How does human-induced environmental change influence host-parasite interactions?

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SUMMARY

Host-parasite interactions are an integral part of ecosystems that influence both ecological and evolutionary processes. Humans are currently altering environments the world over, often with drastic consequences for host-parasite interactions and the prevalence of parasites. The mechanisms behind the changes are, however, poorly known. Here, we explain how host-parasite interactions depend on two crucial steps – encounter rate and host-parasite compatibility – and how human activities are altering them and thereby host-parasite interactions. By drawing on examples from the literature, we show that changes in the two steps depend on the influence of human activities on a range of factors, such as the density and diversity of hosts and parasites, the search strategy of the parasite, and the avoidance strategy of the host. Thus, to unravel the mechanisms behind human-induced changes in host-parasite interactions, we have to consider the characteristics of all three parts of the interaction: the host, the parasite and the environment. More attention should now be directed to unfold these mechanisms, focusing on effects of environmental change on the factors that determine encounter rate and compatibility. We end with identifying several areas in urgent need of more investigations.

Key words: anthropogenic disturbance, global change, infectious disease, pathogen, encounter rate, host-parasite compatibility, virulence, environmental parasitology.

INTRODUCTION

Parasites are ubiquitous in ecosystems (Dobson *et al*. 2008). They influence ecological and evolutionary processes and consequently have a profound impact on the structure and function of ecosystems. The harm that they inflict on their hosts alters population dynamics and the temporal and spatial distribution of both hosts and parasites. The harm also causes antagonistic coevolution between hosts and parasites and, hence, shapes their characteristics, such as morphologies and life-histories (Combes, 2001).

The survival of parasites depends on the successful exploitation of their hosts. This hinges on the encounter rate with hosts and the compatibility between the hosts and the parasite, i.e. on the ability of the parasite to successfully infect the host. Changes in the environment that influence encounter rate or compatibility can alter host-parasite interactions (Thompson, 1994, 2005; Wolinska and King, 2009). Human-induced environmental changes often differ from natural changes in that they are more rapid and occur at larger spatial scales (Turner II *et al*. 1990; Palumbi, 2001). They can be classified into five main categories: climate change, habitat change, introduction of exotic species, human harvesting and pollution (e.g. Sih, 2013). Much evidence currently exists for effects of human-induced environmental changes on the distribution and abundance of parasites (Lafferty and Kuris, 2005). However, our understanding of the underlying mechanisms, i.e. how environmental changes alter encounter rate and compatibility, has remained poor. To improve our knowledge of the consequences of anthropogenic disturbances for host-parasite interactions, we need to clarify effects on these underlying mechanisms. Here, our aim is to review our current knowledge of the mechanisms that regulate host-parasite interactions and examine how humans are altering them, and the consequences that these alterations in turn have for host-parasite interactions. We use examples from the literature to illustrate how humans are altering these mechanisms and the consequences the changes have for both hosts and parasites.

We begin with explaining the importance of host encounter rate and host-parasite compatibility for the viability and evolution of both host and parasite populations. We describe how both processes depend on environmental conditions and, hence, are vulnerable to anthropogenic disturbances. We then proceed to discuss how human-induced environmental changes are influencing encounter rate and compatibility. We first review impacts of humans on encounter rate, through effects on a range of factors, such as the density and diversity of hosts and parasites, the search strategy of the parasite, and the avoidance strategy of the host. We then discuss impacts of humans on host-parasite compatibility,

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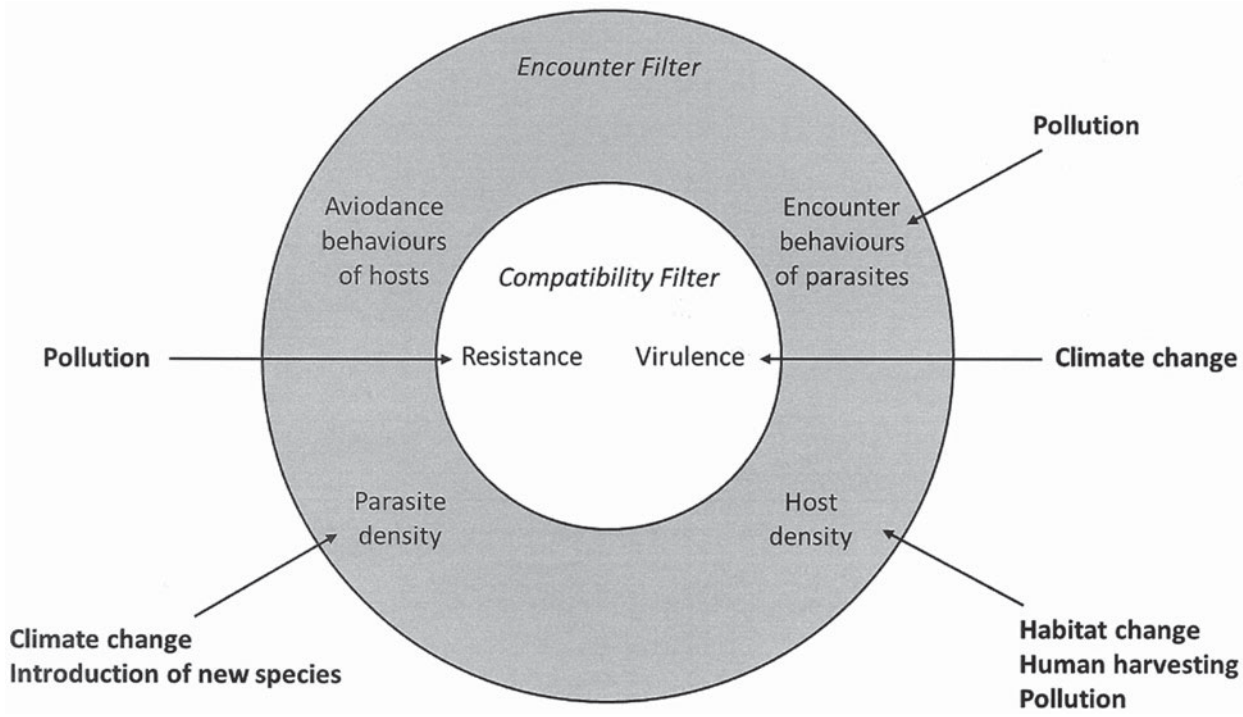

