

CLIMATE CHANGE EFFECTS ON TREMATODE AND NEMATODE DISEASES AFFECTING CHILDREN IN RURAL AREAS OF DEVELOPING COUNTRIES

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Abstract

Among climate change impact on human health, the effects on children living in poor rural areas of developing countries pose a series of question marks and risks related to climate-induced modifications of incidence, prevalence, intensity and geographical distribution of infectious diseases. Parasitic diseases are highly susceptible to climatic variables due to their transmission following the life cycle characteristics and links to abiotic and biotic factors of the environment of both parasite causal agents and transmitting invertebrate vectors. Helminthiasis, mainly trematodiasis and nematodiasis, have recently shown to be also susceptible to changes induced by climate change and global warming. In several, as fascioliasis globally and schistosomiasis in Asia, consequences have already been demonstrated, including increases of disease transmission and human infection, as well as geographical spread. In many others, their transmission characteristics, highly dependent on climatic variables, have allowed to predict similar consequences by means of mathematical modelling, remote sensing from space satellites and geographical information system computer methods. The present review offers a baseline on the interaction of climate change and the characteristics of trematodiasis and nematodiasis known to have a great impact on children. The complexity of climate change variables is analyzed from the point of view of its expected impact on the different transmission phases of the diseases more susceptible to be modified, including fascioliasis, fasciolopsiasis, gastrodiscoidiasis, schistosomiasis, trichuriasis, ascariasis, visceral larva migrans by *Toxocara*, ancylostomiasis, necatoriasis, cutaneous larva migrans by ancylostomatids, lymphatic filariasis and onchocerciasis. Concluding remarks for future research and immediate action are finally added.

Keywords: Climate change, global warming, climate variables, helminth heterogeneity, trematodiasis, nematodiasis, children, rural areas, developing countries.

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Introduction

Within the wide diversity of effects and complex aspects related to climate change, the consequences on human health are among those of most concern. Effects of climate change on health will affect most populations in the next decades and put the lives and wellbeing of billions of people at increased risk. Major threats, both direct and indirect, to global health from climate change are expected through changing patterns of disease, water and food insecurity, vulnerable shelter and human settlements, extreme climatic events, and population growth and migration [1]. Large-scale climate fluctuations are linked with changes in the properties and functions of ecosystem. Thus, climatic factors affect ecological processes at different levels, from the performance of individual organisms, to the dynamics of populations and interactions in and between communities, up to the distribution of species. The ecological consequences of climate change in terrestrial and marine ecosystems are expected to be determined by complex cascading effects arising from modifications in both trophic interactions and competitive relationships.

Among climate change effects on health, the Intergovernmental Panel on Climate Change (IPCC) warned that the climate change could affect infectious diseases as early as 1990, when referring to vector-borne diseases [2]. Changes in climate factors may affect the distribution or ecological range of infectious diseases, whereas the frequency and magnitude of disease outbreaks may change with weather extremes such as flooding and droughts. Evidence-based biological effects of climate change on living organisms, including pathogens and their vectors, comprise [3]: (i) effects on physiology, metabolism or development rate; (ii) effects on distribution; (iii) effects on the timing of life-cycle or life history events; and (iv) adaptation, particularly of the so-called r-strategist organisms. According to the ecological theory on the r and K selection concepts, r strategists are species with short generation times and rapid population growth rates and consequently the most responsive to climate change [4]. This is the case of microparasites, including viruses, bacteriae and protozoans, which have been the pathogens more related to infectious disease emergence [5]. Moreover,

recent evidence indicates that infectious disease agents which are vector-borne in transmission and zoonotic in origin are those whose characteristics are more suitable for climate change impact. It is estimated that 75% of emerging human pathogens are zoonotic [6-8].

Parasitic organisms, both microparasite protozoans and macroparasite helminths and arthropods are known to follow life cycles and transmission characteristics modulated by climate variables since long ago (9). More recently, many studies have emphasized the causal relationship between climate change and parasitic diseases, whether emerging (new infections) or re-emerging (diseases rapidly increasing in either local prevalence and intensities or expanding their geographical distribution) [10,11]. However, a very few years ago, helminthiases were noted as infectious diseases scarcely affected by climate change, when compared to diseases caused by microorganisms in general (viruses, bacteriae, rickettsiae, protozoans). A quantitative analysis of the risk of infectious disease emergence allied to the nature of the organisms, their mode of transmission and source, showed that viruses, bacteriae and protozoans are more likely to emerge than macroparasites, e.g. helminths [5]. The confirmation about the impact of climate change on helminthiases has been reached only very recently [12], despite a very broad literature on the interactions of helminths with abiotic and biotic factors, including both experimental and field studies.

Although helminths also appear to be affected by climate change, their main difference with microparasites lies on the usually longer life cycles of helminths, with longer generation times, slower population growth rates and longer time period needed for the response in the definitive host to become evident. Within the r/K dichotomy and continuum, helminths are also r-strategists, but appear to be less r than viruses, bacteriae and protozoans [13]. Consequently, after a pronounced climate change in a local area, modifications in helminth populations need more time to be obvious or detectable than modifications in microparasite populations. Similarly, the relation of changes in a helminthiasis with climatic factor changes, as extreme events elapsed relatively long time ago, may be overlooked if not concretely searched for. All

indicates that this phenomenon has been the reason for previous analyses to conclude that helminthiases do not constitute priority targets in climate change impact studies [14].

Helminthiases have a tremendous importance because of their large impact on human health whether directly in helminth species specific of humans or indirectly in helminth species proper of animals but able to infect humans, as in the case of zoonotic helminthiases. Additionally, several helminthiases are transmitted by invertebrate vectors, such as snails and insects, whose specificity, population dynamics, ecological requirements and behavioural characteristics markedly define transmission patterns and epidemiological scenarios of the vector-borne helminthic diseases in question.

Many helminthiases are, moreover, within the list of the most important infectious diseases in which concerns morbidity and mortality affecting children in developing countries. This scenario is worse in rural areas of low-income countries, where health infrastructures and minimum care, mainly diagnostic and treatment possibilities, are usually far from those available in urban areas. One wonders which will be the consequences of climate change on the aforementioned helminthiases affecting children in those rural, poor areas where civilisation, man-made infrastructures and appropriate public health systems are not there to deal with adverse outcomes. The present review analyzes the human helminthiases presenting transmission characteristics most suitable to be affected by climate change, by focusing on trematodiasis and nematodiasis of well-known impact on children inhabiting rural areas of developing countries. The aim is to provide a baseline for future action on crucial parasitic diseases pronouncedly affecting rural child health in a climate-changing world.

Helminth transmission strategies and climate change

According to the life-cycle pattern of each helminth species, climate variables are able to affect prevalences, intensities and geographical distribution of helminths both directly influencing on free-living larval stages, as well as indirectly influencing on

mainly invertebrate but also vertebrate hosts of their parasitic stages [12].

Host (or vector) specificity characteristics of each helminth species are crucial. Helminths showing a strict host specificity, that is, only able to develop within a concrete host species, or even concrete host geographical strain, will be very dependent on the influences of climate change on the host population. On the contrary, helminths showing a less marked host specificity, that is, able to develop within different host species, or even phylogenetically distant species, have the possibility to buffer the influence of climate change more or less depending from the different adaptative capacities of the different host species to a given climate modification. However, a wider definitive host spectrum may also play favouring disease transmission speed and modifying disease characteristics as prevalences, intensities and geographical distribution in a faster way, so that climate change impact becomes easier to be detected and measured in a shorter time period. This is the case of several zoonoses, well-known examples of emergence or re-emergence in the last two decades [15,16] and markedly related to climate variability [17], and, within helminthic diseases, of fascioliasis worldwide and schistosomiasis japonica in Asia [14], in which the causal agents are characterized by a very low specificity at definitive host level and, hence, with a very wide animal reservoir species spectrum (see below).

Helminth species affecting humans and domestic animals belong to four systematic groups: digenetic trematodes or flukes, cestodes or tapeworms, nematodes or roundworms and acanthocephalans or thorny-headed worms. These metazoan parasites present very different transmission patterns, ecological requirements and spreading strategies according to the different helminth groups. Their dependence on abiotic and biotic factors is related to their free living stages, and their environment-host population interactions [12]. Among the numerous environmental modifications giving rise to changes in helminth infections, climate variables appear as those showing a greater influence [9].

