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Climate change and infectious diseases of wildlife: Altered interactions between pathogens, vectors and hosts

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Abstract Infectious diseases result from the interactions of host, pathogens, and, in the case of vector-borne diseases, also vectors. The interactions involve physiological and ecological mechanisms and they have evolved under a given set of environmental conditions. Environmental change, therefore, will alter host-pathogen-vector interactions and, consequently, the distribution, intensity, and dynamics of infectious diseases. Here, we review how climate change may impact infectious diseases of aquatic and terrestrial wildlife. Climate change can have direct impacts on distribution, life cycle, and physiological status of hosts, pathogens and vectors. While a change in either host, pathogen or vector does not necessarily translate into an alteration of the disease, it is the impact of climate change on the interactions between the disease components which is particularly critical for altered disease risks. Finally, climate factors can modulate disease through modifying the ecological networks host-pathogen-vector systems are belonging to, and climate change can combine with other environmental stressors to induce cumulative effects on infectious diseases. Overall, the influence of climate change on infectious diseases involves different mechanisms, it can be modulated by phenotypic acclimation and/or genotypic adaptation, it depends on the ecological context of the host-pathogen-vector interactions, and it can be modulated by impacts of other stressors. As a consequence of this complexity, non-linear responses of disease systems under climate change are to be expected. To improve predictions on climate change impacts on infectious disease, we suggest that more emphasis should be given to the integration of biomedical and ecological research for studying both the physiological and ecological mechanisms which mediate climate change impacts on disease, and to the development of harmonized methods and approaches to obtain more comparable results, as this would support the discrimination of case-specific versus general mechanisms [*Current Zoology* 59 (3): 427–437, 2013].

Keywords Climate change, Wildlife, Disease, Host, Pathogen, Vector, Species interactions

1 Introduction

Infectious diseases result from the interactions between hosts, pathogens, and often vectors, which coexist under a given set of environmental conditions (Gilman et al., 2010; Johnson and Paull, 2010). The interactions include both physiological and ecological mechanisms. If there occurs a change of the environmental conditions to which host-pathogen (HP) or host-pathogen-vector (HPV) interactions are adapted to, this will modulate the interactions and can lead to altered disease risks (McMichael et al., 2003; Dobson and Foufopoulos, 2001). In recent times, an environmental alteration that has attracted particular attention is climate change. Variations of climatic factors have been discussed as being responsible for changes in disease prevalence, distribution and intensity, particularly in the case of vector-borne diseases and emerging diseases (Daszak et al., 2000; Harvell et al., 2002; Hofer and East, 2010; Marcogliese, 2008; Randolph, 2009; Rohr et al., 2011; Roque et al., 2008; Rosenthal, 2009). However, if climate change leads to an increase of disease risks remains controversial (Lafferty, 2009; Harvell et al., 2009).

Climate change is defined by the Intergovernmental Panel on Climate Change (IPCC) as "a statistically significant variation in either the mean state of the climate or in its variability, persisting for an extended period (typically decades or longer)". Climate change is usually perceived as global warming, including elevated mean temperatures and stronger temperature variations and extremes, but implicates a variation of environmental factors, including precipitation/humidity, drought frequency, ocean acidification, water quality, and seasonality.

In this article, we aim to review pathways through which climate change can affect host-pathogen-vector interactions, and how this might impact presence or

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emergence of disease. The focus of this review is on wildlife diseases, both terrestrial and aquatic wildlife, since the principal processes are comparable if not identical in the two compartments. There is a diversity of variables and processes of infectious diseases which are sensitive to climate-related environmental variables (Fig. 1) and thus might be impacted by climate change. Importantly, the target processes potentially impacted by climate variables include both pathological processes, e.g., an altered immune response of the host to the invading pathogen, and ecological processes, e.g., a mismatch in spatial overlap between host and pathogen due to shifts in the geographical distribution. Climate factors can have direct actions on distribution, life cycle and physiological status of hosts, pathogens and vectors, and these effects will be addressed in section 2. As disease arises from the interaction of hosts, pathogens and vectors, it is the impact of climate change on these interactions which is particularly critical with respect to altered disease risks. Climate change effects on the interactions between host, pathogens and vectors will be addressed in section 3. Finally, climate change impacts on infectious diseases of wildlife may involve the ecological networks of which HP/HPV systems are part of, and they may involve cumulative effects with other environmental stressors. These aspects will be shortly touched in section 4. An overview of the diseases discussed here and the involved targets and mechanisms of climate change impact on these diseases are provided in Table 1. Although this review is focusing on wildlife, the principal pathways and mechanisms through which environmental change influences disease processes are not different between wildlife and human diseases. Therefore, in line with the ideas of the "one health" concept, knowledge obtained from the study of climate

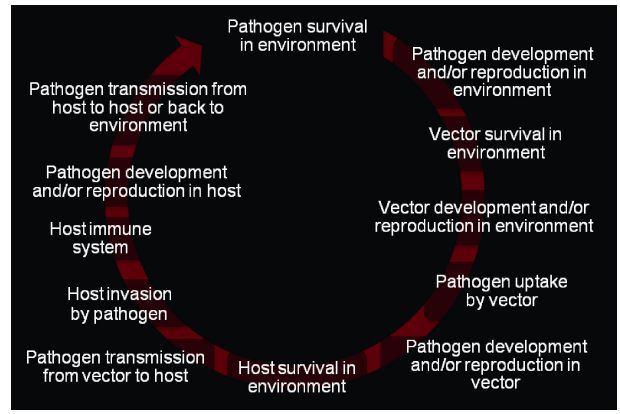

Fig. 1 Key processes in host-pathogen and host-pathogen-vector interactions that might be modified under the influence of climate change