Fig. 1. An outline of the pathways through which human-induced environmental changes influence host-parasite interactions. Alterations in the environment can influence the first step in a host-parasite interaction, the encounter rate between hosts and parasites, i.e. the encounter filter, or the second step, the compatibility between the host and the parasite, i.e. the compatibility filter (adjusted from Combes, 1991). A human-induced environmental change, such as pollution, can influence both filters and several mechanisms within the filters, but for simplicity only a few pathways are presented.

i.e. on parasite virulence and host resistance, considering both plastic and evolutionary effects. Finally, we discuss how complex interactions among multiple parasite species can cause intricate effects of environmental change on host-parasite interactions. We end with pointing out several areas in need of more investigation.

We consider all organisms that cause harm to another during a sustained contact as parasites, including both micro-parasites, such as viruses and bacteria, and macro-parasites, such as ticks and worms (Combes, 2001). We concentrate on human-induced changes to the external environment of the host, and how changes in this in turn cause changes to the internal environment of the host, the immediate environment of the parasite (Thomas *et al*. 2002). We leave out intended changes by humans to the internal environment of the host, through medical or veterinary interventions, as these have been dealt with elsewhere (e.g. Gandon *et al*. 2003; Davies and Davies, 2010).

THE IMPORTANCE OF HOST-PARASITE ENCOUNTERS AND COMPATIBILITY

The specialization of a parasite on a particular host can be described as a two-step process: first, the parasite must pass through an 'encounter filter' to reach the potential host, and second, the parasite has to pass through the 'compatibility filter' and successfully infect the host (Combes, 2001). The first step – passing through the encounter filter – has similarities with optimal foraging as it depends on (1) the spatial and temporal overlap between the parasite and the host, (2) the ability of the parasite to locate and encounter the host and (3) the avoidance behaviour of the host (Lewis *et al*. 2002; Raffel *et al*. 2008; Wajnberg *et al*. 2008). The second step – passing through the compatibility filter – determines whether an infection will occur given an encounter. It includes the specialization of the parasite on a particular host, and the susceptibility of the host to the parasite.

The efficiency of the filters can change over time through antagonistic co-evolution. Parasites are selected to open filters, to increase host encounters and compatibility, while hosts are selected to close filters. Selection on parasites will favour traits that increase the probability of encounters and compatibility. Good examples are parasitic worms that manipulate the behaviour of their intermediate host to facilitate the transmission of their larvae to the final host. Selection on hosts will in turn favour traits that reduce encounters and increase resistance to infection. For instance, the larvae of *Drosophila melanogaster* have evolved foraging strategies that minimize the risk of encountering parasitoids (Carton and Sokolowski, 1992).

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Table 1. Examples of anthropogenic disturbances affecting host-parasite interactions. The disturbances affect various factors that mediate the interaction between hosts and parasites, through their effects on the two filters: host encounters and host-parasite compatibility

Anthropogenic disturbance	Affected factors	Affected filter	References
Climate change	Density and distribution of hosts	Encounters	(Reiter, 2001; Ostfeld, 2009)
	Density and seasonality of parasites	Encounters	(Poulin, 2006; Paull and Johnson, 2011; Macnab and Barber, 2012)
	Virulence of parasites	Compatibility	(Rosenberg and Ben-Haim, 2002)
	Co-infection by multiple parasites	Compatibility	(Munson *et al*. 2008)
Habitat change	Density of hosts	Encounters	(Mbora and McPeek, 2009)
Human harvesting	Density of hosts	Encounters	(Amundsen and Kristoffersen, 1990; Wood *et al*. 2010)
	Density of parasites	Encounters	(Sonnenholzner *et al*. 2011)
	Resistance of hosts	Compatibility	(Arkush *et al*. 2002)
Introductions of exotic species	Diversity of hosts	Encounters	(Kopp and Jokela, 2007; Kelly *et al*. 2009*a*)
	Diversity of parasites	Encounters	(Køie, 1991)
Pollution	Density of hosts	Encounters	(Marcogliese *et al*. 1990; Johnson *et al*. 2007)
	Density of parasites	Encounters	(Kelly *et al*. 2010; Zhao *et al*. 2013)
	Search behaviours of parasites	Encounters	(Morley *et al*. 2005; Desneux *et al*. 2007)
	Infection period of parasites	Encounters	(Johnson *et al*. 2007)
	Immunity of hosts	Compatibility	(Rohr and McCoy, 2010)

Both the encounter filter and the compatibility filter depend on environmental factors, such as host density and characteristics of the habitat (e.g. Poulin, 2003). Changes in the environment that alter these filters also alter host-parasite interactions (see Fig. 1). For instance, habitat fragmentation that reduces host encounter rate reduces infection rate. Changes in host-parasite interactions can in turn induce plastic and evolutionary changes in the traits that determine encounters and compatibility and, thus, cause alterations in species characteristics and in the abundance of parasites and hosts. These changes can have further consequences for the structure and function of ecosystems. Thus, the interaction between ecological and evolutionary processes (eco-evolutionary dynamics) can cause continually changing host-parasite systems, which are influenced by changes in the environment, and which themselves cause further changes to the environment.

