, the eggs hatch in the intestine, but unlike the parasite of humans, their larvae

cannot complete the cycle and lodge in the liver or other organs, occasionally causing visceral larva migrans in the human host (Queiroz et al., 2006).

The human species and some of its ancestors have always distinguished themselves by extensive mobility and conquering new ecosystems. Another characteristic of humans, the invention and constant improvement of new technologies, created extraordinary changes while simultaneously offering opportunities for other parasite species to enter into contact with and install themselves in the human host, due to another human characteristic, namely constant contact with animals.

THE ORIGIN OF HELMINTH PARASITES

Systematic studies on the origin of helminth parasites gained important impetus with the work of Baer (1951) and Cameron (1956). These authors speculated on the domestication of animals and plants and the passage of parasites to the human species. According to Pearce-Duvet (2006), the origin of various human parasites, such as the etiological agents of tuberculosis, measles, smallpox, tapeworm infection, and others were associated with the emergence of agriculture and domestication of animals that accompanied human clustering.

However, this idea does not apply to all parasite species, since (as discussed above) some were inherited by humans from their ancestors, as shown by cladistic studies (Hugot, 1999) and paleoparasitological data (Araújo & Ferreira, 2000).

THE CONTRIBUTION OF PALEOPARASITOLOGY TO STUDIES ON THE ORIGIN OF HUMAN PARASITES

Paleoparasitology provides the means to trace the origin and dispersal of parasites using various methods. Direct evidence of fossil parasites can be obtained from coprolites, latrines, mummies, sediment from archaeological sites, and a wide variety of other materials (Gonçalves, Araújo & Ferreira, 2003; Bouchet, Harter & Le Bailly, 2003). After dating with adequate techniques, the results show the paleogeographic distribution of parasitic infections. Interaction with various other scientific fields has been crucial for paleoparasitological studies. Collaboration with archaeologists, paleontologists, and other specialists is essential for obtaining material and interpreting results. Thus, anthropology, genetics, and molecular biology combine to seek more consistent answers to the evidence from paleoparasitology. Results obtained by recovering genetic material from parasites in archaeological remains provide answers in paleophylogeography, the phylogenetic relations among species over time (Dittmar, Souza & Araújo, 2006).

Another approach involves the relations of current parasites through cladistic studies. Cladistics, or cladism, is the study of kinship between species, based essentially on the analysis of evolutionary relations (Rey, 2003), using morphology or molecular biology, and inferring the species' origins. Some studies resulted in parasite phylogenies using these mechanisms (Iñiguez et al., 2002). The appearance of given parasite species was determined using the molecular clock, a genetic technique capable of determining when two species diverged. Scientists have used the technique to determine how long species took to evolve, and it is still used to study parasitic infections of public health importance (Salemi et al., 2008).

A potentially powerful approach is the study of fossil parasites using molecular biology techniques. This adds a third dimension to findings from paleoparasitology and cladistic studies by reconstructing changes and permanence in gene sequences over time, using molecular biology techniques (Greenblatt & Spigelman, 2003).

Another method to date the emergence of parasites and relate them to host speciation is to superimpose parasites' phylogeny on that of their hosts. If the phylogenies are congruent, one can infer a mutual evolution of the parasite and host species. In such cases, identifying the emergence of parasite species in time and space is based on dating host fossils, either by finding parasite forms in the archaeological or paleontological record or by retrieving genetic material to determine the parasite and host species identification, in a dynamic process of the history of the evolutionary process for each relationship between certain parasite and host species (Araújo et al., 2003).

Parasites found in extinct host species illustrate this line of investigation. Finding nematode larvae in coprolites from a species of hyena that inhabited northern Italy opened this field of investigation (Ferreira, Araújo & Duarte, 1993). Even older parasites were found in Belgium in dinosaurs (iguanodons) from the Cretaceous. Protozoan cysts and helminth eggs were described in coprolites from these animals, dated to millions of years before present (Poinar Jr. & Boucot, 2006).

Possible new parasite species were described in dinosaur coprolites, and protozoan parasites were described in insects preserved in amber, thus demonstrating the potential preservation achieved by these ancient remains (Poinar Jr., 2007, 2008).

When studying the evolution of parasites, it is important to view them as part of the a complex system consisting of the parasite, the host, and the environment in which they are situated, if possible understanding the relationship between a parasite species and its host and how this relationship is affected by the environment. One can thus infer aspects of the ecology of diseases in ancient peoples, or pathoecology (Reinhard, 1992). Therefore, when approaching the various aspects of parasite-human host relations, many situations can be examined and the results can contribute to a better understanding of the origin and evolution of infectious diseases.

ANTIQUITY OF HUMAN PARASITES

Ever since humans emerged as a species several million years ago, we have been parasitized by various organisms such as viruses, bacteria, protozoa, helminths, arthropods, and others. As with all other living beings, human life does not exist without the presence of parasites.

Transmission of a parasitic infection from host to host occurs in various ways, according to the parasite species, and the mechanisms have undergone adaptations throughout the evolution of the parasite-host-environment triad. Such mechanisms can include direct host- to-host transmission, contamination of the environment with infective forms of the parasite, or transmission by vectors like arthropods, mollusks, or other invertebrates, as well as so-called parathenic hosts (Rey, 2003).