Trematodes and nematodes are the helminth groups including parasite species whose life cycle and transmission characteristics are more susceptible to climate change. Among both groups, there are

moreover several species able to infect humans and cause diseases that affect mainly children in rural areas of developing countries. They are, therefore, the main purpose of the present analysis and are treated appropriately below.

Cestodes follow life cycles which are less influenced by climatic conditions and cause diseases not particularly problematic in children as to be considered within helminthiasis whose morbidity affects their development. Additionally, although studies on emergence/re-emergence suggest that climate change may also have an impact on cestodiasis, the only tapeworm disease in which climate change has been found to influence so far is alveococcosis or multilocular hidatidosis by *Echinococcus multilocularis* [12], a disease causing high mortality in humans but which does not appear to be especially focused in children. Another cestode disease frequently affecting children in developing countries and in which climate factors are known to have an influence is hymenolepiasis by *Hymenolepis nana*. However, its low pathogenicity, lack of recognized underdeveloping impact and the absence of field studies hitherto demonstrating or suggesting climate change effects on hymenolepiasis, does not indicate that this disease should be included in the list, at least for the moment.

Acanthocephalans are less important in public health, although they may be very pathogenic. Their very rare infection in humans does not merit a special analysis from the point of view of climate change.

Main climate factors influencing helminthiasis

Analyses on the influence of climatic factors on the transmission and spreading of helminth species have been very numerous since long ago, both experimentally on biological models adapted to laboratory conditions and under natural conditions in field studies. However, this kind of studies have been focused on climate change only very recently, so that the literature on the modulation of helminth parasitism by changing climatic conditions is still scarce [12,14].

It must be highlighted that generalizations about effects of climate change on helminths cannot be

made. On one side, their broad heterogeneous complexity of life-cycle patterns include completely antagonistic strategies, so that given changes of concrete climate variables may give rise to modifications of helminthiasis trends following ‘opposite’ directions even in the same area, that is, increasing the transmission of a given helminth but decreasing the one of another helminth species, and reducing the geographical distribution of a given helminthiasis but expanding that of another helminth. Moreover, the influence of a given climatic factor might be increasing transmission when analysed at a given level but show an opposite consequence when considering another level of the helminth life-cycle, so that counteracting effects may finally give rise to almost no change or no change at all in the transmission.

Additionally, climate changes do not appear to be spatially uniform, so that climate change may influence the same helminthiasis in different directions or with different degrees depending on the geographical area in question. Interestingly also, areas predicted to be the most affected by climate change are those near the current edges of disease’s global distribution (i.e., geographical borders, highland areas) [18].

Temperature increases the helminth development rate. Infection levels and the dynamics of helminth systems are subject to the impact of long term increases in temperature. From the host perspective, if they breed earlier and for longer due to long-term higher temperatures, this will result in the production of more susceptible young individuals and this will lead to an increase in transmission. From the helminth perspective, an increase in the duration and average temperature of the summer season will also increase the window of transmission and development rate of infective stages resulting in increased transmission (19). As a consequence, global warming will lead to increased levels of helminth parasitism.

Modifications of precipitation rates and changes in rainfall may alter humidity giving rise to whether wetter or dryer conditions in given areas. Such changes will greatly influence the survival range, seasonality and viability of many free-living stages of helminths (eggs, soil larvae), but also those developing in intermediate hosts as snails, insect vectors and even small vertebrates, both exothermic

and endothermic. Cloudiness and air pollution interact with sunlight radiation, which is more or less harmful to the exogenous stages of helminths, but may play in an opposite way for given vectors as planorbid and lymnaeid snails which mainly feed on freshwater algae.

Moreover, influences on helminth diseases of changes of each one of these climatic variables cannot be analyzed independently, due to interaction effects. Interactions between temperature and the aforementioned water-related climate variables will give rise to changes in freeze-thaw cycles, modifications of freshwater bodies, or changes in water velocity, so that droughts, floods, and run-offs will increase in frequency. Climatic cascading effects are increasingly being detected, as for instance in extreme latitudes. Such climate change combinations significantly impact ecosystems and the diversity and abundance of the inhabiting invertebrate communities (20).

Trematodiasis

Trematodes follow an heteroxenous life cycle in which the first intermediate host is a specific mollusc. In trematodes following a two-host life cycle, the vertebrate definitive host becomes infected whether through the skin by the snail-released larval stage of cercaria (in schistosomatids), or by ingestion of the metacercaria attached to any carrying substratum (e.g., freshwater plants, in fasciolids). In three-host life-cycles, the vertebrate host becomes infected by ingesting the second intermediate host, usually an invertebrate (molluscs, insects, crustaceans) or an exothermic vertebrate (fishes, frogs, reptiles). Climate conditions whether directly influence free larval stages (eggs faecally shed by the vertebrate host, miracidium development inside the egg, snail-released cercariae, and non-parasitic metacercariae) or indirectly the parasitic larval stages (sporocysts, rediae, cercariae in the snail; metacercariae in invertebrates) [14].

Climate change has been shown to affect trematode transmission at different levels of the parasite's life cycle, including aspects as (i) cercarial output, (ii) cercarial production variability, (iii) magnitude of cercarial production, cercarial size and

snail host size, (iv) cercarial quality, (v) duration of cercarial production increase and host mortality, and (vi) latitude. The common scenario comprises an increase of a few temperature degrees leading to marked increases in cercarial emergence from snail vectors and consequently in disease transmission [14,21].

Although the aforementioned important global-warming-induced impact affects all trematodiasis, data available so far suggests that flukes that follow a two-host life cycle and whose epidemiological characteristics are strongly marked by their zoonotic origin are the trematodiasis showing a higher, or at least faster detectable, climate change impact. Changes in prevalences, intensities and geographical distribution at definitive host level, including both human and other mammal host infection, are more directly influenced in these cases due to the absence of any intermediate host population buffering this effect in between snail vector and definitive host. Moreover, the existence of animal reservoir host species additional to the human host allows to enhance this transmission increase effect in a faster way.

This explains why, within plant-borne trematodiasis, the liver fascioliasis by *Fasciola hepatica* and *F. gigantica* using a large spectrum of herbivorous and omnivorous mammal hosts (see figure 1C,D) are more affected than the intestinal fasciolopsiasis and gastrodiscoidiasis which only use the pig as animal reservoir host. Similarly, the less specific schistosomiasis by *Schistosoma japonicum* using a large spectrum of mammal reservoir hosts (figure 1E) appears to be more affected than the almost strictly human-specific schistosomiasis by *S. mansoni* and *S. haematobium*.

Another curious zoonotic, two-host life cycle trematode disease, cercarial dermatitis or swimmer's itch caused by bird schistosomatid flukes, has also proved to be affected by climate change, although this disease does not target especially on children and does not pose problems in developing countries, but only in northern mild or cold latitudes of Europe and North America (see table 1) [12,14].

Among the rest of important trematodiasis of humans, the Asian food-borne hepatic clonorchiasis by *Clonorchis sinensis* and opisthorchiasis by *Opisthorchis viverrini* and *O. felineus* are dependent

from climate variables [22-24] and will undoubtedly be affected by global warming and also water-dependent factors modifying water collections in the field, although their use of a freshwater fish carrying the infective stage of metacercaria, despite its

dependence from abiotic factors [25], may not allow to transfer the climate change impact at snail vector level to definitive host infection, including human disease, so evidently.



Figure 1. A, B) Amphibious snail vectors of fascioliasis are highly susceptible to climate change, as is the case of *Galba truncatula* at 3900 m high altitude in the Northern Bolivian Altiplano (A) and *Lymnaea viridis* throughout the lowlands of Vietnam (B). C, D, E) Less specific trematodes using a wide spectrum of animal reservoir hosts evidence climate change effects faster: according to the traditions of Aymara inhabitants of the Northern Bolivian Altiplano high endemic area, young children are in charge for the management of livestock (C, D); in the Far East, the combination of livestock with field cultures needing intensive irrigation (see rice fields in the background) facilitates the transmission of schistosomiasis by *Schistosoma japonicum* (E). F) How to tell children in Africa not to bath to avoid infection when the air temperature is around 40 °C? G) Despite efforts in providing electricity (see pylon in the background) and water piping (see pipe crossing canal), women and girls still wash with feet inside water according to centenary traditions in Egypt, thus exposing themselves to schistosomiasis infection. H, I) Consumable vegetables and promiscuous outdoor defaecation (see bottom right) are typical links in soil-transmitted nematodiasis: uncontrolled plant markets are numerous in Asian countries (H); rain and floods contribute to the spread of nematode eggs expelled with stools throughout the environment (I).