In the following sections, we will review how humans are altering the factors and processes that determine encounters and compatibility between parasites and hosts, and how changes in these two steps in turn influence host-parasite interactions. In Table 1, we give an overview of various human-induced environmental changes that have been shown to alter encounter rate and compatibility and that are discussed in this review.

ALTERATIONS OF HOST-PARASITE ENCOUNTER RATE

A parasite's encounter rate with its host depends on a range of factors, such as the spatial and temporal distribution of the host and the parasite, the species composition of the community, the search strategy of the parasite, and the avoidance strategy of the host. These factors can be altered by human-induced environmental changes. Next, we will examine how humans are influencing host-parasite encounters through effects on these factors.

Changes in the density of hosts

A major determinant of the transmission rate of a parasite is the availability of susceptible hosts (Anderson and May, 1979; May and Anderson, 1979; Arneberg *et al*. 1998). This has to exceed a minimum density – the critical threshold – to allow enough transmissions to maintain the parasite population. Human activities that alter the density of hosts can consequently have a major effect on host-parasite encounter rate and, hence, on parasite transmission (e.g. Farnsworth *et al*. 2005).

Human activities that drastically reduce the density of hosts are expected to reduce encounter rate and thereby parasite transmission rate and abundance (Lyles and Dobson, 1993; Keeling and Grenfell, 1997; Arneberg *et al*. 1998; Morand and Poulin, 1998; Dunn *et al*. 2009). In support of this, Altizer *et al*. (2007) found that primates threatened because of various anthropogenic disturbances carry fewer parasite species than sister taxa that are less threatened. Similarly, fish populations that are declining because of overfishing and other human-induced changes are less parasitized than stable populations (Amundsen and Kristoffersen, 1990; Wood *et al*. 2010). For instance, the decline of lake trout populations *Salvelinus namaycush* in the Great Lakes of North America because of intensive fishing correlates with lower parasite prevalence. Inspection of museum specimens revealed that trout caught before

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1925 were more often infected by the nematode *Cystidicola stigmatura* than trout caught after 1925 (Black, 1983, 1985). Amundsen and Kristoffersen (1990) showed experimentally that a reduction in the density of hosts can decrease parasite prevalence. When they reduced the density of whitefish *Coregonus* spp. in Lake Stuorajarvi in Norway, the prevalence of the cestode *Diphyllobothrium ditremum* decreased although the abundance of its intermediate and definitive hosts – copepods and birds – did not change. Further support for an influence of human-induced reductions in host density on parasitism is provided by a literature survey. This found infectious diseases to decrease over time in marine fishes that are declining, but to increase over time in marine taxa that are not declining (Ward and Lafferty, 2004).

Correspondingly, human activities that increase host density are expected to raise encounter rate and, hence, parasite abundance, as a higher host density intensifies contacts among hosts. In support of this, the stocking of Lake Kilpisjärvi in Finland with whitefish increased parasite infections. However, a cessation of stocking did not reduce parasite abundance (Tolonen and Kjellman, 2001). This suggests that other factors than density also influenced the abundance of parasites.

Human activities also can influence parasite transmission rate indirectly, by influencing the density of the predators that prey upon the hosts. For instance, the introduction of the predatory fish salmon *Salmo salar* into Lake Kvernavann in Norway has led to a dramatic decrease in the prevalence of the cestode *Schistocephalus solidus* in the population of threespine stickleback *Gasterosteus aculeatus* in the lake, as the salmon selectively preys upon parasitized stickleback (Jakobsen *et al*. 1988).

Human-induced environmental changes that alter the distribution of hosts and, hence, local density, also alter parasite transmission rate. Habitat fragmentation, for instance, that forces individuals to aggregate in a few localities, can increase encounter rate and, thus, parasite transmission rate (Garnett and Holmes, 1996; McCallum and Dobson, 2002). An example is the recent growth of human populations in eastern Kenya, which has fragmented the habitat of the endemic monkey Tana River red colobus *Procolobus rufomitratus* (Wieczkowski and Mbora, 2000; Mbora and Meikle, 2004*a*, *b*). This has increased the density of monkeys in isolated patches, which in turn has made the species more vulnerable to parasites (Mbora and McPeek, 2009).

Human-induced alterations in the density of a host also can influence encounter rate with the next host in the life-cycle of the parasite, as many parasites infect several host species sequentially. For instance, human-induced increases in the growth of algae in aquatic ecosystems have increased the density and size of planorbid snails, the primary intermediate hosts of the trematode *Ribeiroira ondatrae*, and allowed the snails to tolerate longer infections. This has nearly doubled the number of cercariae larvae that are released from the snails and exposed to the next hosts in their life-cycle, fishes and amphibians (Johnson *et al*. 2007). This has increased the prevalence of malformations in amphibians (Fig. 2, Johnson and Chase, 2004; Johnson *et al*. 2007).

Changes in the density of parasites

Human activities that alter the density of parasites can similarly alter the encounter rate between hosts and parasites and, thus influence parasite transmission rate. Reductions in parasite density are likely to reduce parasite transmission rate, while increases in parasite density can increase parasite transmission rate.

Human-induced environmental changes influence the density of parasites both directly – such as global warming that influences the growth rate of parasites – and indirectly by altering the density of hosts (discussed in the previous section), of competitors, or of predators that prey on parasites. An example of an indirect effect of alterations in predator density on parasite density is the removal by humans of the fishes that prey on the crab *Mithrax nodosus*. The crab is a predator on parasitic eulimid snails – *Sabinella shaskyi* and *Pelseneeria* spp. – that infect the sea urchin *Eucidaris galapagensis*. Thus, an increased density of the crab because of overfishing has reduced the density of the parasitic snails (Sonnenholzner *et al*. 2011). Correspondingly, a recent meta-analysis (Zhao *et al*. 2013) found human use of herbicides to benefit plant-parasitic nematodes by suppressing the density of the predatory nematodes that feed on these parasitic nematodes.