Some parasites are transmitted between hosts, unimpeded by factors from the macroenvironment in which the host lives, such as climate, pH, or soil moisture, since they develop alternative strategies. Among the nematode parasites of humans, *Enterobius vermicularis* is transmitted from one host to another without necessarily passing through the soil. In the *E. vermicularis* life cycle, gravid females migrate from the large intestine to the anal region (especially when the infected person is resting), causing perianal discomfort and itching. The females, full of eggs, burst due to degeneration or when the host scratches, releasing the eggs. Since the eggs are already embryonated, the larvae can hatch and migrate back into the intestine. The eggs can then contaminate the host's hands, infecting him again through hand-to-mouth movements. Other persons thus become infected through close or direct physical contact with the host. One can imagine how many adults have acquired pinworm infection by holding infected children in their laps; the infected children playfully touch the adult's mouth with their hands full of eggs under the fingernails!

Eggs are found in dust and especially in bed clothes, dispersing in the wind and on air currents. In orphanages, barracks, prisons, hostels, and other places with collective sleeping quarters, making up beds and shaking the bed sheets disperses the eggs throughout the environment, quickly contaminating everyone.

Pinworm infection is so well-adapted to humans that it is distributed worldwide, in the widest diversity of biomes, regardless of temperature, humidity, or other transmission factors. The same pinworm species infects the Inuit of Alaska, indigenous peoples from the Amazon rainforest, Australian Aborigines, and indigenous peoples from Patagonia (Araújo et al., 1988).

The history of the evolution of pinworms that parasitize humans has been traced by various paleoparasitological approaches. In association with paleoparasitology, cladistic studies have provided a successful method. Brooks & Glen (1982) and Hugot, Reinhard & Gardner (1999) obtained results from refined cladistic analyses of pinworms of apes and other primates. These studies show that pinworm phylogeny runs parallel to primate phylogeny. Pinworms thus evolved mutually with humans and previously with hominid hosts. The conclusion is that the origin of pinworms predates humans, having evolved in pre-hominid human ancestors.

The paleoparasitological record shows data whose antiquity dates back 10,000 years, in North American indigenous groups from the Great Basin Region (Fry & Hall, 1969). The presence of *E. vermicularis* in such ancient periods confirms that pinworms were introduced into the Americas with the first migrants. Findings have also been recorded in Egyptian mummies, prior to the great Portuguese and Spanish seafaring voyages (Horne, 2002; Bouchet, Harter & Le Bailly, 2003).

Morphologically, the eggs found in archaeological material are identical to those in the current human population. However, some differences have been found in their genetic makeup in certain South American human populations (Iñíguez et al., 2002). These studies point to distinct origins of the parasite strains in the Americas, with implications for the peopling of the American continent.

Reinhard (1990) showed that the characteristics of interactions with the environment adopted by certain groups facilitated the conditions for the increase or decrease in risk of pinworm infection. In some groups of hunter-gatherers, a diet rich in plants with anthelmintic activity apparently limited various helminths infections, including *E. vermicularis*. In contrast, the construction of buildings, as in the case of the Ancestral Pueblos in Arizona and the Incas in Chile, along with the reduction in the ingestion of plants with anthelmintic activity, caused a significant increase in *E. vermicularis* infection.

The construction of apartment-style buildings in densely grouped (although relatively small) populations, combined with the fact that pinworm infection can be transmitted by egg transport on air currents, created a new ecological situation that favored pinworm parasitism. Thus, the evolution of pinworm transmission was intimately related to human behavior and characteristics during a period in which human populations were sparse and small. Changes in human ecology, like the adoption of collective dwellings, enhanced the parasite's transmission by concentrating more hosts in confined spaces (Reinhard, Ambler & McGuffie, 1985; Ferreira et al., 1989).

E. vermicularis is one example among many, like other nematodes that live their cycle in the soil, called geohelminths, which took their evolutionary paths by following the human host ever since the species emerged on the African continent.

LICE IN HUMANS

Lice are another interesting example of parasites inherited from pre-human ancestors. Like pinworms, lice of humans are transmitted directly between hosts, and the infection is found in human populations in the most diverse places on the planet. The same louse species or phylogenetically proximate subspecies can infect the Inuit in Alaska, indigenous peoples in the Amazon, and Australian Aborigines (Araújo et al., 1988; Light et al., 2008).

Lice have parasitized primates for at least 25 million years. Approximately 6 million years ago, when chimpanzees and humans diverged, the two host species inherited and shared genus *Pediculus* (Reed et al., 2007; Raoult et al., 2008). Various studies have traced the origins of lice infection in humans, showing that head lice, *Pediculus humanus*, coevolved with humans since a pre-hominid, and as occurred with *Enterobius vermicularis*, spread to other parts of the world, when humans dispersed out of Africa. Paleoparasitological findings have confirmed these assumptions. Lice have been found in archaeological sites in the Southeast United States, Central Mexico, the Aleutian Islands, Peru, Brazil, and Greenland, in times prior to Christopher Columbus' arrival in the Americas (Rick et al., 2002a).

Like *Enterobius vermicularis*, lice of humans suffered less influence from conditions in the macroenvironment but had to adapt to changes introduced by their host in the microenvironment. For example, when humans began to wear clothes, change hygiene habits, and adopt haircuts or use wigs and elaborate hairdos that went months without changing, the human host changed the microenvironment in which the parasite lived.