Table 1 Overview of the main examples discussed in the text for climate change effects on infectious diseases of wildlife

Disease	climate-related environmental variables act upon			climate-related environmental variables modulate interaction between				physiological mechanism	ecological mechanism
	H	V	P	H-P	V-P	H-V	Ecological network		
parasite disease (*P. marinus*) of oysters			x						alteration of geographic distribution
parasite disease (*U. pallikuuken-sis*) of musk ox			x					alteration of pathogen development	
bluetongue		x			x	x			alteration of geographic distribution, vector switch
avian influenza virus			x					altered pathogen survival	
(bacterial) diseases of corals	x		x	x				altered host immunity and pathogen virulence	
malaria		x	x		x	x		alteration of vector immunity, of vector biting frequency and of pathogen development	alteration of geographic distribution
Rift Valley Fever		x						alteration of vector reproduction	alteration of vector population growth
distemper of harbour seals	x								alteration of intraspecific aggregation
chytrid fungus infection of amphibians	x		x	x				alteration of host immunity and of pathogen development,	
parasite disease (*P. tenuis*) of deer	x		x	x					alteration of geographic distribution
Parasite-stickleback-birds	x	x		x			x	alteration of pathogen development	alteration of host behaviour and of trophic relations
Proliferative Kidney Disease	x		x	x			x	alteration of host immunity and of pathogen development	alteration of host geographical distribution, density, and of pathogen transmission
West Nile Virus		x				x	x		alteration of vector population growth, and of trophic relations

Abbreviations: H = host, P = Pathogen, V = vector.

change effects on wildlife diseases is relevant and applicable for human diseases as well.

2 Impact of Climate-Related Environmental Variables on Physiological and Ecological Traits of Hosts, Pathogens or Vectors

Environmental change can have direct impacts on physiological and ecological traits of species such as pathogen resistance, life cycle parameters or geographic range. Responses of species to environmental change include physiological acclimation (within their reaction norms) as well as evolutionary adaptation. This chapter discusses on a few examples how climate change variables may interfere with the distribution and performance of hosts, pathogens or vectors.

2.1 Climate change affects geographic distribution of host, vectors and pathogens

Climate variables act as environmental filters with direct influence on the geographic distribution of hosts, pathogens and vectors. A well documented example of climate change-related geographic expansion is the northward movement of an oyster parasite, the protozoan *Perkinsus marinus*. In the 1990s, winter temperatures of surface waters along the Atlantic coast of North America increased. This was accompanied by an expansion of the parasite from its original range along the southeast coast to the northeast coast (Cook et al., 1998; Harvell et al., 2009). The association between the northward migration of *P. marinus* and the warming of sea water is suggestive of climate change as a causative factor. However, alternative explanations must not be overlooked, for instance, the northward expansion of *P. marinus* could be an evolutionary based cold adaptation of the parasite. Ford and Chintala (2006) tested the evolutionary hypothesis and found no evidence to support it; thus, the causative factor for the northward migration of *P. marinus* indeed appears to be increased water temperature. Notably, expansion of the thermally suitable range of a species does not necessarily result in an increase of geographic distribution, as other factors besides climate may be limiting, for instance, barriers to dispersal or predation (Lafferty, 2009).

Climate change factors can result not only in range expansions but also in range shifts (Lafferty, 2009). This distinction is important in assessing the consequences of altered geographic distribution for the presence of disease. For instance, in tropical countries malaria is less endemic in high altitude areas, since the relatively low temperatures of mountain regions reduce generation time and biting frequency of the insect vectors (Lafferty, 2009; Pascual and Bouma, 2009). Altered environmental temperatures also influence developmental rates of the pathogen inside the ectothermic vector. With increasing temperatures due to global warming, the presence of malaria in tropical mountain areas is expected to increase. At the same time, however, climate change may lead to decreased presence of malaria at the warmer, more arid boundaries of its distribution, because in those areas vector survival is reduced due to the increasing temperatures, together with more frequent rainfall events (Paaijmans et al., 2007). Through the opposing developments in tropical mountain areas and subtropical semi-arid areas, climate change would cause a shift but not an expansion of malaria distribution and endemics.

2.2 Climate change affects life cycle traits of host, vectors and pathogens

Climate variables can modulate survival, growth, developmental rates or reproduction of hosts, pathogens and vectors thereby influencing disease dynamics. A very direct consequence of altered climate conditions is reduced survival of the pathogen in the environment. Survival time of Avian Influenza A Virus (AIV) of birds, which is transmitted mainly via faeces-contaminated water, varies with water temperature. Brown et al. (2007) found an inverse relation between increasing water temperature and AIV survival. Therefore, increases in water temperatures are expected to reduce infection cases of birds by AIV. In addition, changes of water salinity, as they may occur as a consequence of altered hydrological cycles under conditions of climate change, were found to influence environmental AIV persistence (Brown et al., 2007).