Table 1. Climate change effects on different trematodiasis and nematodiasis affecting children

Disease causal agent	Effects on free living stages of the parasite	Effects on larval development inside vector	Effects on vector host	Effects on intermediate (or paratenic) host	Effects on zoonotic transmission	Impact on children	Impact on human development
TREMATODIASIS:							
<i>Fasciola hepatica, F. gigantica</i>	++++	++++	++++	---	++++	++++	++++
<i>Clonorchis sinensis</i>	++	++++	+++	++	++	++	+++
<i>Opisthorchis viverrini, O. felinus</i>	++	++++	+++	++	++	++	++++
<i>Paragonimus spp.</i>	++	++++	+++	++	++	+	+++
<i>Fasciolopsis buski</i>	++++	++++	+++	---	+	+++	+++
<i>Gastrodiscoides hominis</i>	++++	++++	+++	---	+	+++	+++
<i>S. mansoni, S. haematobium</i>	++++	++++	+++	---	---	++++	++++
<i>Schistosoma japonicum</i>	++++	++++	++++	---	++++	++++	++++
Cercarial dermatitis	++++	++++	+++	---	++++	+	+
NEMATODIASIS:							
<i>Trichuris trichiura</i>	+++	---	---	---	---	++++	++++
<i>Ascaris lumbricoides</i>	+++	---	---	---	+	++++	+++
<i>Toxocara canis, T. cati (VLM)</i>	+++	---	---	--- (+)	+++	+++	+
<i>A. duodenale, N. americanus</i>	++++	---	---	---	---	++++	++++
Cutaneous larva migrans	++++	---	---	--- (+)	+++	+++	+
<i>W. bancrofti, B. malayi</i>	---	++++	++++	---	---	++	++++
<i>Onchocerca volvulus</i>	---	++++	++++	---	---	++	++++
<i>Loa loa</i>	---	++++	+++	---	---	+	+
<i>Dirofilaria immitis, D. repens</i>	---	++++	++++	---	+++	+	+
<i>Enterobius vermicularis, E. gregorii</i>	+++	---	---	---	---	++++	+
<i>Strongyloides stercoralis</i>	++++	---	---	---	---	+++	++
<i>Angiostrongylus cantonensis</i>	++	++++	++++	++	++++	+	+
<i>Angiostrongylus (M.) costaricensis</i>	++	++++	++++	++	++++	+	+

+ = low impact; ++ = middle impact; +++ = high impact; ++++ = very high impact. --- = does not apply.

A similar observation may be made with the food-borne, pulmonary paragonimiasis caused by several species of *Paragonimus* mainly in Asia, but also in Africa and the Americas [26]. Moreover, none of these food-borne trematodiasis focuses especially on children, although *C. sinensis* in some endemic areas of China and *O. felineus* in Russia and Ukraine may reach relatively high prevalences in children locally [22]. These food-borne trematodiasis have been mentioned to emerge in recent times [27], although nothing indicates that a climate change impact may be in the background of these emergences in spite of their zoonotic origin, at least so far (see table 1).

Fascioliasis

Fascioliasis is a highly pathogenic disease caused by *Fasciola hepatica*, present in Europe, Africa, Asia, the Americas and Oceania, and *F. gigantica*, mainly distributed in Africa and Asia. This disease is typically rural, has a great spreading power thanks to the large colonization capacities of its causal agents and vector species, and is at present emerging or re-emerging in many countries, including both prevalence and intensity increases and geographical expansion. Today, fascioliasis is the vector-borne disease presenting the widest latitudinal, longitudinal and altitudinal distribution known. Human cases have been increasing in 51 countries of the five continents, with estimates of up to 17 million people affected or even higher depending from the hitherto unknown situations in many countries, mainly of Asia and Africa [28-30]. Different human endemic and epidemic situations with long-term, high morbidity effects have been described. Children and females appear to be the most affected in human high endemic areas [31,32].

The two-host life cycle of both fasciolids is similar. It comprises four phases [22]: A) a very wide spectrum of herbivorous (sheep, cattle, goats, equines, etc.) and omnivorous (pigs, humans, etc.) mammals act as definitive host; infected by ingestion of metacercariae with vegetables or drinking water, they harbour fluke adults in biliary canals and gall bladder; eggs reach the external milieu with faeces; in man, the long chronicity problem in endemic areas is due to the

fluke life span of up to 13.5 years; B) the transit between mammal and snail hosts includes the long resistance phase of egg and short active phase of miracidium in freshwater of appropriate physico-chemical characteristics (mainly temperature of 15-25° C); C) vectors are specific freshwater lymnaeid snail species; the intramolluscan larval development finishes with the shedding of cercariae into water; the prepatent period (38-86 days) is dependent on temperature, higher temperatures reducing the period; D) the transit between snail and mammal host includes the short swimming phase of cercaria and the long resistance phase of metacercaria attached to freshwater plants or water surface; the shedding process takes place between 9° and 26° C, independently of light or darkness; metacercarial cysts become infective within 24 hours and remain viable for months, even more than a year. Thus, liver fluke development is very dependent of the environmental characteristics according to phases B, C and D, and markedly influenceable by human activities at phase A. The large heterogeneity of transmission patterns and epidemiological scenarios seems to be related to different lymnaeid vector species [30,32,33].

Fascioliasis fulfills all adequate requirements for an helminthic disease to be highly and relatively rapidly (in comparison to other helminthiasis) affected by climate change: (i) two host life cycle without any intermediate host between snail vector and mammal host; (ii) very dependent on climatic variables in most of its life cycle; (iii) amphibious snail vectors very dependent on climatic conditions (see figure 1 A, B); (iv) high zoonotic component due to the very low specificity at mammal host level (figure 1 C, D). This is why fascioliasis has always been the model most used to illustrate helminth-climate interactions [9], as well as to develop climate forecasting methods and evaluate their usefulness.

The incidence of fascioliasis has been related to air temperature, rainfall and/or potential evapotranspiration. There are climatic fascioliasis forecast indices which are calculated with different equations which take into account variations in these climatic factors [34-37]. Several have been successfully applied to animal fascioliasis in different areas of Europe, Africa and the USA [38]. Recently, they were also successfully applied to human

fascioliasis in Bolivian highlands, after introducing a modification in the aridity calculation deduced from climatediagrams in the way to adapt the indices to high altitude and low latitude [38]. The validation was performed by using data about human and animal fascioliasis as well as lymnaeid vector distribution and peculiar physiographic characteristics of the very high altitude covering the whole 3800-4100 m altitude human hyperendemic area of the Northern Altiplano [39]. The values of one index allowed even to classify the degree of disease transmission into low, moderate and high risk areas. Worth noting is that the only Altiplanic lymnaeid vector snail species appears to be almost exclusively linked to permanent water bodies, because of the high altitudinal evapotranspiration leading temporal water bodies to quickly disappear thus unabling lymnaeids to adapt and develop [39]. This explains why the transmission on the Altiplano takes place throughout the year, opposite to the typical fascioliasis seasonality in northern hemisphere countries.

In other regions, different factors have been used in the models developed. Bayesian hierarchical models of the spatial distribution of bovine fascioliasis in Victoria, Australia, were developed using data of liver fluke infection in cattle together with environmental aspects. Rainfall was found to have an inconsistent relationship with the fluke prevalence data, whereas irrigation was the variable that best described the observed distribution of the disease [40].

A more complex suite of environmental factors related to fascioliasis and available from space satellites may be used for forecasting by means of Remote Sensing (RS) and Geographic Information System (GIS) methods [41]: (i) temperature, air, soil and surface water (diurnal temperature maximum and minimum, diurnal temperature difference, sea/water/land surface temperature), (ii) water, including soil moisture, standing water and atmospheric water vapor; (iii) condition of vegetation canopy over the earth, (iv) structure and dynamics of the lower atmosphere plus composition and dimensions of airborne particles (aerosols) contained, and (v) topography and mineralogy, i.e. terrain relief and bedrock/soil types. In RS-GIS for animal fascioliasis, surface hydrology, vegetation indices and temperature data based on previous knowledge have

proved to be very useful (see review in 42). Annual normalized difference vegetation index (NDVI) values together with a climatic index were initially proposed for human fascioliasis in Chile [43] and later successfully applied and validated for the Northern Bolivian Altiplano high human hyperendemic area [44]. The prediction capacity of the RS map appeared to be higher than that from forecast indices based only on climatic data [38]. A GIS forecast model to conduct an epidemiological analysis of human and animal fasciolosis in the central part of the Andes was proposed [45]. NDVI data maps represent a step further in the way to reach a GIS based on various parameters which could accurately fit real epidemiological and transmission situations of fascioliasis in high altitude endemic areas in Andean countries [46]. More recently, levels of vegetation have been also reported as a positive predictor of *F. hepatica* in Switzerland [47].