Paleoparasitological findings show that lice were present in what is now Brazilian territory some $10,640 \pm 80$ years ago (Araújo et al., 2000). These data, as well as the oldest data for *E. vermicularis* (Fry & Moore, 1969), indicate that human lice infection was introduced into the Americas with the first migrants more than 10,000 years before the arrival of the first Europeans on the continent (Araújo et al., 2000).

Archaeological and paleoparasitological reconstructions of the archaeological site where lice were found in what is now Arizona, USA, dated 600 AD (Reinhard, unpublished data), indicate that this human group consisted of numerous adults and children that subsisted on diversified agriculture.

Meanwhile, studies in the Great Basin, where lice infection was also found, showed that the infected population consisted of small groups of nomadic hunter-gatherers that fed on a limited variety of animals and plants. The data thus show that lice infection existed in societies with different degrees of complexity.

Lice infection in Andean societies that used sophisticated hairdos was common and perhaps related to the trade and control of groups dominated by Inca society. There are documents referring to taxes paid with tiny bags of nits and adult lice (Souffez, 2001).

An interesting aspect of lice infection is that geographic isolation provided distinct opportunities for evolution of the head and body lice strains. Some researchers in systematics have even postulated variations of the current species *Pediculus humanus* when comparing indigenous peoples of North and South America (Ewing, 1926). These studies have continued recently with the work of Yong et al (2003), Kittler, Kayser & Stoneking (2003), Leo & Barker (2005), and Leo et al (2005).

The lice that parasitize human hair, belonging to genus *Pediculus*, present two distinct lineages. One is only found parasitizing hair, while the other can be found in both hair and clothing. The louse species that parasitizes chimpanzees, *Pediculus schaeffi*, and the lineage of *Pediculus humanus* found in both the hair and on the body shared a common ancestor some 6 million years, consistent with the their host species' diversification (Reed et al., 2007). The other lineage of *Pediculus humanus*, found only in hair, parasitizes humans in the New World, having diversified

by geographic isolation some 1 million years ago (Reed et al., 2004). The latter research group has studied the genetic diversity of modern louse specimens collected in diverse regions, concluding that three lineages exist, A, B, and C, with different geographic origins on the various continents. They concluded that lineage B has an American origin (Light et al., 2008).

Such diversification can be used for lice found in archaeological material, especially in studies using molecular biology techniques, comparing genetic sequences between modern and ancient lineages to elucidate the geographic origin of the parasites and human groups.

The discussion should include another genus of lice, *Pthirus*, including species *Pthirus pubis*, a parasite of humans, and *Pthirus gorillae*, a parasite of gorillas. While species from genus *Pediculus* are only found in humans and chimpanzees, genus *Pthirus* is found in humans and gorillas, but not in chimpanzees. There are some inconsistencies in the time at which the two *Pthirus* species separated, failing to coincide with the divergence of their hosts (Reed et al., 2007).

Specimens of the two genera have been found in human remains in both the Old and New Worlds (Rick et al., 2002b; Mumcuoglu et al., 2003). An interesting line of study focuses on nits in well-preserved hair from mummified bodies, as found in the Atacama Desert in Chile, some cases in Brazil and the United States, and even on some shrunken heads, used as trophies by some South American indigenous groups. As shown by Linardi et al (1988), the eggs remain attached to the hair shaft for a long time and can be studied to estimate the time of infection of the individual according to the position in relation to the hair root.

EXAMPLES OF OTHER PARASITES

Trichuris trichiura or whipworm, a geo-helminth nematode that parasitizes the large intestine of humans, also reached the human species through pre-hominid ancestors. *Trichuris* eggs are transmitted by fecal contamination. They require specific environmental conditions like soil characteristics – moisture, pH, and temperature – for a period of time, until embryonating and becoming infective, and are ingested by (and infect) a new human host. The eggs are resistant but remain infective for a limited time.

There were two alternative hypotheses for the origin of human infection with *Trichuris trichiura*, reviewed by Confalonieri et al (1985). According to one, *Trichuris trichiura* infection originated with the domestication of pigs (*Sus scrofa*), and the species is derived from *Trichuris suis* (Samsonov, 1969). According to this hypothesis, the two species diverged recently and thus display very similar morphological characteristics, although detailed analyses show that they are distinct species. The two parasite species have completely diverse hosts.

The parasite of swine is found in *Sus scrofa domestica* and *Sus scrofa nigripes*, respectively domestic swine and wild boars (European boar). *Trichuris trichiura* infects great apes in nature, including species from genera *Pongo*, *Pan*, and *Hylobates*, and two Cercopithecoidae, *Macaca* and *Papio*.

Other *Trichuris* species evolved in Old World prosimians and primates. *Trichuris cynocephalus* parasitizes *Papio hamadryas* and *Papio cynocephalus*, *Trichuris presbyticus* is found in *Presbytis arvunculus*, and *Trichuris lemuris* in *Cheiroglaeus major*, *Lemur catta*, *Lemur macaco*, and *Daubentonia madagascariensis* (Ooi et al., 1993).