The Arctic musk ox *Ovibos moschatus* is parasitized by the strongyloid worm *Umingmakstrongylus pallikuukensis*. While the adult parasites live in the lungs of the musk ox, the larvae develop outside the host. Their developmental rate is directly temperature-dependent (Kutz et al., 2005). Already a moderate temperature increase of 1°C has the potential to shorten the two-year cycle for the development of *U. pallikuukensis* larvae to a one-year-cycle. Such an increase in ambient temperature has been observed in Artic Canada between 1978 and 2000, which implicates that the infection pressure on musk ox by *U. pallikuukensis* is likely to increase in the future.

The importance of climatic factors beyond tempera-

ture for the dynamics of diseases may be illustrated by the example of Rift Valley Fever (RVF). This is a mosquito-borne viral disease, which is widely distributed in Eastern and Western Africa (Martin et al., 2008). It mainly causes disease in humans and domestic livestock such as sheep and cattle, but can also lead to abortions in wildlife, for example in buffaloes (Pfeffer and Dobler, 2010). The etiological agent is a RNA virus of the genus *Phlebovirus*, which is transmitted by a range of mosquito species, including insects of the genus *Aedes* (Turell et al., 2008). In the Horn of Africa, where RFV has been originally described, the disease occurs in epidemics which correlate with heavy rainfall events (Martin et al., 2008). The underlying mechanism is the biology of the *Aedes* vector: These insects are floodwater-breeding species laying eggs in pond and river mud. Eggs can survive desiccation for many years. RFV virus is transferred transovarially into the eggs and persists in the eggs during dry periods. When the eggs get flooded again, insects hatch in huge numbers giving rise to the emergence of a large, infected vector population and to a new endemic cycle (Martin et al., 2008). As pointed out by the IPCC report (Trenberth et al., 2007), heavy rainfall events are expected to become more frequent in the future, and therefore an increase in frequency and severity of RFV outbreaks might be expected. Climate change may affect vector transmission of RFV not only by modulating the frequency of emergence events, but also through other aspects of *Aedes* biology, for instance, by impacting egg production or the length of the extrinsic incubation period. Such effects have been demonstrated in laboratory experiments, although their relevance under field conditions remains to be demonstrated (Martin et al., 2008).

2.3 Climate change effects on physiological capacities of hosts, vectors and pathogens

A physiological mechanism through which host susceptibility to a pathogen can be altered is the environmental modulation of host immunocompetence (Acevedo-Whitehouse and Duffus, 2009; Dobson, 2009; Martin et al., 2010). While ecological factors such as spatial distribution decide on whether hosts and pathogen co-occur, host immune capacity influences the success and severity of the infection. Climate variables are known to modulate immune functions, and this has consequences for the establishment, survival and reproduction of the pathogen in hosts and vectors. There is evidence for a role of altered immunocompetence in an increasing number of disease cases (Martin et al., 2010; Mydlarz et al., 2010; Murdock et al., 2012). Climate impact on immunity has not only direct negative consequences for the host, but possibly also indirectly in that the energetic costs of the immune response lead to trade-offs such as impaired reproduction (Bradley and Jackson, 2008). Climate effects on host immunity may have implications also for pathogen evolution: Since the immune system is an important selection mechanism for pathogens, climate-induced alterations of host immunocompetence may modify pathogen evolution and give rise to the emergence of new virulent strains. This would indirectly lead to an alteration of the host-pathogen interaction (Sorci et al., 2013).

A laboratory example on the impact of climate-related variables on host immunity comes from the study of Seppälä and Jokela (2010) with pond snails *Lymnaea stagnalis*. The animals were exposed for one week to 30°C warm water (a realistic scenario for small ponds during hot summers) and their immune capacity was compared to that of snails kept at 15°C. In snails kept at 30°C, phenoloxidase activity and antibacterial activity of the haemolymph were significantly reduced. When snails were exposed to microorganism-enriched water, phenoloxidase activity increased at 15°C but not at 30°C. In other words, snails kept in warm water were not able to activate their immune system under pathogen challenge.

The probably best studied field case of a H/P system in which temperature-modulated host immunity plays a role comes from bacterial diseases of corals. In recent years, worldwide an increased frequency and severity of infectious coral diseases has been noted, including coral bleaching, i.e. the loss of the obligate algal symbionts, and coral mortality (Hoberg et al., 1995; Kushmaro et al., 1997; Brown, 1997). Coral disease outbreaks often follow heat waves. The immune response of corals is modulated by temperature (Martin et al., 2010; Mydlartz et al., 2010). Mydlarz et al. (2010) found that when healthy sea fan corals *Gorgonia ventalina* were exposed to increasing water temperature, they increased their amoebocyte activity. Granular amoebocytes are a part of the coral's cellular immune response (Ellner et al., 2007). At the same time, water temperature influences virulence of the infective bacteria, as it has been shown, e.g., for *Vibrio corallilyticus*, which shows temperature-dependent pathogenicity (Rosenberg and Ben Haim, 20902; Kimes et al., 2012): At water temperatures above 27°C, the bacterium upregulates a number of virulence factors concurrent with phenotypic changes in motility, haemolysis or cytotoxicity. The disease outcome in interaction between the coral host and the pathogenic

bacteria will depend on the balance of the temperature-dependent changes in host immunity and pathogen virulence.