Global warming because of anthropogenic activities is expected to have positive effects on the abundance of many parasites, as temperature can accelerate their growth and maturation rates (reviewed in Chubb, 1977, 1979, 1980, 1982). Accordingly, elevated temperature has been found to accelerate the development rate of trematode eggs and allow trematodes to complete their life-cycles more rapidly. This has increased the production and transmission rate of trematodes (Poulin, 2006; Paull and Johnson, 2011). Elevated temperature was also found to accelerate the growth rate of the cestode *S. solidus* in its secondary intermediate host, the threespine stickleback (Macnab and Barber, 2012). As higher parasite weight increases the fecundity of the parasite in its definitive host, birds (Tierney & Crompton, 1992), elevated temperatures could increase egg production and thus parasite transmission rate.

Anthropogenic pollution is another factor with major effects on parasite abundance and thereby on the transmission of parasites to hosts. For instance, Kelly *et al*. (2010) showed that the exposure of the snail *Potamopyrgus antipodarum* to moderate levels of

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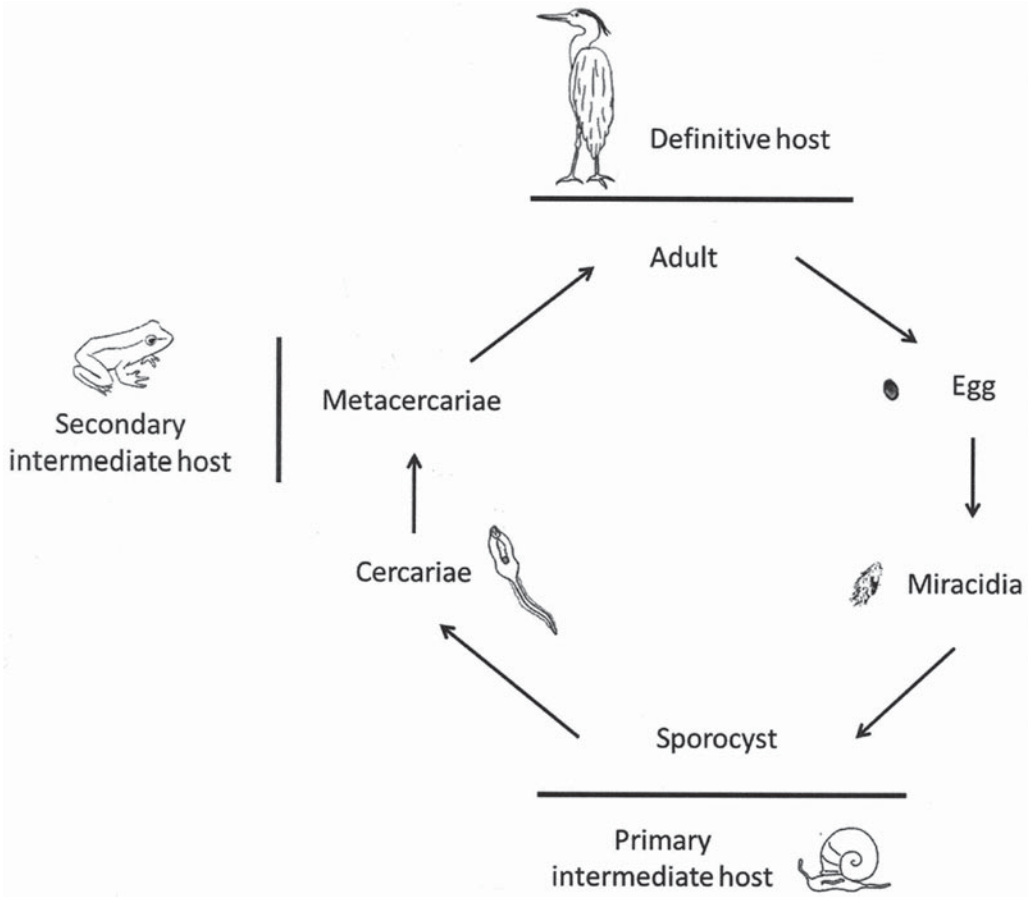

Fig. 2. An example of a complex life-cycle of a parasite. The life-cycle of the digenetic trematode *Ribeiroia ondatrae* involves both free-living stages, which are directly exposed to environmental perturbations, and parasitic stages, which rely on other organisms for development and reproduction and, hence, are indirectly influenced by effects on these organisms. The miracidia larvae infect aquatic snails, in which they develop to sporocysts. The sporocysts produce cercariae asexually, which are released into the water where they search for amphibians to infect. In the frogs, the cercariae develop into metacercariae, which cause malformations in amphibians. Predation by birds transmits the metacercariae to the definitive bird host, where the metacercariae mature and reproduce sexually. Anthropogenic disturbances that affect at least one of the different stages can compromise the completion of the whole life-cycle of the parasite.

the common herbicide glyphosate increases the production and release by the snail of the infective cercarial stages of the trematode *Telogaster opistorchis*. This raises in turn the density of parasites for the next host in the life-cycle of the trematode, juveniles of the freshwater fish *Galaxias anomalus*. Moreover, synergistic effects between the herbicide and the parasite amplify the negative impact of the parasite on infected fish, causing malformations and death of fish (Kelly *et al*. 2010).