Data layers of environmental variables including inundation, elevation, slope and distance from river were used in a GIS model for mapping risk of fascioliasis in Cambodia, where a combination of draught animals and the cultivation of irrigated rice in the periphery of flooded areas provide a suitable habitat for lymnaeid vectors and their infection. Interestingly, temperature was excluded from the model because it fluctuates little during the year in Cambodia and persists in the range favourable to snails. Similarly, rainfall was also excluded because annual floods were associated with melting snow rather than rainfall [48,49].

The strong dependence of fascioliasis from weather factors indicate that climate change may have a marked influence on this disease. In South America, global warming effects have already been described in the Northern Bolivian Altiplano high human hyperendemic area. Fast shrinkage of glaciers and perpetual snows are expected to modify the hydrological characteristics of the endemic area, with consequences on lymnaeid vector distribution and fascioliasis transmission [12,14]. The El Niño-Southern Oscillation (ENSO) phenomenon and associated precipitation modifications, drought and floods are expected to modify fascioliasis transmission in Andean countries as Ecuador, Peru and Bolivia. Animal fascioliasis outbreaks were already detected in Ecuador after the great climatic

irregularities taken place after the 1997/98 ENSO phenomenon [12,14]. The typical extreme climatic events in the Caribbean region, as for instance hurricanes, are also capable to give rise to human and animal fascioliasis outbreaks due to the pronounced r-strategist characteristics of the widely distributed snail vector *Lymnaea cubensis*. In Cuba, several human outbreaks have been described which characterize the Caribbean transmission pattern and epidemiological scenario [32]. The increasing frequency of such climatic events in recent years may increase the frequency of fascioliasis outbreaks.

In Europe, the appearance of human outbreaks after heavy rainfall in the previous year or season has been reported repeatedly [22]. Modifications of raining rates including temporary concentration of rainfall and consequent floods may influence fascioliasis transmission in the areas affected and cause epidemics. Recently, global warming has been noted as the cause of increased animal fascioliasis in UK [50-53] and France [54].

In Africa and Asia, predicting future scenarios of fascioliasis related to climate change becomes more difficult due to the overlap of the distributions of *F. hepatica* and *F. gigantica*, together with the widespread presence of hybrid intermediate forms which may not necessarily follow known thresholds for the pure species, as e.g. minimum temperature thresholds for larval development of 10 °C for *F. hepatica* and 16 °C for *F. gigantica* [14]. The Nile Delta in Egypt, Gilan province in northern Iran, and Vietnam are examples of endemic areas where forecasting initiatives will be jeopardized by the genetic complexity of the fasciolids [14]. Forecast and risk models made for areas where both fasciolid species overlap and hybrids are present, such as Ethiopia [55], east Africa [36] and Cambodia [48, 49] should be re-assessed in the future once development thresholds of the local hybrid forms become known after appropriate experimental studies.

Fasciolopsiasis

The Giant Asian intestinal fluke *Fasciolopsis buski* is one of the largest digeneans infecting humans. It inhabits the duodenum and jejunum in light infections and also much of the intestinal tract, including the

stomach, in moderate and heavy infections [56]. Pigs are the only animal reservoir of any significance [28,29]. Fasciolopsiasis affects several million people in Asia, widely expanded in central and south China, Hong Kong, Taiwan, Bangladesh, India, Vietnam, Laos, Cambodia, Thailand, Kampuchea, Singapore, Burma, Malaysia, the Philippines, and Indonesia [28,29]. In humans, mortality has been reported in children with heavy infections in India, China, and Thailand, and massive infections are responsible for clinical symptoms, intestinal disturbances, malnutrition, edema, and malabsorption [57].

In the endemic areas, the disease is underreported and is most prevalent in remote rural places and semi-urban areas. Fasciolopsiasis is most prevalent in school-age children (see review in 28), in which the number of worms per child can exceed 800 [58]. Prevalences reported in children ranged from 57% in mainland China to 25% in Taiwan and from 60% in India and 50% in Bangladesh to 10% in Thailand [28,29].

The transmission of fasciolopsiasis follows the same pattern as in fascioliasis. The life cycle phases which develop in water are extremely susceptible to climate. Temperature and water-related climate variables greatly influence the embryonation of eggs in freshwater. The miracidium development period is 16-77 days, with a mean of 22 days, the optimum being 27-30 °C of water temperature and 6.5-7.2 as pH range [28].

The small planorbid snail vectors involved are extremely sensitive to desiccation, their survival limit out of water at 25 °C and 50% humidity being 25 hours [59]. Exposure of 2 hours to drying usually kills them, but they are able to live for some time in slightly moist mud. Moreover, the parasite larval development within the snail vector is markedly dependent on abiotic factors such as temperature. Incubation periods recorded were 46-59 days at 22-24 °C, and longer, of 85-100 days at 18-22 °C [59]. Additionally, cercarial emergence from the snails is dependent on light, cercariae being strongly phototactic, with a great variation having been noticed in the daily emergence patterns of cercariae [60].

The disease occurs focally, is wide-spread and is linked to freshwater habitats with stagnant or slow moving waters [58,61]. The disease is therefore susceptible to climatic changes in precipitation rates

as well as rainfall and extreme events as floods and drought which may modify freshwater bodies and water velocity.

It appears to follow a seasonality, with a peak between June and September declining thereafter to a low level during winter and early spring (November-March), being absent during January and February, at least in a humid subtropic hilly city of north-east India where rearing of pigs is a common household practice [62]. A local climate change implying a modification of the current seasonality, by enlarging the yearly transmission window, would pronouncedly affect the epidemiological characteristics of fasciolopsiasis in the area, with increase in prevalences, intensities and geographical spread of infection both in humans and pigs.

In endemic areas, the disease appears associated with common social and agricultural practices and aggravated by poverty, malnutrition, poor sanitation, other helminthiasis, declining economic conditions and an explosively growing, inspection-lacking free-food market [58,61,63]. Differences of incidence are due to factors such as economic status, educational background, standard of health and way of life [28,29].

Control programs focus on school-aged children with large community therapy initiatives [63], including educational efforts directed primarily toward school-age children because they are less entrenched in their food and eating habits, behaviour, and customs [61]. Unfortunately, despite control programs implemented and sustained in the communities, fasciolopsiasis still remains a public health problem in endemic areas [63]. And in areas where it was thought to be fully controlled, there are reports of a re-emerging infection in recent years (64,65).

Gastrodiscoidiasis

The trematode *Gastrodiscoides hominis* infects the caecum and colon of both pig and man [66]. The pig is the normal host and only important reservoir, sporadically infected mammals (mainly wild boars) and locally infected rats being without broad epidemiological implications [28,67]. It has a large distribution in the Palaearctic Region mostly

overlapping fasciolopsiasis, including India, Pakistan, Burma, Thailand, Vietnam, Philippines, China, Kazakstan and the Volga Delta in Russia [57,66,68,69]. Its records in Africa need confirmation [28,67].

Infection by this trematode species causes illness in a large number of persons, and deaths among untreated patients, especially children, have been attributed to this infection (66). In human infection, a picture similar to that detected in pigs might be expected [28,67].

This fluke follows a diheteroxenous life cycle similar to those of *F. hepatica*, *F. gigantica* and *F. buski*. Eggs when laid include an embryo in a very early stage of segmentation. The miracidium appears fully mature on day 9 at a temperature of 24-33 °C. Hatching takes place between days 9 and 14 depending from temperature. Higher temperatures appeared to be detrimental for miracidium development. A longer maturation period of 4 weeks was required in April-May. Longer periods of up to 3 months for hatching have also been described [28, 67].

The tiny freshwater planorbid snail *Helicorbis coenosus* (= *Segmentina coenosus*) is the only vector species known. In this snail, the prepatent period ranges between 28 and 152 days, this variation depending on the seasonal variations of temperature, i.e. 51 days at a mean temperature of 24 °C (variation 20-30 °C) and 74 days at 22 °C (variation 17-27 °C). This period is shortest in summer and longest in winter. The longevity of the snails varies from 10 to 147 days after the infection becomes patent, and the snails shed cercariae intermittently for 6-40 days. Positive snails stop shedding when it becomes cold [28, 67].