The susceptibility of the host to pathogen infection can be altered through physiological as well as ecological mechanisms. Ecological mechanisms which enhance host susceptibility to and interaction with pathogens are, among others, changes in animal distribution and interactions. Seasonal migration of animals is considered to reduce parasite prevalence in the host species (Harvell et al., 2009). Weather extremes such as drought favour aggregation of animals to water holes, and this will increase rates of pathogen transmission and support maintenance of infections in a population (Schöning et al., 2013). A similar mechanism is discussed to have led to an epidemic of distemper among northern European harbour seals *Phoca phoca* in 1988. Lavigne and Schmitz (1990) compared mean monthly air temperatures during the years of high mortality with mean monthly air temperatures for the preceding ten years. According to their data, each outbreak began after a three-month-period of unusual warmth, during which mean temperatures had been 1.0°C to 3.0°C higher than the preceding ten-year average for the same months. Lavigne and Schmitz (1990) suggested that this may be due to higher seal densities on shore during warm periods. The unseasonably warm temperatures could have triggered the seals to assemble on shore. The resulting high animal densities would have then favoured pathogen transmission and disease outbreaks.

3 Impact of Climate-Related Environmental Variables on Interactions between Hosts, Pathogens or Vectors

As discussed for several of the examples above, a climate effect on either host, pathogen or vector does not necessarily translate into an alteration of the disease. As infectious disease results from the interaction of the pathogen, the host and – in the case of vector-borne diseases - the vector, it is the climate effect on these interactions which is particularly critical with respect to the consequences of climate change for infectious diseases of wildlife. In the following, we will provide a few examples on how climate variables can impact HP/HPV interactions and what the consequences for the disease outcome are.

Murdock et al. (2012) and Paaijmans et al. (2012) studied how changing environmental temperatures affect vector-borne malaria of rodents. The insect vector is ectothermic, and therefore it is expected that environmental temperature directly affects vector traits like metabolic rate, egg production, biting frequency. Temperature should also affect pathogen development inside the vector. In fact, parasite developmental rates were found to increase linearly with increasing temperature over the 20–26°C temperature range, suggesting that parasite transmission potential should increase with warming temperature. However, the temperature effect on the pathogen development is only one side of the story. There is also a temperature effect on vector competence, i.e., the proportion of infectious mosquitos with sporozoites in their salivary glands. Surprisingly, the percentage of infectious mosquitos decreased with increasing temperature. To understand this effect, we have to take into account the thermal physiology of the mosquitos. Higher temperatures appear to activate the immune capacity of the vector, which opposes the temperature effect on pathogen proliferation in the mosquitors (Murdock et al., 2012). The overall effect of increasing temperature on transmission dynamics of the disease is thus the result of the contrasting temperature effects on pathogen development and vector competence (Mordecai et al., 2012; Paaijmans et al., 2012). A similar example is reported by Oki and Yamamoto (2012) who performed a modelling study to predict the consequences of global warming for dengue viral disease. They found that the probability of dengue epidemics will be overestimated if only the temperature effect on vector reproduction is considered, without taking into account the temperature effect on host population immunity.

Raffel et al. (2013) studied the differential response of the pathogenic chytrid fungus *Batrachochytrium dendrobatidis* and its amphibian hosts to environmental temperature change. The authors hypothesized that parasites will acclimate more quickly to temperature shifts due to their smaller body size and the faster tissue metabolism. The faster acclimation of the parasite implicates that under conditions of unpredictable temperature fluctuations, the parasite will be able to respond, but not the host. This opens a “window of opportunity”, i.e., a period of suboptimal host immune capacity when the parasite may show enhanced growth during periods of suboptimal host immunity. This hypothesis was substantiated by field data from Latin America, where the best climatic predictor of *B. dendrobatidis*-related frog

declines was the month-to-month variation in temperature (Raffel et al., 2013). Under conditions of longer-term, predictable environmental change, also the host will be able to acclimate and perform better in the fight against the pathogen. This expectation could be confirmed by Raffel et al. (2013) in a series of laboratory experiments, which showed that *B. dendrobatidis* grew better in culture at a constant temperature of 25°C than at 15°C, but fungus growth on frogs kept constantly at 25°C was reduced, indicating that under these conditions the host was able to enhance its resistance and thereby could counteract the stimulating effect of temperature on fungus growth (Raffel et al., 2013).

Above we discussed that climate change can influence infectious diseases via altering geographical distribution of host, pathogens or vectors. Importantly, an increase in the geographic range of the disease will only be possible if the distribution responses of hosts, pathogens and vectors to changing climate conditions are similar; otherwise an ecological mismatch will happen (Rosenthal 2009). An interesting modeling study on how changing climate may affect spatial host-parasite dynamics was provided by Pickles et al. (2013). These authors studied possible shifts in the geographic distribution of the protostrongyloid nematode *Parelaphostrongylosis tenuis*, which is commonly found in white-tailed deer in North America, and whose life cycle involves a free-living stage and a gastropod intermediate. The model output indicated that climate change will lead to increased niche breadth for all three species, but at the same time, mismatches in habitat suitability will happen. It appears that the free-living parasite larvae can only survive in a subset of the range of its hosts. Thus, the niche extension of the individual species does not necessarily translate into an extension of the disease distribution. Climate-related variables do not only modify spatial interactions between hosts, pathogens and vectors, but they can also modify temporal interactions by influencing the timing of phenologies of the disease players (Harvell et al., 2002; Roque et al., 2008; Paull et al., 2012).