The distribution of *Trichuris* species in primates indicates mutual evolution with the primate hosts. The diversification of *Trichuris* species parallels the adaptive radiation of primates (Sarwar, 1959).

Trichuris trichiura speciated with the evolution of Hominoidea, and like *Enterobius vermicularis*, it already existed in hominids when they appeared.

Paleoparasitological findings of *Trichuris trichiura* eggs in mummified bodies and human coprolites support the hypothesis that the species precedes the estimated date for the domestication of pigs. The famous mummy Ötzi from the Tyrolean Alps was infected with *Trichuris trichiura*, as were mummified bodies found in European turf bogs before the presumed dates for the domestication of pigs (Bouchet et al., 2003). In the New World, *Trichuris trichiura* eggs were found in human coprolites dated to 5,000 BP (Confalonieri, 1988).

The necessary environmental conditions for maintaining the parasite's life cycle point to an origin in tropical regions. For embryonation to occur, the eggs must be in soil with adequate humidity, temperature, and shade. Such conditions are consistent with the tropical and subtropical environment in which hominids evolved and where humans parasitized by this species are currently found.

PLEISTOCENE DATING OF PARASITISM BY *ASCARIS LUMBRICOIDES*

In other cases, paleoparasitological studies have refuted assumptions on the origin of certain parasites. The morphological similarity between the intestinal nematodes *Ascaris lumbricoides* and *Ascaris suum*, the ascarid parasites of humans and swine, respectively, led researchers to accept that the evolution of these parasites was somehow related. Genetically, the two parasites differ very little from each other and can be considered sibling species. In fact, it was proven that *Ascaris suum* can experimentally infect humans and that *Ascaris lumbricoides* can experimentally infect swine (Leles et al. 2008). The evolutionary separation may have occurred more recently, and there are doubts as to whether they are really two distinct species.

Since Cameron's pioneering work on *Ascaris lumbricoides*, it was accepted that the parasite originated from the species found in swine. The domestication of pigs was thought to have provided human contact with ascarids, and that *Ascaris lumbricoides* subsequently emerged as a species.

However, infection with *Ascaris lumbricoides* has been confirmed in archaeological sites in North and South America. The oldest known date for this parasite is 5,000 BP. As far as we know, *Ascaris suum* does not infect South American wild pigs under natural conditions (Artiodactyla, Tayassuidae). In addition, no record of *Ascaris lumbricoides* has been found in regions where wild pigs were autochthonous. The domestication of pigs must have occurred in the Old World around 7,000 years ago. Therefore, the presence of *Ascaris lumbricoides* in the New World is inconsistent with an evolutionary origin of *Ascaris lumbricoides* from *Ascaris suum* with the domestication of pigs.

The data suggest that the evolutionary origin of *Ascaris lumbricoides* is older than previously believed. However, the data from America are circumstantial. Direct evidence from the Old World was needed to definitively confirm infection with *Ascaris lumbricoides* in humans prior to the domestication of pigs.

Such evidence was finally found in human coprolites excavated in France, dated 28,000 BP (Loreille & Bouchet, 2003). The analyses were positive for *Ascaris lumbricoides* eggs, thus proving that *Ascaris lumbricoides* parasitized humans since the Pleistocene, long before the domestication of pigs.

One can conclude that if *Ascaris lumbricoides* and *Ascaris suum* had a common evolutionary history, the latter would have originated from the human parasite after the domestication of swine, through human contact with these animals. In other words, precisely the opposite of what was believed.

Ascaris eggs remain infective in the soil for many months or even years, depending on conditions in the environment (Rey, 2008), but resisting changes from intense heat to intense cold, for example on the European continent. While the macroenvironment changed, the microenvironment (i.e., the host's organism) remained the same. This allowed infection with *Ascaris lumbricoides* to be maintained in the small bands of hunter-gatherers that characterized human prehistory.

If a temporary camp were contaminated, the parasites' eggs could remain viable and infective for more than a year and infect new hosts. This parasite-host-environment relationship was enhanced when human populations became urban.

Paleoparasitological data on *Ascaris lumbricoides* indicate a long history of infection in Europe, since very ancient periods, still in the Neolithic. However, the infection became much more common under the unhealthy conditions and crowding of Medieval Europe (Fernandes et al., 2005). After establishing itself as the most common helminth infection in humans, it dispersed with the Europeans that colonized other regions of the globe. Disordered urbanization, fostering conditions of environmental contamination by fecal matter, made *Ascaris lumbricoides* infection an inevitable part of urban life.

An interesting aspect of *Ascaris lumbricoides* is its relative scarcity in parts of the prehistoric world where *Trichuris trichiura* is commonly found. Both during the medieval period and in modern times, *Ascaris lumbricoides* and *Trichuris trichiura* are frequently associated. The two have similar life cycles, as well as resistant eggs that can remain infective for long periods, months or years (Rey, 2005). Both proliferate in crowded and unhealthy conditions.

Even so, in prehistoric times they were not always associated or their eggs were not preserved identically in archaeological sites, indicating a subtle difference in the two species' parasite-host-environment relations or in their preservation in the archaeological record.

Ascaris lumbricoides eggs have only been found in two prehistoric sites in the New World, one in the Southwest United States and the other in Northern Peru. There was also a single finding in Southeast Brazil (Gonçalves, Araújo & Ferreira, 2003). In contrast, *Trichuris trichiura* eggs are found in many sites in the Americas.