Cercarial emergence takes place in morning hours. The free swimming life of cercariae varies from 1 hour to more than 24 hours, at the end of which it encysts. Encystation generally takes place on the bottom. A few of them encyst on the shell of the snail host or any other substrate available. Human contamination may occur when encysted metacercariae are swallowed with tainted vegetation (aquatic plants) or with animal products, such as raw or undercooked crustaceans, squid, molluscs, or amphibians [57, 69].

The prevalence in pigs is of great epidemiological significance. In endemic areas, the molluscan vector appears to abound in the water reservoirs around the pigsties [66]. In surveys of pigs in north-east India, gastrodiscoidiasis showed a seasonal occurrence trend similar to that of fasciolopsiasis. Their prevalence rose to a peak during the months from June to September, declining thereafter to a low level during winter and early spring (November-March). The infection by *G. hominis* was not present during the first 3 months of the year [62].

However, high infection rates have sometimes also been detected in humans in areas where pigs were very scarce, as the 41% prevalence and high individual intensities detected in mainly children in northern India. These results suggested that the infection was maintained in the human population without participation of pigs [28,67].

Summing up, climate change may affect gastrodiscoidiasis in a way similar to fasciolopsiasis, due to the similar life cycle, transmission characteristics, identical animal reservoir species, similar latitudes and overlapping geographical distribution.

Similarly as in fasciolopsiasis, besides treatment and educational measures, methods in control campaigns should include (i) prevention of human infection; (ii) efforts at human level to cut disease dissemination by humans; (iii) control at pig reservoir level; and (iv) efforts at snail vector level. To prevent human infection, the most practical method is to avoid eating raw, water-derived food. Unfortunately, the reality shows how difficult it is to change century-old traditions and therefore the importance of educational efforts at the level of school-age children [28,67].

Schistosomiasis

Schistosomiasis or bilharziasis is caused by trematode species infecting the circulatory system of humans, mainly by three species of *Schistosoma*, *S. mansoni* in Africa, the Caribbean and South America, *S. haematobium* in Africa, and *S. japonicum* in Asia. Four other species affect humans only sporadically or in more restricted areas, as *S. intercalatum* and *S. guineensis* in tropical Africa, and *S. mekongi* and *S. malayensis* in South East Asia. This disease is one of

the most important human helminthiasis due to its very high morbidity [70]. Only in sub-Saharan Africa, the 192 million cases represent that schistosomiasis is the second most important after hookworm, accounting for 93% of the world's number of cases of schistosomiasis and possibly associated with increased horizontal transmission of HIV/AIDS [71].

Schistosomiasis was the first trematodiasis to be included among the diseases able to increase both its local infection and geographic expansion with climate change, mainly with global warming [6,72,73]. This is in part related to the peculiarity of the larval development of schistosomes within their snail vectors, including an infinite cercarial production capacity related to larval stage replication processes [74].

There are different environmental factors that impact on the distribution of schistosomiasis. Temperature, water body type, rainfall, water velocity and altitude can all have a significant effect on the schistosome life-cycle and survival of the intermediate snail host [75]. Climatic changes are likely to affect the known geographical distribution of freshwater snails, such as *Biomphalaria* species, the vector hosts of African schistosome species transmissible to humans [76].

However, up to the present, only schistosomiasis by *S. japonicum* in Asia has shown to be affected by climate change [14]. In China, for instance, schistosomiasis has re-emerged in mountainous and hilly regions in Sichuan, where it had been controlled previously by intensive interventions [77]. The resurgence of *S. japonicum* infection in the past few years is taking place despite 50-year intensive control activities targeted against the amphibious snail vector, *Oncomelania hupensis*, and large-scale chemotherapy campaigns using praziquantel.

Results of a study on a time-series from 1972 to 2002 for 39 counties of eastern China, where *S. japonicum* is endemic, showed that temperature increased over the past 30 years in all observing stations. Prediction methods showed temperature increases for the entire area studied, with an increase from north to south, and suggested an impact on the frequency and transmission dynamics of schistosomiasis japonica [78,79].

Moreover, environmental changes resulting from global warming but also from the Three Gorges dam

were expected to result in a widening of the habitat of *O. hupensis*. Unfortunately, predicting the climate-change-induced geographical spread of this vector was not as simple as initially expected, due to the complexity and heterogeneity of the snail species involved. The considerable variation of snail habitats, from mountainous habitats in the west to flood plain habitats in the east, proved to be associated with different subspecies of *O. hupensis* [80]. Thus, the existence of different *O. hupensis* vector subspecies in the region hampered the predictive models of the spatial distribution of schistosomiasis. Additionally, the prediction of schistosomiasis risk to identify the habitats of *O. hupensis* in mountainous regions was complicated by the occurrence of seasonal flooding [81]. This is a good example about how global warming influencing both (i) the development of the parasite larval stages and consequently the transmission of the disease and (ii) the spread of the snail vectors of the schistosome and consequently the geographical distribution of the disease, might jeopardize a long-term successful control program [82-85].

Whereas climate change has already shown to influence a pronouncedly zoonotic schistosomiasis in northern temperate latitudes in Asia (figure 1 E), the question is still posed about whether climate change may modify, and up to which level, non-zoonotic schistosomiasis by *S. mansoni* and *S. haematobium* in tropical and subtropical latitudes of Africa (see figure 1 F,G) (or additionally the Americas in the case of *S. mansoni*). Schistosomiasis has re-emerged many times in Africa in recent times. Anyway, in all these situations re-emergence was related to global change instead of to climate change, that is, in response to environmental and sociopolitical changes such as hydrological changes, e.g. construction of dams, irrigation canals, reservoirs, etc., that establish suitable new environments for the intermediate host snails that transmit the parasites [11].

Mapping schistosomiasis in Africa has been a priority since long ago [86]. Computer modelling has been applied to schistosomiasis in different African countries, such as Egypt [87] and South Africa [88], although focused on the geographical characterization rather than on the prevalence or intensity of infections. Only few attempts have been made thus far to predict changes in the frequency and transmission

dynamics of schistosomiasis due to climate change in Africa [89,90]. The lack of long-term, high-quality datasets, among other reasons, have been argued to explain the discrepancy reported in given studies which did even come to different conclusions regarding the extent of schistosomiasis transmission under the scenario of a warmer climate [89,90].

The marked differences between Africa and Asia with regard to the ecological characteristics of the respective freshwater snail vectors shall also be taken into account. The vectors of *S. mansoni* and *S. haematobium* are species of *Biomphalaria* and *Bulinus*, both pronouncedly more aquatic than *O. hupensis*. The latter Asian snail is of amphibious behaviour, similar to that typical of lymnaeid snails transmitting the liver fluke *F. hepatica* and snails which have already proved to be susceptible to climate modifications. Thus, schistosomiasis in Africa and the Americas are a priori susceptible to be influenced by climate change effects, although climate-change-induced modifications on schistosomiasis in Africa and the Americas may not be similar to those seen in Asia.

Furthermore, in Africa new strains of schistosomes are indeed progressively detected through natural hybridizations between different species of schistosomes from humans [91], from humans and rodents [92], and from humans and cattle [93]. The question immediately rises about which will be the development thresholds of these hybrid forms with regard to the different climatic variables. This means that thresholds assessed for African human pure schistosome species time ago may not be further extrapolated to the schistosome hybrid forms, in a way similar to the same development question posed by fasciolid hybrids [30].

Nematodiasis

Nematodes present from very simple up to complex life cycles. Trichurids (*Trichuris*) and ascarids (*Ascaris*, *Toxocara*) are monoxenous with a definitive mammal host and the egg as only free living stage depending on environmental factors (pseudogeoelminths). Ancylostomatids and *Strongyloides* are also monoxenous but present active free-living larval stages highly dependent from abiotic

factors (geohelminths) (see figure 1 H,I). Other nematodes present a two-host life-cycle including vector-borne parasites transmitted by biting dipteran insects (filarids and *Onchocerca*). Diheteroxenous protostrongylidae are transmitted by strongly climate-dependent snails. Thus, nematodiasis are amongst the helminthiasis which will presumably be more affected by climate change (table 1).