Climate-induced changes in disease distribution can lead to host or vector switches. An example comes from the recent invasion of the midge-borne bluetongue virus (BTV) into southern Europe (Purse et al., 2005, 2008; Wilson and Mellor, 2008). BTV is a RNA virus of the family *Reoviridae*, which can replicate in all ruminants. It is transmitted by biting midges, primarily by *Culicoides* species. Historically, endemic areas of BTV are North Africa and the Middle East, with occasional brief sporadic invasions into southern Europe (Purse et al., 2005). BTV infections in southern Europe all occurred within the northern range limit of the main vector species *Culicoides imicola.* Temperature and moisture modulate key events in the life cycle of *Culicoides* vectors, and climate change-related alterations of these environmental variables have the potential to (i) increase the range, abundance and seasonal activity of the vector, (2) increase the proportion of competent vector individuals, and (3) increase the development rates of the virus within the vector (Purse et al., 2008). All these processes probably have contributed to the fact that from 1998 onwards, BTV entered into parts of Europe that were clearly north to the traditional distribution (Purse et al., 2005; Wilson and Mellor, 2008), and likely represent a key mechanism in the invasion of BTV in Europe. However, the changes in *C. imicola* biology were not the only mechanism driving the northward spread of bluetongue. A second mechanism is an extension of the vector spectrum: in the newly invaded areas, additional *Culicoides* species such as *C. pulicarus* and *C. obsoletus*, became new vectors of BTV. These species are more cold-tolerant, and have a higher overwintering ability; therefore they can extend the BTV range more northward than *C. imicola* could do (Purse et al. 2008). Thus, the recent invasion of BTV in Europe appears to result both from climate impact on the traditional vector and the switch to new vectors.

Climate effects on host-pathogen interactions can be particularly complex in multi-host systems. MacNab and Barber (2011) studied a multi-host systems composed of the tapeworm *Schistocephalus solidus*, which undergoes a pleroceroid growth phase in its intermediate host, the stickleback *Gasterosteus aculeatus*, but completes its life cycle and reproduces only following transmission to the definitive host, usually a piscivorous bird. The fitness of the parasite is related to the size that the pleroceroids attain in the stickleback host: only after having reached a size of 50 mg or more, the pleroceroids become infective for the avian host. Elevated water temperatures promoted parasite growth in the sticklebacks: at 20°C, with all pleroceroids reached a body size of > 50 mg within eight weeks after infection, whereas at 15°C, none of the pleroceroids reached this size. As a result, the parasites could complete their infection cycle only at 20°C, but not at 15°C. At the same time, the parasite appeared to manipulate the behaviour of the fish host in that fishes harbouring infective pleroceroids

showed significant preferences for warmer temperatures. As warmer water temperatures are typically found at the surface and the margins of lakes, parasitized sticklebacks will prefer those areas, what makes them more susceptible to predation by piscivorous birds. Thus, the influence of water temperature on parasite transmission was mediated through two mechanisms: on the one hand through the growth-promoting effect of elevated water temperature upon the parasite in the fish host, leading to a higher percentage of fish containing infective parasites, and, on the other hand, through a behavioural modification of the fish hosts increasing their susceptibility to predation by the final host, piscivorous birds. While increased feeding rates of the birds on sticklebacks will enhance pleroceroid transmission rates, they also may cause a population decline of sticklebacks due to increased predation pressure. Declining stickleback populations will result in a dietary shift of the birds to other fish prey species, and this would then lead to a decrease of plerocercoid transmission rates. The final outcome of the temperature impact on the parasite-stickleback-piscivorous bird system is thus a balance between changes in host-parasite and host-host relationships (Paull and Johnson, 2011).

Proliferative Kidney Disease (PKD) of salmonids is another case where climate change gets effective not through just one mechanism or one target, but affects several disease processes and interactions (Okamura et al., 2011). This disease is caused by the myxozoan endoparasite *Tetracapsuloides bryosalmonae*. The myxozoan life cycle involves both invertebrate and vertebrate hosts (Fig. 2). Infection of the vertebrate host (salmonid fish) occurs via penetration of the gills by parasite spores, followed by amoeboid sporoplasm invasion of host tissues, particularly the excretory kidney. Spores which mature in the renal tubular luminae and collecting ducts, are released in urine, and finally infect the invertebrate host, the bryozoans. Bryozoans are colonial filter-feeding organisms with a seasonal life-history. Colonies expand prolifically during summer and regress to dormant, asexual overwintering stages (statoblasts) in the autumn. *T. bryosalmonae* development in bryozoans increases in the spring and early summer, leading to a peak of infective spore release which in turn results in (re-) infection of trout. Disease severity shows a clear temperature-dependency: in rivers, where mean water temperatures during summer remain at 12–15°C, parasite spore development in the fish host takes place without causing mortalities (Bettge et al., 2009). The summer-cold rivers are the preferred habitats of brown trout. In contrast, in rivers with summer temperatures of 15°C and higher, PKD can cause losses of up to 90% among young-of-the-year trout (YOY). Interestingly, in Switzerland PKD is found mainly in rivers in lowland regions (Wahli et al., 2008), which experienced an increase of water temperatures over the last decades (Hari et al., 2006) and it is in these regions where a severe decline of brown trout stocks has been observed. (Burkhardt-Holm et al., 2005). There are several mechanisms through which climate change-related environmental variables may influence PKD. On the side of the fish host, water temperatures higher than 15–16°C are increasingly stressful to trout, and thereby may impair trout immunocompetence (Koellner and Kotterba, 2002). This will enhance susceptibility of trout to infection and will compromise trout's ability to handle and survive the infection. In addition, development of the parasite in the fish host may be promoted by increased temperatures. On the side of the invertebrate host, increasing water temperatures may provoke earlier and stronger development of infective spores thereby prolonging the period and intensity of trout exposure to infective spores released by the bryozoa. In addition, increasing water temperatures are likely to favour the geographic distribution of bryozoans, so that the disease may spread to previously PKD-free river stretches or watersheds. Finally, climate change-related alterations of river hydrological regime can influence spring spore