Changes in the temporal distribution of hosts and parasites

The often ephemeral distribution of hosts forces parasites to adjust their temporal distribution to that of their hosts (Lewis *et al*. 2002). For example, helminth parasites time the hatching and emergence of their larvae to abiotic factors associated with the presence of susceptible hosts, such as temperature, light and humidity (Pietrock and Marcogliese, 2003). This tracking of the presence of hosts can cause highly seasonal parasite epidemics (Altizer *et al*. 2006). Human-induced changes in abiotic factors that alter the temporal distribution of hosts will consequently also alter that of parasites. This can in turn induce evolutionary changes in the phenology of both hosts and parasites (Lafferty, 2009).

A growing human-induced environmental problem that is affecting the phenology of both hosts and parasites is global warming (Rogers and Randolph, 2006). For instance, higher temperature has been found to prolong the time window during which mosquitoes can breed and extend the period when mosquito-borne parasites are transmitted to humans (Reiter, 2001). This prolonged transmission period has been suggested to have contributed to the spread of the bluetongue virus in Europe during recent years (reviewed in Purse *et al*. 2005).

Global warming can also reduce the reliability of environmental cues as indicators of the ideal timing of life-history events (Schweiger *et al*. 2008). This

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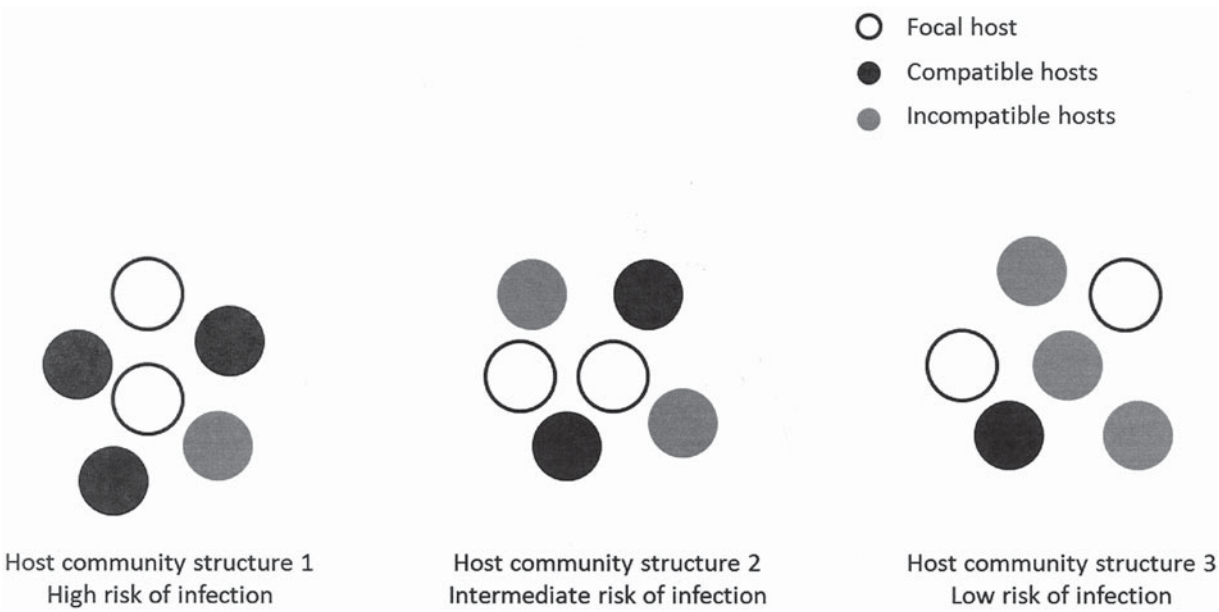

Fig. 3. The dilution of infection risks through increases in the density of incompatible hosts. Individuals of the white host population carry one parasite species able to differentially infect other host populations in the community. Black hosts are compatible hosts for the parasite (i.e. sources for the parasite population), while grey hosts are incompatible hosts (i.e. sinks for the parasite population). Although the population of white hosts remains constant under the three community structures, alterations in the composition of the host assemblage affect infection risk for the white hosts.

mis-timing can have particularly deleterious consequences for parasites that spend part of their life-cycle outside the host, where the host's internal temperature does not buffer them against changing environmental conditions. Little evidence exists, however, of mis-timed phenologies between hosts and parasites, probably because of the scarcity of long-term data series for the prevalence and abundance of parasites (Møller, 2010).

Another anthropogenic disturbance that can have profound effects on the temporal distribution of both hosts and parasites is thermal pollution of aquatic ecosystems. For instance, a long-term study by Aho *et al*. (1982) found thermal discharges in cooling reservoirs to extend the transmission period of the metacercariae of the eyefluke *Tylodelphys scheuringi*. This increased infections in populations of mosquitofish *Gambusia affinis*.

Changes in the diversity of hosts and parasites

The encounter rate between a parasite and a host depends not only on the density of the target host, but also on that of alternative hosts and non-hosts, i.e. on the composition of the community (Thieltges *et al*. 2008*a*; Johnson and Thieltges, 2010). Human-induced introductions or removals of species can consequently have positive or negative effects on native host-parasite interactions, depending on how the change influences encounter rate with compatible hosts.

Human-induced introduction of novel host species promotes parasite transmission if a new compatible host-parasite association is formed from which parasites can be 'spilled back' to native hosts (reviewed in Kelly *et al*. 2009*b*). This can occur when the introduced and the native hosts are ecologically similar, i.e. the encounter filter is open, and when the two hosts are closely related so that the probability of compatibility with local parasites is high, i.e. the compatibility filter is open. Both the native and the introduced host will then experience higher parasitic pressure. The host that suffers the greatest negative impact might eventually go extinct (Anderson and May, 1979), or diverge ecologically and evolve lower overlap.