Many nematodiasis strongly dependent on climate characteristics, which mainly affect children and which represent a serious handicap for the development of rural communities in developing countries are analyzed in the following. There are other nematodiasis, however, which are also affected by climate variables and mainly infect children but whose impact on child development is low, as strongyloidiasis or anguillulosis by *Strongyloides stercoralis* and oxyuriasis or enterobiasis by the ageohelminth species *Enterobius vermicularis* and *E. gregorii*. Additionally, both the snail-borne angiostrongyliasis or eosinophilic meningoencephalitis by *Angiostrongylus cantonensis* and the snail-borne abdominal angiostrongyliasis by *Angiostrongylus (Morerastrostrongylus) costaricensis*, as well as the mosquito-borne dirofilariases by *Dirofilaria immitis* and *D. repens*, are nematodiasis which have already been verified to be affected by climate change [12], but children are not particularly infected by these diseases. Strongyloidiasis and oxyuriasis are human-specific diseases, whereas angiostrongyliases and dirofilariases are zoonotic, with rats and dogs and cats as main definitive animal hosts, respectively (see table 1).

Trichuriasis, ascariasis and toxocariasis

The two pseudogeohelminth species *Trichuris trichiura* (whipworm) and *Ascaris lumbricoides* (roundworm) are soil-transmitted by eggs and mainly distributed in tropical and subtropical regions of the developing world where adequate water and sanitation are lacking. The greatest numbers of infections occur in sub-Saharan Africa, East Asia, China, India and South America. Recent estimates suggest that *T. trichiura* infects 795 million people and *A. lumbricoides* 1221 million [94].

The development of the adult stage in the human host is similar in the two species, with an adult life span of 1-2 years and a basic reproduction number R_0 (= average number of female offspring produced by one adult female parasite that attains reproductive maturity, in the absence of density dependent constraints) with values of 4-6 for *T. trichiura* and somewhat lower, of 1-5, for *A. lumbricoides* [95]. Considering that the nematode adult life inside the host is in fact a refuge from the external environment, *T. trichiura* and *A. lumbricoides* are protected from outside temperatures only throughout a 1-2 year period, which means that the chances of their transmission stages to be deposited and develop in suitable thermal conditions are less increased than, for instance, in hookworms whose adult stage life expectancy is of 3-4 years [96]. The development to sexual maturity is also similar in *T. trichiura* and *A. lumbricoides*, of 50-80 days [95], although egg production capacity appears to be pronouncedly higher in *A. lumbricoides* than in *T. trichiura* (10,000-200,000 and 2,000-20,000 eggs/female worm/day, respectively) [97-99].

Environmental conditions strongly influence the transmission of both nematodes, so that the free-living egg stages present in the environment develop and die at temperature-dependent rates [97]. According to experimental studies, the maximum development rates of free-living infective stages occur between 28 and 32°C, with the development of both species arresting below 5 and above 35-39 °C [100,101]. Eggs of *A. lumbricoides* appear to be more resistant to extreme temperatures than those of *T. trichiura*, with a life expectancy of the free-living infective egg stage of 28-84 days for *A. lumbricoides* and of only 10-30 days for *T. trichiura* [97-99]. This development in the soil (figure 1I) appears to be less rapid than that of hookworm larvae, and consequently they have a lower probability of surviving to infect hosts, according to the observed relationship between prevalence and the number of days in the year below the thermal threshold. The prevalence of *T. trichiura* and *A. lumbricoides* is generally low in locations where temperatures fall below the thermal threshold for less than 35-40 days, and increases with increasing number of days [96].

The larval development time inside the egg up to infective stage shows a wide range (*T. trichiura*: 20-

100 days; *A. lumbricoides*: 8-37 days) [100, 101], which is also influenced by soil moisture and relative atmospheric humidity. A higher humidity is associated with a faster egg development, and at a low humidity of less than 50% the eggs of both species do not even embryonate [96].

These different development and survival rates will influence parasite establishment in the human host and consequently the infection levels. A climate-induced increase in the rate of establishment, while holding parasite mortality constant, causes the parasite equilibrium to rise [102]. Although transmission may present seasonal dynamics, the fluctuations may be of little significance, because the life span of adult worms is much longer than the year periods during which R_0 is less than 1. In that way, R_0 on average will be greater than 1 and maintain the overall endemicity [97]. Thus, spatial variability in long-term synoptic environmental factors will have a greater influence on transmission success and patterns of nematode infection than seasonal variability in a location [96].

The importance of climate on the transmission explains the statistical relationships observed between environmental factors and spatial patterns of infection by these two nematode species. There are many reports on the ecological associations between the distributions of these nematodes and temperature, rainfall and altitude [103].

RS and GIS have been used successfully to describe the environmental factors associated with infection patterns by *T. trichiura* and *A. lumbricoides* in selected geographical areas, and have helped in identifying the importance of different environmental factors in determining geographical distributions [104-109]. A clear relationship exists between infection prevalence and remotely sensed land surface temperature [110]: *T. trichiura* and *A. lumbricoides* prevalences are generally less than 5% in areas where land surface temperature exceeds 38-40° C. This is opposite to what happens with hookworms, despite all these nematodes presenting a similar thermal thresholds. The eggs of *T. trichiura* and *A. lumbricoides* are non-motile and cannot consequently escape from high surface temperatures resulting in egg dying from desiccation [96].

Models applied for *T. trichiura* and *A. lumbricoides* including independent variables as

satellite-derived mean land surface temperature, Normalized Difference Vegetation Index (NDVI) and altitude [96,111], have provided impressive descriptive accuracies both of low and high transmission situations. Satellite data can therefore help define their large-scale distributions, which are demonstrated to be influenced by heterogeneities in climate. Unfortunately, other factors as human behaviour, personal hygiene, differences in sanitation and socio-economic status, have to be considered when analysing smaller scale levels.

Other zoonotic ascarid species are also of great public health importance, affect predominantly children and might be affected by climate change by influencing on the egg development in the external environment, although no concrete studies on that subject seem to have been performed up to the present,

Toxocariasis is a zoonotic infection caused by the larval stages of two cosmopolitan species of the ascarid genus *Toxocara*, *T. canis* and *T. cati*. Their one-host life cycle is similar to that of *A. lumbricoides* [112,113], with the exception of the possibility of neonatal and transmammary infection in *T. canis* [114, 115] and the participation of rodents as paratenic hosts [116,117]. Hosts are infected either with infective eggs developing and surviving in the environment or with larvae from paratenic hosts. *Toxocara canis* is fairly age-specific and therefore hosts of nematode adults are usually puppies, which contaminate the environment with large number of eggs [118]. Puppies are infected by the intrauterine or the lactogenic way with larvae activated in the organism of pregnant bitches since the 6th week of pregnancy. Rodents, as paratenic hosts, often significantly contribute to the circulation and maintenance of toxocariasis, as *Toxocara* larvae survive in their organism and are also transmitted to their progeny. *Toxocara cati* parasitizes in all categories of feline carnivores, and unlike puppies, kittens may contract infection only after their birth by lactogenic way.

Transmission of these two animal ascarids to humans primarily results from the ingestion of food or soil contaminated with embryonated eggs. Non-embryonated eggs are shed in the faeces by dogs harbouring the adult worm, mainly massively-infected puppies [119]. Although human infection by *T. cati*

might be underestimated considering the high *T. cati* infection rate in cats [120], *T. canis* is generally considered the main agent of human toxocariasis [121]. In many parts of the USA the prevalence of toxocariasis is almost 100% in puppies less than 6 months of age [122]. In developed countries, children, typically 1-4 year old, often come in contact with *T. canis* eggs while playing in sandboxes and on playgrounds that were contaminated by a family pet. In developing countries, infection in children, in rural areas where dogs and cats are present, may be higher due to mainly the lack of veterinary control of these domestic animals. In humans, *Toxocara* worms never reach the adult stage, their larval stage causing both visceral and ocular larva migrans [123]. Visceral larva migrans is mostly a disease of toddlers and young children, whereas ocular larva migrans is more common in 5-10-year older children. Both the habitat of geophagia and having a litter of puppies in the home have been identified as significant relative risk factors for the development of toxocariasis [124, 125].