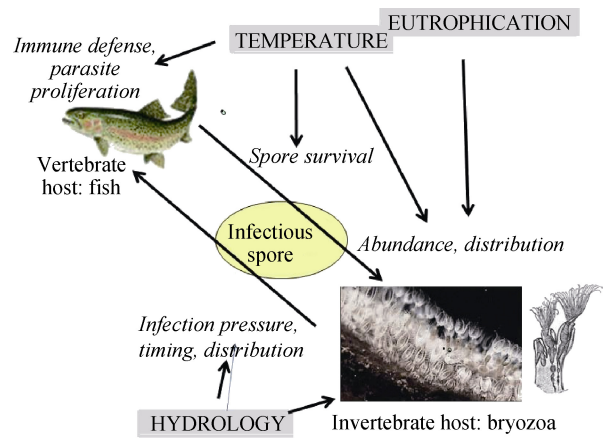

Fig. 2 The infective cycle of of Proliferative Kidney Diseases (PKD)

The etiological agent, the myxozoan Tetracapsuloides bryosalmonae, cycles between invertebrate hosts (bryozoa) and vertebrate host (salmonid fish). Transmission, infection as well as intra-host development of the parasite is modulated by environmental drivers including temperature, hydrology and eutrophication, all of them being influenced directly or indirectly by climate change.

transmission between bryo zoans and fish, as altered water flow and timing of spring flood can modulate spore density and spatial distribution of spores, In addition, the hydrological regime may have an indirect effect in that it can affect the eutrophication status, which influences bryozoan abundance (Okamura et al., 2009). Overall, climate change has the potential to modulate the trout-bryozoan-myxozoan interactions through multiple processes at multiple sites.

4 Impact of Climate Change on Infectious Diseases: The Role of Ecological Networks And Multiple Stressors

The previous chapters exemplified that hosts, pathogens and vectors respond differentially to climate shifts and that this can lead to complex, non-linear effects on their interactions and the disease outcome. Since infectious diseases are inherent components of ecosystems, they cannot be considered in isolation, but have to be understood in their ecological context and as part of ecological networks (Johnson and Paull, 2010). Effects at disparate sites within the ecological community can lead to indirect and cascading effects on hosts, pathogens and vectors. For instance, altered climatic conditions may favour geographic expansion of a HP/HPV system, but the establishment of an endemic life cyle in the new area may be limited through interactions with other species in the new community. Climate-induced alterations of ecological networks can shift infection pathways. For example, prolonged drought in a region of the USA reduced the population of rodent predators what in turn led to an increase of the rodent population, and this again led to an increase of zoonotic hantavirus infections in humans (Rocque et al., 2008). A similar case has been reported for West Nile Virus (WNV) infection. This is a vector-borne disease caused by a *Flavivirus* which is transmitted by mosquitos (mainly from the genus *Culex*) and causes neurological symptoms in birds, especially corvids, as well as in horses and humans. Usually, WNV circulates between birds and mosquitos. Birds are the main virus amplifiers, and most of the time they do not display disease signs. In the eastern United States, WNV outbreaks were found to increase with increasing precipitation, while in the western United States, precipitation and WNV incidence were negatively correlated (Landesman et al., 2007). The contrasting observations may be related to regionally differing consequences of climate change: (i) In the eastern United States climate change is associated with increasing precipitation, which favours larval breeding habitats, and this then leads to an increase of the vector population and, consequently, more pathogen transmission. (ii) In the western United States, climate changes is associated with reduced precipitation, which alters food-web interactions in a way that predator pressure on the mosquitos increases, this leads to a declining vector population and, consequently, less pathogen transmission. While in the first case, the climate impact is mediated through a direct effect on the vector population, in the later case the effect is mediated indirectly via the food web (Landesman et al., 2007).

A controversially discussed hypothesis with respect to the role of ecological networks for infectious diseases is the hypothesis that higher host diversity will reduce disease prevalence. The reasoning behind this hypothesis is that higher diversity reduces the relative abundance of the competent host in relation to the non-competent hosts, and this would result in an elevated percentage of "wasted" transmission events (Johnson et al., 2008). Findings from both modelling and empirical studies appear to support the hypothesis that high host diversity can decrease disease risk (Keesing et al., 2006), but further research is needed to confirm or reject this hypothesis.

Also interactions between diseases may modulate the dynamics of pathogen systems. As described above, in the Arctic, with increasing ambient temperatures, nematode parasites of musk ox complete their life cycles much more quickly than previously (Kutz et al., 2005). This produces much higher worm burdens in the hosts, associated with enhanced morbidity and mortality. At the same time, warming of the Arctic region has allowed species such as elk to expand northwards into areas that overlap with the southern range of musk ox and this leads to the introduction of new pathogens for musk ox, so that this host species is now challenged with an increasing burden of its "traditional" pathogen as well as with new pathogens (Dobson et al., 2003; Kutz et al., 2005).