Ascaris lumbricoides was absent from Japan until the introduction of rice farming, although *Trichuris trichiura* was present in the ancient Jomon cultures (Matsui, Kanehara & Kanehara, 2003). Considering the ubiquity of *Ascaris lumbricoides* infection in ancient urban settlements and in the modern world, its scarcity or absence in certain parts of the world and during certain periods requires explanation. Conditions in the parasite-host-environment system may have made human infection relatively rare until urban settlements and agricultural practices developed.

Meanwhile, the taphonomic process influences organic structures of diverse origins in different ways (Timothy et al., 2003). Thus, in South American sites previously considered negative for *Ascaris lumbricoides* eggs (Gonçalves, Araújo & Ferreira, 2003), molecular biology techniques showed positive results with the recovery of genetic material from the parasite (Loreille & Bouchet, 2003; Leles et al., 2008, 2009).

Considering only the dates, *Ascaris lumbricoides* infection most likely spread across Europe during the Pleistocene, was introduced into parts of the Americas in the Holocene, but only penetrated into Japan with rice farming (50 AD). Thus far we lack data on Africa that allow a more precise evaluation on its origin in pre-hominids or in human ancestors closer to our species.

Finally, *Ascaris lumbricoides* is more susceptible to anthelmintics than *Trichuris trichiura*. Adult *Ascaris lumbricoides* worms live in the small intestine and remain there due to muscle movements. Adult *Trichuris trichiura*

burrow their thinner anterior portion into the mucosa of the large intestine, leaving the posterior portion projecting into the lumen. Some anthelmintics temporarily paralyze the parasites. Temporary paralysis of *Ascaris lumbricoides* leads to its expulsion from the intestine, which may not occur with *Trichuris trichiura*, since it remains attached to the intestinal mucosa. Thus, by using plants with active ingredients that cause paralysis in worms, human populations could have altered the environmental conditions for *Ascaris lumbricoides*, limiting infection by the parasite, but the use of these same plants would have no effect on *Trichuris trichiura* (Chaves & Reinhard, 2003).

THE ANTIQUITY OF HOOKWORM INFECTION AND ITS ANCIENT DISTRIBUTION

The clinical condition known as ancylostomiasis is associated with the presence of *Ancylostoma duodenale* or *Necator americanus* in the human intestine. These species can be found alone or in association in the same individual. *Ancylostoma duodenale* and *Necator americanus* are considered anthrophilic, thus more adapted to the human host. However, parasitism can occur with adult forms of *Ancylostoma ceylanicum*, and by larvae and rarely adult forms of *Ancylostoma caninum* and *Ancylostoma braziliense* (Rep, 1963).

The Southeast region of the Sahara Desert in Africa is considered the center for the dispersal of human infection with *Necator americanus*. Dispersal of *Ancylostoma duodenale* began from some point in Northern Africa, Southern Europe, or Southern Asia. After the increase in communication among peoples, especially during the 19th century, the limits in the distribution of the two species became less clear (Manter, 1967).

Cameron (1927) was the first to discuss the origin of hookworm species that parasitize humans. According to him, wild canids and later domestic dogs were the source of an ancestral species of *Ancylostoma duodenale*. Humans would thus have acquired this parasite after the domestication of dogs.

According to Zeuner (1963), the first relations between wolves, wild dogs, and hunter-gatherer humans could not have been very close, given the presumed competition between them. The author hypothesized that domestication of the dog occurred in Europe, possibly during the Paleolithic, but certainly by the Mesolithic, some 9,000 years ago. Canine and human skeletons have been found in association, dated to 11,000 BP in Arabia and 11,500 BP in Persia (Protsch & Berger, 1973).

According to one hypothesis, *Necator americanus* originated from parasites of African ungulates, and a pre-hominid ancestor was parasitized in the savannah-forest ecotone, in the same habitat as zebras and gnus. Thus, *Ancylostoma duodenale* would have emerged in *Homo sapiens*, while *Necator americanus* already infected human ancestors. However, this view was not unanimous. Fonseca, Filho (1972) contended that both parasite species were already found in *Homo sapiens* when the latter speciated, since they exist in African great apes (*Pan (Homo) troglodytes*, *Gorilla gorilla*). These primates thus acquired the parasite from a common ancestor. Meanwhile, this common ancestor became parasitized, probably by the ecological route, by occupying habitats with infected hosts, since the closest species to *Necator americanus* are found in animal hosts that are not phylogenetically close to primates, such as the ungulates (Chitwood, 1970; Dunn, 1970).

Hoagland & Schad (1978) studied the origin of parasite species inherited by the phylogenetic route, using the biological characteristics and parasite-host relations observed in *Necator americanus*. Their results point to the parasite's long association with humans. The parameters verified in the comparison included infection and reproduction strategies, as well as low pathogenicity and virulence.

The presence of *Ancylostoma duodenale* in prehistoric populations in the Americas, especially in Northeast Brazil, dated $7,230 \pm 80$ BP, is strongly indicative of an older association between dogs and humans than previously assumed if Cameron's hypothesis (1927) were correct. In this case, the origin of *Ancylostoma duodenale* would have been long before 7,000 BP, since both the human host and the parasite originated in the Old World (Araújo, 1988).