Ancylostomiasis, necatoriasis and cutaneous larva migrans

Among soil-transmitted nematodes, the two ancylostomid geohelminth species *Ancylostoma duodenale* and *Necator americanus* (hookworms) are transmitted by free-living larvae. Hookworms are present in tropical and subtropical regions of the developing world lacking appropriate hygienic conditions (see figure 1I). Recent estimates indicate that hookworms infect 740 million people, the majority in areas of sub-Saharan Africa, East Asia, China, India and South America (94). Hookworm infection occurs in almost half of the poorest people in sub-Saharan Africa, including 40–50 million school-aged children and 7 million pregnant women, in whom it is a leading cause of anemia [71].

For hookworms, the estimated values of the basic reproductive number R_0 are between 2 and 3, and consequently lower than for the pseudogeohelminths *T. trichiura* and *A. lumbricoides* (95). Compared to the two pseudogeohelminths, hookworm adult life span is longer (3-4 years), adult development to sexual maturity is shorter (28-50 days) [95], and egg production is lower (3,000-20,000 eggs/female

worm/day) [97]. Their long adult survival is a crucial factor, as life within the host represents a parasite life period not influenced by environmental conditions. This characteristic pronouncedly increases the chances of hookworm transmission stages to be deposited and develop in appropriate temperature conditions.

Hookworm free-living larval stage development and survival pronouncedly depend on environmental conditions [97]. The time needed for larvae to develop up to infective stage is of 2-14 days [126] and the life expectancy of the free-living infective larval stages is of 3-10 days [97], both markedly shorter than in *Trichuris* and *Ascaris*. Thus, the probability of hookworm larvae surviving to infect hosts is enhanced by their more rapid development in the soil. This is related to the observed relationship between prevalence and the number of days in the year below the thermal threshold. When compared to *Trichuris* and *Ascaris*, hookworms require a much smaller (8 day) window of thermal suitability for transmission and consequently they are able to persist even when the period available for development is of only 10 days [96]. The abundance of hookworm larvae is also related to soil moisture and relative atmospheric humidity, maximum survival rates of hookworm larvae, that is proportion of surviving larvae, being within the 20-30 °C range, their development ceasing at 40 °C [126]. These development and survival rates will influence parasite establishment in the human host and consequently infection levels [97].

Hookworm infection appears to be highly prevalent throughout the upper end of the thermal range, which is opposite to *Trichuris* and *Ascaris* in spite of having similar thermal thresholds. The hookworm capacity to survive under hotter conditions may be related to the ability of their mobile larvae to migrate to more suitable thermal and moisture conditions. The motility of hookworm larval stages, although limited, enables them to avoid desiccation by moving downward into the soil [127].

Ancylostomids are peculiar because of their capacity to enter in hypobiosis, which enables them to survive periods that are not suitable for transmission [128]. However, in human ancylostomids hypobiosis only occurs for *A. duodenale* [129] and not for the sub-Saharan Africa predominant hookworm species *N. americanus* (130). Therefore, hypobiosis has been

excluded as a possible explanation for hookworm's apparent wider thermal tolerance [96].

The relationship between climatic factors and hookworm development is the base to understand the associations detected between hookworm geographical distributions and environmental characteristics [103]. This baseline has been applied for RS analyses and GIS development for identifying the importance of the climatic and other environmental factors in the hookworm distributions in concrete geographical areas [104-109,131]. These studies may be useful in analyzing the future effects of climate change on hookworm prevalences, intensities and geographical dispersal. However, models including independent variables as satellite-derived mean land surface temperature, NDVI and altitude [96,111], have provided only moderate accuracy when applied for hookworms, a probable reflection of the apparent wider distribution of hookworms than *Trichuris* and *Ascaris* for which those models appeared to be very accurate. Unfortunately, the application of such models at smaller scale levels becomes more complicated, as factors not easily quantifiable as those related to behavioural characteristics of human communities shall be taken into account (96).

Hookworm infections would typically not be considered new or re-emerging as they are highly prevalent throughout the developing world. Infection levels tend to be stable because of the lack of sanitary waste disposal and proper hygiene practices. However, under appropriate conditions, geohelminth infections can re-emerge in areas of low prevalence.

A rapid increase in hookworm prevalence that coincided with environmental change including flooding, altered water drainage patterns and saturation of soil near homes, was reported in Haiti [132]. The prevalence of hookworm infection increased markedly from 0% to 12-15% over a 6-year period, most of this increase taking place in 3 years. Analyses lead to conclude that the temporally-coincident local environmental change including moister soil conditions because of the flooding favoured hookworm transmission allowing a rapid increase.

This case, although not of climate origin, clearly suggests that climate change may have important

consequences on hookworm infection at least at local level.

Climate change may be of higher impact on other ancylostomid species of animals which, besides tropical and subtropical regions, also inhabit temperate and colder regions where climate change is expected to be more marked. The species specific and common of cats, dogs and other canids *Ancylostoma braziliense*, *A. caninum*, *A. ceylanicum* and more sporadically *Uncinaria stenocephala* are the main causal agents of cutaneous larva migrans or creeping eruption [133,134]. *Ancylostoma braziliense* appears to be the most widely distributed species and the human syndrome it causes is called "larbush" in Africa. The life cycle pattern and dependence from environmental factors of these ancylostomid species is similar to that of *A. duodenale*, excepting the participation of paratenic rodent hosts in *A. braziliense* [135,136] and the possibility of neonatal and transmammmary transmission in *A. caninum* [114,115,137].

Developmental arrest or hypobiosis allows nematode larvae to persist within the somatic tissues of the host and to reactivate at opportune periods. Reactivation results in resumption of development and self-reinfection or dissemination of the parasite to the environment or to newborn offspring [128,138]. The ubiquity of *A. caninum* in the domestic dog populations, related to its neonatal transmission, is of concern because of its ability to cause not only cutaneous larva migrans but also gastroenteritis in humans [139].

An emergence of human cutaneous larva migrans was detected in Berlin, Germany, in summer 1994 when extraordinary climatic conditions were observed, leading to the extremely high number of 378 sun-hours in July.

During this period, the mean surface air temperature in the area of Berlin was 6 °C higher than the average values of this century and the absolute air humidity was up to 19 g water/m³ air (average value 10 g/m³). The study concluded that increasing local temperatures resulting from climate changes and the threat of global warming may give rise to an emergence of the cutaneous larva migrans syndrome due to the ubiquitous presence of these zoonotic hookworms [140].

Filariases and onchocerciasis

Lymphatic filariases by *Wuchereria bancrofti* (Bancroftian filariasis or wuchereriasis) and *Brugia malayi* (brugiasis) and onchocerciasis or river blindness by *Onchocerca volvulus* are highly pathogenic vector-borne nematode diseases transmitted by biting insects belonging to different dipteran families (culicid mosquitoes and *Simulium* blackflies, respectively) and distributed in tropical and subtropical regions of the developing world excepting eastern Asia where they expand northward into temperate areas. Lymphatic filariasis (46–51 million cases) and onchocerciasis (37 million cases) are also widespread in sub-Saharan Africa, each disease representing a significant cause of disability and reduction in the region's agricultural productivity [71]. Loiasis by *Loa loa* is another filariasis in Africa, but of low pathogenicity and transmitted by tabanid dipterans.

The most obvious clinical impact of these disease is during adulthood. Therefore, they significantly decrease the socioeconomic status of the affected communities, as expressed in their disease burden estimate in disability-adjusted life years (DALYs) [141]. Consequently, children living in these communities are indirectly affected by the disease impact. Additionally, although human prevalences increase with age and are therefore usually not considered problematic diseases in children, infection by *W. bancrofti* in children appears associated with the infection status of both parents, implying differences in exposure at the household level and not in utero exposure per se as the major determinant of infection in children. A similar familial clustering has also been observed in *B. malayi* infection [142]. Moreover, prevalence differences with regard to age are known to be related with transmission intensity in the endemic area in question. Thus, in high wuchereriasis transmission foci adult subjects are those more affected, whilst in low transmission foci prevalences grow in young children to become stable around 15 years age and more [143].

In humans, adult worms follow a long development, with beginning of offspring microfilariae production after a year or longer, and have a very long life span of several years. On the contrary, the development within the vector is short,

of only a few weeks. The duration of the parasite development inside the vector may vary according to vector species or strain, but mainly depending on environmental temperature.