When humans introduce species that are not compatible with native parasites, the introduced species will experience a low risk of infection, in lines with the enemy release hypothesis (Torchin *et al*. 2002, 2003; Torchin and Lafferty, 2008). This can dilute infection risks also for native hosts by increasing the parasite's encounters with and infection attempts on incompatible hosts and, thus, reduce the abundance of the parasite (Fig. 3, Keesing *et al*. 2006; Johnson and Thieltges, 2010). An example of this is the introduction by humans of the European freshwater snail *Lymnaea stagnalis* to New Zealand at the end of the 19th century (Hutton, 1881). The introduced snail is less compatible than the native snail *P. antipodarum* with the native trematode *Microphallus* sp., i.e. the encounter filter is open but the compatibility filter is closed (Kopp and Jokela, 2007). Thus, increased infection attempts on the introduced, incompatible snail has reduced the prevalence of the parasite, which in turn has reduced encounters

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with the compatible, native snail and released it from infections (Kopp and Jokela, 2007). Similar dilution effects because of human-introduced species have been reported for various parasites of molluscs, fishes and mammals (e.g. Telfer *et al*. 2005; Thieltges *et al*. 2008*b*; Kelly *et al*. 2009*a*; Paterson *et al*. 2011).

When human-introduced species bring with them non-indigenous parasites, these can be 'spilled over' to native hosts and affect them negatively. The topic has received considerable attention in the literature (Prenter *et al*. 2004). A classic example is the massive mortality of amphibians worldwide because of global trade with African-clawed frogs *Xenopus* sp. The frogs, which are used in research, as pets, and to conduct pregnancy tests, carry the chytrid fungus *Batrachochytrium dendrobatidis* on their skin, which is spread to native species when the frog is introduced into novel environments (Weldon *et al*. 2004; Ouellet *et al*. 2005; Rachowicz *et al*. 2005). Another classic example is the worldwide spread of the swim-bladder nematode *Anguillicola crassus* with the commercial export of Japanese eel *Anguilla japonica* (Køie, 1991). The low specificity of the nematode for intermediate hosts has allowed it to rapidly spread to other eel species, where it causes pathological damage to the swimbladder (Moravec, 1996; Moravec and Škoriková, 1998). This could have contributed to the dramatic decline of European eel *Anguilla anguilla* populations in recent years (Køie, 1991).

Changes in search and avoidance strategies

The search strategy of the parasite and the avoidance strategy of the host depend crucially on environmental conditions. Human disturbances that influence these strategies can consequently alter host encounter rate. An insidious human-induced problem that is currently altering the behaviour of both parasites and hosts is chemical pollution. Chemical cues are often used by free-living stages of parasites to locate their hosts (Lewis *et al*. 2002). This means that human activities that influence the chemical composition of the environment also alter host-parasite interactions. For instance, the increased use of pesticides has impaired the search behaviour of parasitic wasps by affecting their longevity, activity and orientation (Desneux *et al*. 2007).

Human-induced increases in the concentration of heavy metals pose a serious threat to host-parasite interactions, as the metals often influence the behaviour of both parasites and hosts. For example, Morley *et al*. (2005) showed that a mixture of zinc and cadmium influences the energy expenditure of the cercarial larvae of the trematode *Diplostomum spathaceum*. The larvae normally shed their tails when their energy store is almost depleted in order to reduce energy use. When the larvae were exposed to a single metal, the frequency of tail losses increased with age. However, when the larvae were exposed to a mixture of metals, tail losses were delayed (Morley *et al*. 2002, 2005). This is expected to increase energy use and reduce energy store, and, hence, impair the activity and transmission rate of the parasite. Together with a reduction in the release of larvae from the intermediate snail host population, because of negative effects of heavy metals on snails (Coeurdassier *et al*. 2004), this could drastically reduce the prevalence of the parasite.

Changes in parasite avoidance behaviour of hosts because of human-induced environmental changes can be categorized into two main groups: (1) changes in pre-contact avoidance behaviour, such as habitat choice and selective foraging, and (2) changes in post-contact avoidance behaviour, such as grooming (Thieltges and Poulin, 2008). These changes are expected to influence host-parasite interactions. However, the impact that human-induced environmental changes have on avoidance behaviour has received surprisingly little attention. One exception is the study by Rohr *et al*. (2009) on the influence of the herbicide atrazine on parasite avoidance behaviour of tadpoles of the American toad *Bufo americanus*.

ALTERATIONS OF HOST-PARASITE COMPATIBILITY

In the preceding section, we discussed how human-induced environmental changes can influence the probability that a parasite encounters a compatible host. We now turn to discuss how human-induced changes in the environment can influence infection success, and the severity of the infection, through effects on the compatibility between the parasite and the host, i.e. through effects on parasite virulence and host resistance. Virulence and resistance are determined by environmental and genetic factors and develop through antagonistic coevolution between the parasite and the host. Human-induced changes in the environment can induce immediate plastic changes, or longer-term genetic changes, both of which can alter host-parasite interactions.

Parasite virulence can be defined as the degree to which a parasite harms a host, or more exactly, reduces its fitness (Ebert and Herre, 1996; Ebert and Bull, 2003; Alizon *et al*. 2009). According to the transmission-virulence trade-off hypothesis, higher virulence limits the transmission rate of the parasite, as most hosts will die before the parasite has been transmitted to a new host. Parasite strains with high virulence may therefore quickly go extinct (Ewald, 1983; Lipsitch and Moxon, 1997; Alizon *et al*. 2009). Human-induced increases in host density can allow the evolution of higher virulence, as growth rate is then not limited by encounter rate, but by replication rate.