In nematode parasites, it is possible to assess the antiquity of parasite-host relations according to the parasite's ontogenic characteristics and pathogenicity (Chabaud, 1955). Hoagland & Schad (1978) studied these characteristics in *Ancylostoma duodenale* and *Necator americanus*. They aimed to determine which species was better adapted to the human host, basing their analysis on the r and K selection characteristics (MacArthur & Wilson, 1967). More opportunistic species are more involved in a process of conquering new habitats, and are considered to be dominated by r selection patterns. K-selected species are more stable in the environment. The analysis concluded that *Necator americanus* displays patterns of greater stability when compared to *Ancylostoma duodenale*. However, this analysis is limited by the fact that it compares parasite species that are not closely related.

Therefore, the same procedure was adopted with *Ancylostoma duodenale*, a parasite of humans, and *Ancylostoma caninum*, a parasite of canids (Araújo, 1988). The two species' morphological and biological patterns were compared to determine which was better adapted to its specific host. The results showed that the canine parasite has more r selection attributes than *Ancylostoma duodenale* in humans.

Other data favoring the hypothesis of an ancient association between *Ancylostoma duodenale* and humans is the finding of this species (or very closely related species) in other members of the Hominidae family (Dunn, 1966).

Genus *Ancylostoma* is distributed across carnivores, primates, edentates, rodents, and swine (Lichtenfels Jr., 1980). It probably emerged as a parasite of carnivores, acquiring other hosts over the course of its evolution. However, *Ancylostoma caninum* does not appear to be older or better adapted to parasitism in canids than *Ancylostoma duodenale* in *Homo sapiens* (Araújo, 1988).

The origin of parasitism by *Ancylostoma duodenale* in humans must be found (as with *Necator americanus*) in a phylogenetic route coming from pre-hominids. Recent phylogenetic studies based on DNA sequences appear to confirm these hypotheses by showing phylogenetic relations that proved an older history for *Ancylostoma duodenale* than for *Necator americanus* (Blaxter, 2000).

In summary, paleoparasitological findings indicate that a large share of current human parasites have lived for a long time with the human species. In the Old World, malaria parasites and Trypanosomatidae have a long evolutionary history with hominids. Thus, human populations emerged and evolved concomitantly with a whole complex of parasites.

THE EVOLUTION OF TRYPANOSOMATIDAE

Paleoparasitologists have described several more complex relations between parasite, host, and environment in detail. Lambrecht (1985) studied paleontological evidence on species of genus *Glossina* (tsetse fly) in Africa. *Glossina* species act as the vector for *Trypanosoma rhodesiense* and *Trypanosoma brucei*, the etiological agents of sleeping sickness. His analysis showed that genus *Glossina* originated in the Pliocene. Based on the characteristics of human resistance to different species of *Trypanosoma*, Lambrecht (1985) presents convincing evidence that at least one species of *Trypanosoma* parasitized hominids for millions of years. The author's arguments thus suggest that genus *Trypanosoma* is another ancestral parasite of the group of hominids. However this was not the route in

the case of *T. cruzi*, since this parasite only began to be transmitted to humans after the peopling of the Americas, according to the paleoparasitological data.

The reconstruction by Lambrecht (1985) was verified by molecular analysis of some species of *Trypanosoma*. Stevens, Noyes & Gibson (1998) analyzed rRNA sequences from four species of *Trypanosoma* of human and non-human primates. The studies showed that *T. brucei* originated between five and 15 million years ago and coevolved with hominids.

A comprehensive study on the origins of human infection began in the Americas, developed independently by different research teams. Suspected clinical cases of Chagas disease were described in South American mummies (Fornaciari et al., 1992), marking preliminary paleopathological studies in mummified bodies. Some were partially proven by histopathology, but without confirmation as to whether the observed structures were in fact amastigote forms of *Trypanosoma cruzi*.

The advent of molecular biology techniques has led to great progress in this field, exemplified by the chapter dedicated to the origin and evolution of infection with *T. cruzi* (see Chapter 26, dedicated to Chagas disease).

Capasso (1998) conducted an evolutionary study on mosquito vectors preserved in amber. Analyzing the diseases transmitted by different genera of mosquito vectors with infectious agents, he deduced the antiquity of important human parasitic diseases. His analysis showed that the genera of mosquito vectors evolved in the Pliocene and inferred that malaria was prevalent in hominids. Thus, by analyzing the vector's antiquity, he reached a conclusion on the antiquity of parasitism by *Plasmodium* in human populations.

Studies also began in Brazil with insect vectors preserved in amber, leading to the description of new sand fly species (see Chapter 10, on Arthropods and Parasites in Amber).

PARASITES OF ANIMALS IN HUMAN COPROLITES

As humans began to conquer a wide range of environments, they encountered parasites that infected other animals. Such parasites are called etiological agents of zoonoses, or diseases of animals that are transmitted to humans. However, in the case of helminth infections, we prefer to call them parasites of animals with the potential to infect humans, since the archaeological material does not allow distinguishing between true infections (when the parasite actually establishes itself in the host) and so-called false infections (when helminth eggs from parasites of animals are excreted in the human feces for several days, but without true infection) (Carvalho-Costa et al., 2009). Paleoparasitological data in the Americas have shown the wide distribution of zoonotic parasites among pre-Columbian hunter-gatherers. One can only speculate on the range of these or similar parasitic infections in Africa, where the paleoparasitological data are scarce (Dittmar & Steyn, 2004; Horne, 2002).