Wuchereriasis appears concentrated in foci. Infection by filarids can only take place when transmission conditions are very adequate, among which temperature and abundance of surface waters for mosquito vector development are the most important factors [143]. Infected mosquitoes maintained at 16 °C survive for months but filarid parasites do not develop. The minimum temperature threshold for filarid development inside the vector is 18 °C; at this temperature they take 48 days to complete their larval development until infective stage. At 20 °C the development is completed in 27 days, at 25 °C in 14 days, and at 30 °C in only 10 days. At higher temperatures of 32–33 °C, the parasite does not appear to reach a viable infective stage, which occurs parallelly to a high mortality of female mosquitoes. Thus, temperature acts on both parasite development and vector survival, mean temperatures of 23–27 °C appearing to be the most appropriate for the transmission. The influence of temperature on transmission intensity is so high that it is sufficient by itself to clearly design the geographical distribution of the disease by interacting with both latitude and altitude, with only a very few exceptions [143,144].

For the disease to be intensely transmitted, vectors shall also be abundant, which occur when larval development sites are numerous at least during a short period (heavy rainfall on impermeable flat soil) or when several larval development sites are maintained throughout the year (permanent water bodies). Extreme climatic events strongly modifying the stable ecology of the aquatic environment give rise to quick mosquito population decreases. In many areas, it has been observed how wuchereriasis distribution appears linked to the frequency of precipitations and to the abundance and long-term stability of surface waters [143,144]. The broad literature dealing with the potential impact of climate change on mosquito vectors can be extrapolated to filariases.

In French Polynesian archipelagos, wuchereriasis transmission potential and resulting disease manifestations in humans proved to be correlated with ambient temperature [145]. In East Africa, a marked

seasonal variation in vector abundance and transmission potential contributes to a complex transmission pattern, with indices being higher during and shortly after the rainy seasons. Considerable differences in *W. bancrofti* transmission were thus observed within a relatively small geographical area, reflecting in the marked differences in infection level in the human populations [146]. Differences in infectivity rates of Bancroftian filariasis vectors also appear between the wet and dry seasons in Kenya [147], similarly as in India [148].

RS and GIS have been attempted for filariasis [103,106,107], loasis [149] and onchocerciasis [150-152]. These studies have focused on the use of RS data to identify ecological correlates of infection and develop statistical models of disease risk.

A rapid mapping method has been developed for wuchereriosis. A Rapid Geographical Assessment of Bancroftian Filariasis (RAGFIL) has been developed by TDR/WHO. This is based on the use of a spatial sampling grid with either 25 km or 50 km between sampled communities, rapid prevalence assessments, and geostatistical methods for predicting the distribution of filariasis throughout the target area [153]. Prevalences in four countries in West Africa have been predicted using this method [154].

Onchocerciasis has also been included within the list of diseases which may increase with global warming [73]. Blackflies breed in areas close to fast-flowing and well-oxygenated rivers and seldom travel more than 15 km in search of a bloodmeal. This means that high-prevalence communities are located close to breeding sites. Consequently, not only global warming but also climate change effects linked to water-related variables, such as rainfall or extreme climatic events as well as droughts, able to modify freshwater bodies and their water velocity, may have an impact on onchocerciasis.

In western and southwestern Ethiopia, different models based on altitude, temperature, rainfall, evapotranspiration, NDVI and terrain slope were useful to predict high to severe risk areas, including suitable areas for onchocerciasis transmission even outside known endemic areas [151]. In southern Venezuela, GIS tools and a landscape epidemiology approach showed striking differences in the transmission dynamics of onchocerciasis between different river courses. A significant relationship with

temperature and influences by the geologic substrate, kind of landscape and vegetation were observed. Different kinds of landscapes associated with different vector species were linked with different transmission intensities [152].

Rapid Epidemiological Mapping of Onchocerciasis (REMO), developed by TDR (Tropical Disease Research)/WHO, has been a key geographic tool for the control of onchocerciasis [155,156]. REMO uses geographical information, particularly the locations of river basins, and makes it possible to assess which communities are at high onchocerciasis risk and where they are located. The robustness of REMO following several rounds of interventions remains, however, to be fully investigated since there has been little validation of the approach since its initial development [96].

Concluding remarks and future work

Helminthiasis are nowadays included within the so-called neglected tropical diseases (NTDs), a group of chronic, debilitating, and poverty-promoting parasitic, bacterial, and some viral and fungal infections, which are among the most common causes of illness of the poorest people living in developing countries. Their control and elimination is now recognized as a priority for achieving United Nations Millennium Development Goals and targets for sustainable poverty reduction [157]. Helminths together comprise the most common infectious agents of humans in developing countries. The collective burden of the common helminth diseases, including from dramatic sequelae to the more subtle but widespread effects on child development, pregnancy, and productivity, rivals that of the main high-mortality conditions such as HIV/AIDS or malaria [158].

Around 85% of the NTD burden for the poorest 500 million people living in sub-Saharan Africa results from helminth infections. The DALYs for total helminth infections in sub-Saharan Africa is 5.4–18.3 million in comparison to 40.9 million DALYs for malaria and 9.3 million DALYs for tuberculosis [71]. In the Latin American and the Caribbean region, approximately 40% of the estimated 556 million people inhabiting that region live below the poverty line. Relative to sub-Saharan Africa and Asia, the

character of poverty in the Latin American and the Caribbean region is unique. Of the Latin American and the Caribbean region's estimated 213 million impoverished people, around one-third live in rural poverty as subsistence farmers, ranchers, and fishermen [159], typically in communities of indigenous and African descent where they face a high level of social exclusion and social inequity, including lack of access to safe water and health care services. Two-thirds of the region's poor live in urban and peri-urban communities where poverty combines with the conditions of unsafe water, poor sanitation, and the proliferation of rodent animal reservoirs and vectors [160]. Poverty is not the only major determinant for risk of acquiring NTDs in the Latin American and the Caribbean region. Instead, it combines with other inequities related to ethnicity (e.g., indigenous groups and people of African descent), age and gender (i.e., children and women), and a patchwork of unique ecological niches to establish sometimes highly focal epidemiological NTD "hot spots." This has important implications for the control of NTDs in the Latin American and the Caribbean region, which may differ from the integrated NTD control currently being advocated for and tested in sub-Saharan Africa and elsewhere [157].

Yet, research into helminth infections has not received nearly the same level of support. This is partly because helminthiases are diseases of the poorest people in the poorest regions, but also because these pathogens are difficult to study in the laboratory by comparison to most model eukaryotes and many other pathogens [71].

Climate change has been highlighted as the biggest global health threat of the 21st century (1). As it has been shown above, effects of climate change on trematodiasis and nematodiasis will unavoidably interact with efforts to be made to achieve the United Nations Millennium Development Goals. A new advocacy and public health movement is needed urgently to bring together governments, international agencies, non-governmental organisations (NGOs), communities, and scientists and academics from many disciplines to face the effects of climate change on health. Management of the climate change effects on helminthiases will require inputs from all sectors of government and civil society, collaboration between

many scientific and academic disciplines, and new ways of international cooperation.

Broad integrated and multidisciplinary initiatives are in need to be organized to assess and counteract these effects where they can be more devastating, as in poor rural areas and remote communities of developing countries. Action should be taken to launch large and long-term multidisciplinary projects including several year studies in both the field and the laboratory to assess how climate change will modify the present scenarios of prevalences, intensities and geographical distribution of diseases of such high impact on rural children as trematodiasis and nematodiasis. Obtaining such new knowledge becomes crucial for the establishment of forecasting measures, for decision makers to conclude priorities on where and when to intervene, and for governments and health officers to design the appropriate public health systems that should be put into place to deal with the future adverse outcomes.

Fortunately, we already have the sufficient base knowledge as well as the tools for research, assessment and monitoring needed for such an action. However, many aspects do not conform an easy scenario, due to the long duration of the initiatives needed, the high cost of field and laboratory research activities in both remote rural areas and high technologies as parasite life cycle experimental reproduction, molecular characterization of parasites and vectors, and large computer requirements for mathematical modelling, RS and GIS analyses, and the evident difficulties in starting broad international collaboration initiatives between experts of disciplines not used to interact. Among all this scenario, the importance of re-increasing efforts on field work in the rural areas has been recently highlighted [161].

Helminth infection takes long time to react to climatic and environmental changes, even also after extreme catastrophic events. It will not be easy to adapt to long-term efforts, both for funding institutions not to become tired in keeping support and for scientists not to be frustrated due to the slow climate-change modifications in disease characteristics during long periods, in the present society always in hurry and increasingly demanding short-term production and success. But future risks represented by climate change effects on children living in rural areas of developing countries are too

important as to ignore them. Our responsibility towards future generations requires immediate action. A hard work is in front of us.

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