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Plastic changes in virulence and resistance

The degree to which human-induced environmental changes cause plastic alterations in parasite virulence and host resistance depends on the genetic constitution of the individuals, as genes determine reaction norms and, thus, how traits vary across environments. Common causes of plastic adjustments of parasite virulence are alterations in host condition or in the intensity of competition for hosts (e.g. Tseng, 2006; Tschirren *et al*. 2007; Choisy and de Roode, 2010). Plastic changes in parasite virulence can in turn cause plastic changes in host resistance.

Human-induced global warming is increasingly recognized as a potential cause of increased virulence of parasites, as temperature often acts as an 'on-off' switch for the expression of virulence genes (Konkel and Tilly, 2000; see Marcogliese, 2001; Mitchell *et al*. 2005). This is currently contributing to the worldwide bleaching of corals – the loss of endosymbiotic zooxanthellae – through effects of temperature on the expression of virulence factors in bacteria that inhibits photosynthesis of the zooxanthellae (reviewed in Rosenberg and Ben-Haim, 2002). For instance, the current decline of the coral *Oculina patagonica* is caused by global warming activating the expression of several virulence factors in the coral-bleaching bacterium *Vibrio shiloi* (reviewed in Rosenberg and Falkovitz, 2004).

Similarly, various forms of human-induced pollution alter virulence and resistance by causing physiological changes in parasites and hosts. Chemical pollutants, in particular, can impair immune responses of hosts by altering the production, longevity, structure and function of the cells and proteins of the immune system (Schuurman *et al*. 1994; Banerjee, 1999; Blakley *et al*. 1999; Jorgensen, 2010). For example, chemical compounds that impair the production of the mucus that protects the gills of fishes can hamper resistance, as the mucus contains compounds that trap and inhibit the growth of microorganisms (see Shephard, 1994; Bols *et al*. 2001; Alvarez-Pellitero, 2008 and references therein). Petroleum hydrocarbons, for instance, impair mucus production in cod, which increase the prevalence of gill parasites, such as ciliates and monogeneans (Khan and Kiceniuk, 1988; Khan, 1990). Another chemical pollutant that hampers the functioning of the immune system in a range of fishes and amphibians is the herbicide atrazine (Rohr and McCoy, 2010). It triggers the degeneration of macrophages in mullets (Biagianti-Risbourg, 1990), lowers the respiratory burst activity of circulating phagocytes in rainbow trout (Rymuszka *et al*. 2007), and reduces the abundance of T cells in a number of species (e.g. Christin *et al*. 2003; Christin *et al*. 2004; Rymuszka *et al*. 2007). A meta-analysis found the herbicide to reduce 77% of the immune responses that were included in the analysis (Rohr and McCoy, 2010). On the other hand, the herbicide has positive effects on the immune system of some species, through complex interactions between the herbicide and physiological functions (e.g. Chakrabarty and Banerjee, 1988; Sures, 2006; Sures, 2008).

Anthropogenic disturbances can influence host resistance also indirectly, through trade-offs between resistance and other fitness functions (Martin *et al*. 2010). For instance, Adamo and Lovett (2011) showed that increasing temperatures because of global warming increases reproductive output, mass gain and the activity of the immune system in the cricket *Gryllus texensis*. Because of physiological trade-offs between reproduction and disease resistance, the increased effort reduces resistance to some parasites. This suggests that global warming could cause crickets to become more susceptible to some parasites.

Evolutionary changes in virulence and resistance

Human activities that cause longer-term changes in the environment can induce evolutionary changes in virulence and resistance if genetic variation in the direction of selection exists, or is introduced through gene flow or mutations. The influence of human activities on the evolution of parasite virulence is especially pronounced at farms where the density of hosts is high, as high host density favours higher parasite virulence (Murray and Peeler, 2005; Mennerat *et al*. 2010). In aquacultures, the density of one species can even be a thousand times higher than in the wild (Pulkkinen *et al*. 2010). An example of a parasite that has evolved more virulent strains is the salmon louse *Lepeophtheirus salmonis* at salmon farms (Mennerat *et al*. 2012). After the rapid growth of aquaculture, the more virulent strains have amplified and spread to wild salmonid populations, where they have had adverse effects on the natural stocks (Krkošek *et al*. 2007; Costello, 2009). Another example of the evolution of more virulent strains is the bacterial fish parasite *Flavobacterium columnare*, which frequently causes severe parasite outbreaks at fish farms (Kunttu *et al*. 2009; Pulkkinen *et al*. 2010).

A classic example of human-induced coevolution between host resistance and parasite virulence is the release of the myxomatosis poxvirus in Australia to control the population growth of the introduced European rabbit *Oryctolagus cuniculus*. The most lethal strain of the virus, originating from America, was released during the 1950s. This caused dramatic mortality among the rabbits, with over 99% of the infected rabbits dying. Within 10 years, a less virulent strain of the virus had established itself, which killed only 50% of infected rabbits (Fenner and Marshall, 1957; Marshall and Fenner, 1960). The higher survival of the infected rabbits enhanced the transmission of the less virulent strain, which in turn selected for enhanced host defence (Massad, 1987). This led to the evolution of resistant rabbits, which in

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turn selected for higher virulence (Best and Kerr, 2000).