In the Americas, the following parasites have been found in populations of hunter-gatherers: *Moniliformis clarki*, *Diphyllbothrium pacificum*, *Echinococcus granulosus*, *Trichinella spiralis*, *Paragonimus mexicanus*, *Echinostoma* sp., *Parapharyngodon sceleratus*, and an unknown tapeworm species. These parasites circulate in wild animals, infecting humans that eat poorly cooked meat or insects (Rey, 2008).

Infection with *Moniliformis clarki* results from ingesting raw or poorly cooked insects. Its focus of infection in prehistory was situated in the Great Basin Region of North America. The ingestion of raw or poorly cooked marine life can result in infection with *Diphyllbothrium pacificum*, which appears to be distributed mainly on the South

American Pacific Coast (Ferreira et al., 1984; Reinhard & Urban, 2003), but with cases described in populations on the Aleutians Islands (Bouchet et al., 1999).

Hydatid cyst results from ingesting *Echinococcus granulosus* eggs. The highest prevalence rates of hydatidosis are found in modern-day Africa, where some human groups eat dog intestine slightly seared over flames. This cooking process is light and insufficient to kill the embryos inside the eggs, leading to the ingestion of thousands of the tapeworm's eggs (Garcia, Moro & Schantz, 2007).

Trichinella spiralis generally causes a severe disease, and infection in humans appears to date to very ancient times (Owen et al., 2005). Infection with *Paragonimus mexicanus* results from eating poorly cooked freshwater crustaceans. Abundant eggs from *Echinostoma* sp. were found in a coprolite associated with megacolon in a mummified body in which the presence of *T. cruzi* was diagnosed with molecular biology techniques. Species of this parasite are found in mammals that ingest fish or crustaceans contaminated with its larvae and thus develop the infection. The infection is common in modern-day Asian countries, but has still not been reported in the Americas, except for the case described above in prehistory (Sianto et al., 2005).

Eggs from an unidentified tapeworm species were found in prehistoric sites in Arizona and Utah, in human coprolites and latrine sediments. The eggs may be from *Dipylidium caninum*, which has canids as its definitive hosts and rodents as its intermediate hosts. Humans are rarely infected, but some cases have been described (Neafie & Marty, 1993).

Zoonoses in Europe during the Neolithic and Post-Neolithic must have been a real problem for human groups whose subsistence strategies included raw or poorly cooked meat (Le Bailly et al., 2005, 2007). Foraging cultures have been particularly well-studied in the Americas and can provide general analogies for other parts of the world where there are no available data. Studies in prehistoric American populations suggest that ancient African hunter-gatherers were also exposed to similar infections. Certain species of *Echinococcus* and *Trichinella* are endemic in Africa. Other agents of zoonoses such as *Toxocara canis*, *Toxoplasma gondii*, and various tapeworms must have infected the ancestral African populations.

In relation to infection with *Toxoplasma gondii*, it is interesting that there are no records in ancient populations of humans or animals, although it is now one of the most widely disseminated infections in the world (Tamma, 2007). Genetic material has been successfully recovered from the tissues of experimentally infected and mummified rodents (Terra et al., 2004), and the same technique is still being tested in ancient material. Toxoplasmosis could be one of the oldest infections in humans and other animals ever since the dawn of Africa, but we still lack concrete data to confirm this hypothesis.

Bouchet et al (2003) found *Toxocara canis* eggs in organic sediments of human and other animal origins, dated 500,000 to 300,000 BP in Europe. Carnivores such as hyena and wolf species, together with humans, inhabited the same cave in which the eggs were found. Since they shared the space, even though at different moments, it is assumed that toxocariasis (*Larva migrans visceralis*) occurred in humans since this time. These data are consistent with findings that show *Homo neanderthalensis* butchering animals inside caves in Europe (Mellars, 2006; Metcalfe, 2007).

THE DAWN OF AGRICULTURE AND THE DISSEMINATION OF INFECTIONS BY FECAL MATERIAL

Cockburn (1973) demonstrated that agriculture led to the exposure of populations to various levels of health risk. Changes in parasite ecology with the introduction of horticulture have been well-studied by paleoparasitology. Various studies have proven Cockburn's view on the influence of horticulture. The horticulturists of the Colorado Plateau,

United States, were parasitized by a much wider range of species than the ancient hunter-gatherers (Reinhard, 1988; Reinhard, Hevly & Anderson, 1987). Diseases from fecal contamination intensified with agriculture, and some of them must have emerged in humankind during this period. Anal-oral infection became a problem in the emerging small villages, as exemplified by pinworm infection, discussed in the next chapter (Hugot et al., 1999).

During the medieval period, infections with *Ascaris lumbricoides* and *Trichuris trichiura* were so common in Europe that Andrew Jones found concentrations of up to 400 eggs per ml of soil sediment (Jones, 1985). Diseases of fecal contamination had apparently become a common and normal characteristic of urban life. Various records performed by paleoparasitologists confirm this point on parasitism in the medieval period (Bouchet, Harter & Le Bailly, 2003).