Finally, climate change is not the only environmental factor of relevance for infectious diseases but they are under the influence of multiple anthropogenic stressors (Marcogliese, 2008; Becker, 2008; Lafferty, 2009). Habitat alteration, invasive species, appearance of pesticide-resistant vector populations, pathogen introduction with travel and global trade, or migration all can impact disease dynamics and it is difficult to sort out the rela-

tive contribution of individual factors. This has been exemplified by Ward and Lafferty (2004) analysing the causes of increased disease incidences in six marine taxa. As the increases occurred in parallel with an increase of global ocean temperatures, climate change was suspected to be the key causative factor, however, warming was responsible only for the increased disease frequency in corals and sea turtles, while different factors explained the increase of diseases in the other taxa. A prominent case for which a climate change-related increase of disease has been postulated as causative factor, are the widespread amphibian declines (Pounds et al., 2006; Rohr and Raffel, 2010). Although changing climate variables are able to increase the disease risk from the pathogenic fungus *B. dendrobatidis* (Raffel et al., 2013), there exists evidence for a role of cumulative effects of multiple stressors in the amphibian decline. For instance, Rohr et al. (2008) observed that the decline of *Rana pipiens* correlated with both agrochemical exposure and parasite infection. One of the agrochemicals had a direct immunosuppressive effect on the amphibians, thereby rendering them more susceptible to parasite infections. At the same time, the agrochemicals favoured snail intermediate hosts of the parasite, thereby increasing the infection pressure to the amphibians. Thus, the stressor combination became effective through a direct interaction on the immune-competence of the amphibians, and an indirect interaction through which the agrochemicals enhanced the parasite infectivity.

5 Conclusions

The discussion above highlights the complexity in the relation between climate change and infectious diseases of wildlife, how difficult it is to predict the influence of climate change on infectious disease dynamics. First, climate change may affect HP/HPV systems in various ways and through different mechanisms. Second, climate change is only one among multiple stressors that impacts HP/HPV systems. Third, diseases involve complex interactions not only between host, pathogens, and vectors but also within their ecological networks, and all these players and interactions may show different response curves to changes in climatic factors. The impact of climate change on infectious diseases is unlikely to arise from a linear effect of elevated temperature on one specific physiological or ecological process in the host-pathogen-vector interaction, but it can involve multiple targets, it can be counteracted by phenotypic acclimation and/or genotypic adaptation, it can depend by the ecological context of the host-pathogen-vector interactions, and it can be modulated by cumulative impacts of other stressors. Given this complexity, it is not surprising that responses of biological systems to climate change are often non-linear, and reactions with abrupt changes are likely to occur (Lafferty, 2009; Rohr et al., 2011). Likewise, it is not surprising that there exist contrasting views on the consequences of climate change on diseases, from “no effect” to “increases” to “decreases”.

In order to advance our understanding of the relation between climate change and disease, research should give more emphasis on the integration of ecological approaches focussing on the ecological mechanisms by which climate factors influence host-pathogen-vector interactions, with biomedical approaches studying the molecular and pathological processes through which climate change alters the balance between the disease players. Also, it is important not to focus too exclusively on temperature and neglecting other climate-related variables – although the existing literature is strongly biased towards the temperature factor. Furthermore, the impact of stressors beyond climate change and possible cumulative effects of stressor combinations definitely need more attention. A possible way forward would be to go beyond the observation of specific diseases and cases, but to head for a more systematic risk factor analyses, comparing different regions characterized by different sets of environmental factors (see Patz et al., 2004). As discussed in Schöning et al. (2013), this need to be accompanied by the use of harmonized methods and approaches in order to make results more comparable, as this would support the discrimination of case-specific versus general mechanisms.

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References

Acevedo-Whitehouse K, Duffus ALJ, 2009. Effects of environmental change on wildlife health. Phil. Trans. R. Soc. B 3364: 3429–3438.

Becker N, 2008. Influence of climate change on mosquito development and mosquito-borne diseases in Europe. Parasitol. Res. 103 (Suppl. 1): S19–S28.

Bettge K, Segner H, Burki R, Schmidt-Posthaus H, Wahli T, 2009. Proliferative kidney disease in rainbow trout: time and temperature-related renal changes of *Tetracapsuloides bryosalmonae* DNA in the kidney. Parasitology 136: 615–625.

Bradley JE, Jackson JA, 2008. Measuring immune system variation to help to understand host-pathogen community dynamics. Parasitology 135: 807–823.

Brown BE, 1997. Coral bleaching: Causes and consequences.

Coral Reefs 16: 129–138.

Brown JD, Swayne DE, Cooper RJ, Burns RE, Stallknecht DE, 2007. Persistence of H5 and H7 avian influenza viruses in water. Avian Dis. 51: 285–289.

Burkhardt-Holm P, Giger W, Güttinger H, Ochsenbein U, Peter A et al., 2005. Where have all the fish gone? Environ. Sci. Techn. 39: 441A–447A.

Cook T, Folli M, Klinck J, Ford S, Miller J, 1998. The relationship between increasing surface water temperature and the northward spread of *Perkinsus marinus* disease epizootics in oysters. Estuarine Coastal Shelf Sci. 40: 587–597.

Daszak P, Cunningham AA, Hyatt AD, 2000. Emerging infectious diseases of wildlife-threats to biodiversity and human health. Science 287: 443–449.