For parasite virulence and host defences to evolve, they need to be heritable and express genetic variation in the direction of selection. Declining populations often suffer from the loss of genetic variation. This can hamper the evolution of host defences against parasites and further worsen the probability of survival of the populations. For instance, several threatened vertebrate taxa show less variation in the genes of the major histocompatibility complex, MHC, which is involved in parasite recognition (e.g. Hedrick *et al*. 1999, 2000; Giese and Hedrick, 2003). An example of this is captivity inbred winter-run chinook salmon *Oncorhynchus tshawytscha*, which are less resistant to three species of parasites than outbred populations (Arkush *et al*. 2002). This is particularly evident for salmon that are homozygous for the MHC genes. Surprisingly, wild Chinook populations show high allelic diversity for the MHC genes compared with other genes, despite also being inbred (Garrigan and Hedrick, 2001).

THE INFLUENCE OF CO-INFECTIONS

We have so far focused on single-parasite infections where one parasite infects a host. However, hosts are often infected by several different parasite species (multi-specific infections) or different strains of a parasite (multi-strain infections). Interactions between these can influence the outcome of the different infections. This is particularly the case when parasites exploit overlapping niches and niche switches within the host are not possible (Mideo, 2009; Rigaud *et al*. 2010; Bordes and Morand, 2011; Eswarappa *et al*. 2012). Facilitation and competition between the co-infecting parasites can then select for higher parasite virulence, which in turn can select for changes in host defences and cause coevolution between the host and the multiple parasites (Bradley and Jackson, 2008; Horrocks *et al*. 2011).

Anthropogenic disturbances can alter these interactions among multiple parasite species through two different pathways: (1) by changing the diversity and distribution of the parasite species and the host, which can alter the probability of co-infections, and (2) by causing modifications in parasite virulence and host resistance. Our current knowledge of multi-parasite interactions is still in its infancy (Rigaud *et al*. 2010), but a recent study on *Babesia* infections in lions *Panthera leo* in the Serengeti and Ngorongoro Crater suggests that climate change could amplify negative effects of co-infections on parasite abundance. The study found severe outbreaks of the tick-borne haemoparasite *Babesia* to correlate with epidemics of canine distemper virus in lions (Munson *et al*. 2008). However, the immunodepression induced by the canine distemper virus could not alone explain the severity of the *Babesia* infections. Instead, the extreme drought that preceded the canine distemper epidemic must have weakened the herbivores that carried the ticks that transfer *Babesia* to lions. This could have allowed the tick population to grow, and increased the encounter rate with lions when the rains resumed. A simultaneous outbreak of the canine distemper virus reduced the resistance of the lions, which magnified the *Babesia* infections. Thus, the climate extreme disrupted a stable host-parasite system and caused mass mortality of lions.

CONCLUSIONS AND FUTURE DIRECTIONS

In this review, we have examined how human-induced environmental changes influence host-parasite interactions through effects on the two main steps of infection: host encounters and host-parasite compatibility. The effect of environmental change can be both direct and indirect (through effects on other species), and induce both immediate plastic and longer-term genetic changes. It is obvious that the ultimate influence of human disturbance depends on a range of abiotic and biotic factors. Thus, to unravel the impact of humans on host-parasite interactions, and to reveal the mechanisms behind the effects, we have to consider the characteristics of all three components of the interaction: the parasite(s), the host(s) and the surrounding environment.

Human disturbance is likely to have the most profound impact on host-parasite systems where parasites have multiple, successive hosts. This is because multiple hosts increase the probability that at least one host will be affected by the disturbance (Marcogliese, 2001), or that gene flow will hamper local adaptation (e.g. Louhi *et al*. 2010). Similarly, human disturbances are expected to affect specialist parasites more than generalists, as specialists require an evolutionary host switch before they can use another host.

The ultimate consequences of human-induced alterations of host-parasite interactions on the structure and function of ecosystems are poorly known. Parasites mediate many species interactions and changes in host-parasite interactions could therefore have profound impacts on ecosystems (Marcogliese, 2004). More investigations are currently needed on the mechanisms behind the effects of man-made changes on host-parasite interactions, and their consequences for the structure and function of communities and ecosystems. We end this review with a few suggestions on topics that are in particular need of more research.

First, researchers should attempt to link human-induced changes at the two steps of infection to each other, i.e. link changes in host encounter rate to changes in compatibility, and vice versa. Much research has focused on coevolution between virulence and resistance, but the co-evolution between the two

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steps, encounter rate and compatibility, has received little attention. The whole life-cycle of the parasites should here be considered, as investigation of a restricted number of life-history stages may not reveal the ultimate effect of changes in the environment.

Second, further investigations are needed on the influence of human-induced environmental change on co-infections by multiple parasite species (or strains) and their effects on host-parasite interactions. Co-infections are common in nature and by focusing on single parasite infections we may severely underestimate the influence of human activities on both hosts and parasites.

Third, researchers have to consider how humans impact host-parasite interactions through effects on the community of species. Human-induced environmental change may cause parasites to switch between hosts, through plastic or evolutionary responses, while changes in the parasite fauna may induce competition and facilitation among parasites. These changes may further alter host-parasite interactions. More investigations are particularly needed on the consequences of changes in the density of human populations for plastic and evolutionary changes in host-parasite interactions.

Fourth, more attention should be paid to the influence of humans on the trophic cascades that shape host-parasite systems, considering both top-down and bottom-up processes. Humans are currently having major effects on the structure and function of ecosystems through effects on trophic cascades, but the influence that humans are having on these cascades through effects on host-parasite interactions has received surprisingly little attention.

Fifth, we need to spend more effort on synthesizing available research results, for instance through meta-analyses. This would allow us the better estimate which anthropogenic disturbances have the most adverse effects on host-parasite interactions, if the effects are general or idiosyncratic, which host-parasite systems are most sensitive to particular forms of anthropogenic disturbances, and which pathways are most sensitive to human-induced perturbations. These are major goals in our attempt to elucidate the consequences of human activities for ecosystems and in finding solutions to prevent or minimize the negative long-term effects that our activities may have.

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