In North America, infection with *Hymenolepis nana* and *Hymenolepis diminuta* was probably associated with agriculture. These tapeworm species follow two different types of cycles to maintain their circulation in their hosts (Rey, 2008). One cycle in the case of *Hymenolepis diminuta* involves a two-host system, with a vertebrate as the definitive host and an invertebrate as the intermediate host. It parasitizes rodents, generally ruderal mice and rats. This type of association usually involves a species of weevil that is commonly found in stored grain and rodents. As discussed by Reinhard, Hevly & Anderson (1987), agriculture and grain storage facilitated this life cycle. A direct transmission cycle developed in *Hymenolepis nana*, so the parasite is transmitted between humans, but cases of autoinfection also occur.

The direct life cycle of *Hymenolepis nana* is unique among tapeworms that parasitize humans. All other tapeworm parasites of humans have a multiple life cycle, with more than one host. The direct cycle of *Hymenolepis nana* probably emerged recently from the two-host cycle. This emergence was associated with human behavior. Analyses of interspecific variations in isoenzyme patterns between different species of *Hymenolepis* showed that *Hymenolepis microstoma* was the common ancestor of *Hymenolepis diminuta* and *Hymenolepis nana* (Novak, Taylor & Pip, 1989). This analysis showed that *Hymenolepis nana* emerged more recently and that *Hymenolepis diminuta* is an intermediate form. Later studies on cross-immunity confirmed this hypothesis. The two hymenoleptids of humans, *Hymenolepis nana* and *Hymenolepis diminuta*, display phylogenetic proximity, but *Hymenolepis nana* emerged more recently (Palmas, Eccia & Gabriele, 1993).

Paleoparasitology made new contributions to the understanding of evolutionary pressures that gave rise to the direct cycle of *Hymenolepis nana*. The limiting factor for the maintenance of this species' transmission is that the eggs are highly dependent on conditions in the environment. Under hot and humid conditions, the eggs can remain viable for many weeks, but in dry environments they are only viable for a few hours. Thus, in the ecology of the parasite-host-environment system for *Hymenolepis nana*, the environment determines the likelihood of infection.

Hymenolepis nana eggs have only been found thus far in New World archaeological sites. They were present in prehistoric coprolites in Arizona, on the coast of Peru, in the Atacama Desert in Chile, and in the semiarid region of Northeast Brazil (Gonçalves, Araújo & Ferreira, 2003). Importantly, all these sites correspond to societies of horticulturists/farmers, and hunter-gatherers in Northeast Brazil.

Eggs of this parasite were also found in latrine sediments in Arizona (Reinhard, Hevly & Anderson, 1987). Two sites, one in Arizona and the other in Chile, were positive for nematode parasites with a direct cycle. Thus, for the two sites, fecal transmission must have been an efficient mechanism of infection. However, in two other sites, one of which was also in Arizona and the other in Peru, there is no evidence of other parasites transmitted by direct contamination from fecal matter. This may suggest that direct transmission was not effective in these locations. Thus, for these sites, the cycle involving two hosts, insect and rodent, would have maintained the infection cycle,

and humans would have become infected by fortuitously ingesting the intermediate host arthropod, probably grain weevils or fleas (Reinhard, Hevly & Anderson, 1987).

OTHER PARASITES OF ANIMALS CAPABLE OF INFECTING HUMANS

The environment is the determinant factor for infection by parasites. Population concentration causes sanitary problems that affect parasites, both specific to humans and those of animal origin. When more feces of infected individuals accumulate, the environment is more likely to be contaminated with eggs. This potentiates infection by certain zoonoses. For example, 16th-century paleoparasitological findings in Japan (Matsui, Kanehara & Kanehara, 2003) show that humans were infected with *Metagonimus yokogawai* and *Clonorchis sinensis*, among other parasite species. *Metagonimus yokogawai* has two intermediate hosts, first a snail (*Semisulcospira*) and later various species of freshwater fish.

Likewise, human infection with *Clonorchis sinensis* is limited by the distribution of the snail, generally *Parafoossarulus manhouricus*, and a fish species, serving as intermediate hosts. The fact that the intermediate host is restricted to the Far East means that distribution of the infection is ecologically limited. However, a case was described in the United States during the period of Chinese migration to America (Reinhard et al., 2008). In 16th-century Japan the population was already considerably large, and fecal deposition was widespread, with no sanitary infrastructure (Matsui, Kanehara & Kanehara, 2003). Fish were an important source of protein and were consumed raw. The parasite-environment subsystem thus generated a major risk of infection for the human host.

It is not surprising to find eggs of parasites of animals in human coprolites, due to eating habits that changed over time (thus representing cases that could be either false parasitism or true infection). For example, the fact that fragments of arthropods or even nearly entire specimens are found in human coprolites demonstrates intentional ingestion by the individuals, which could lead to infection by microorganisms (Johnson et al., 2008).

Paleoparasitology can contribute greatly to studies on the origins of parasitic infections, both in humans and in other animals. The review by Sianto, Chame & Silva (2009) shows the first steps to understanding these relationships, offering possibilities for dating the appearance of certain eating habits in the prehistoric population according to the presence of specific parasites of animals.

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