Dobson A, 2009. Climatic variability, global change, immunity, and the dynamics of infectious diseases. Ecology 90: 920–927.

Dobson A, Foufopoulos J, 2001. Emerging infectious pathogens of wildlife. Phil. Trans. R. Soc. Lond. B 356: 1001–1012.

Dobson AP, Kutz S, Pascual M, Winfree R, 2003. Pathogens and parasites in a changing world. In: Lovejoy LJHT ed. Climate Change and Biodiversity: Synergistic Impacts. New Haven: Yale University Press, 33–38.

Ellner SP, Jones LE, Mydlarz LD, Harvell CD, 2007. Within-host ecology in the sea fan *Gorgonia ventalina*: Modelling the spatial immune-dynamics of a coral-pathogen interaction. Am. Nat. 170: 143–161.

Ford SE, Chintala MM, 2006. Northward expansion of a marine parasite: Testing the role of cold adaptation. J. Exp. Mar. Biol. Ecol. 151: 119–133.

Gilman SE, Urban MC, Tewksbury J, Gilchrist GW, Holt RD, 2010. A framework for community interactions under climate change. TREE 25: 325–331.

Hari RE, Livingstone DM, Siber R, Burkhardt-Holm P, Güttinger H, 2006. Consequences of climatic change for water temperature and brown trout populations in Alpine rivers and streams. Global Change Biology 12: 10–26.

Harvell D, Mitchell CE, Ward JR, Altizer S, Dobson AP et al., 2002. Climate warming and disease risks for terresrtrial and marine biota. Science 296: 2158–2162.

Harvell D, Altizer S, Cattadori IM, Harrington L, Weil E, 2009. Climate change and wildlife disease: When does the host matter the most ? Ecology 90: 912–920.

Hoberg EP, Polley L, Gunn A, Nishi JS, 1995. *Umingmakstrongylus pallikuukensis* gen. nov. et sp. nov. (Nematoda: Protostrongylidae) from muskoxen *Ovibos moschafus* in the central Artic, with comments on biology and biogeography. Can. J. Zool. 73: 2266–2282.

Hofer H, East ML, 2010. Impact of global climate change on wildlife hosts and their pathogens. Nova Acta Leopoldina NF 111: 105–112.

IPCC, 2007. Intergovernmental Panel on Climate Change. 4th Assessment Report. Cambridge: Cambridge University Press,

Johnson PTJ, Paull SH, 2010. The ecology and emergence of diseases in fresh waters. Freshwater Biology 56. 638–657.

Johnson PTJ, Hartson RB, Larson DJ, Sutherland DR, 2008. Diversity and disease: Community structure drives parasite transmission and host fitness. Ecol. Lett. 11: 1017–1026.

Keesing F, Holt RD, Otfeld RS, 2006. Effects of species diversity on disease risk. Ecol. Lett. 9: 485–498.

Kimes NE, Grim CJ, Johnson RJ, Hasan NA, Tall BD et al., 2012. Temperature regulation of virulence factors in the pathogen *Vibrio corallilyticus*. ISME J. 6: 835–846.

Koellner B, Kotterba G, 2002. Temperature dependent activation of leucocyte populations of rainbow trout *Oncorhynchus mykiss* after intraperitoneal immunisation with *Aeromonas salmonicida.* Fish Shellfish Immunol. 12: 35–48

Kushmaro A, Rosenberg E, Fine M, Loya Y, 1997. Bleaching of the coral *Oculina patagonic*a by Vibrio AK-1. Mar. Ecol. Progr. Ser. 147: 159–165.

Kutz S, Hoberg EP, Polley L, Jenkins RE, 2005. Global warming is changing the dynamics of Artic host-paraiste systems. Proc. R. Soc. B 272: 2571–2576.

Lafferty KD, 2009. The ecology of climate change and infectious diseases. Ecology 90: 888–900.

Landesman WJ, Allan BF, Langerhans RB, Knight TM, Chase JM, 2007. Inter-annual associations between precipitation and human incidence of West Nile Virus in the United States. Vector Borne Zoon. Dis. 7: 337–343.

Lavigne DM, Schmitz OJ, 1990. Global warming and increasing population densities: A prescription for seal plagues. Mar. Poll. Bull. 21: 280–284.

MacNab V, Barber I, 2011. Some (worms) like it hot: Fish parasites grow faster in warmer water, and later host thermal preferences. Global Change Biology 18: 1540–1548

Marcogliese DJ, 2008. The impact of climate change on the parasites and infectious disease of aquatic animals. Rev. Sci. Tech. 27: 467–484.

Martin V, Chevalier V, Ceccato P, Anyamba A, DeSimone L et al., 2008. The impact of climate change on the epidemiology and control of Rift valley Fever. Rev. Sci. Tech. 27: 413–426.

Martin LB, Hopkins WA, Mydlarz LD, Rohr JR, 2010. The effects of anthropogenic global changes on immune functions and disease resistance. Ann. N.Y. Acad. Sci. 1195: 129–148.

McMichael AJ, Campbell-Lendum DH, Corvalan CF, Ebi KL, Githeko AK et al., 2003. Climate Change and Human Health. Risks and Responses. WHO Report. Geneve: WHO.

Mordecai EA, Paaijmans KP, Johnson LR, Balzer C, Ben-Horin T et al., 2012. Optimal temperature for malaria transmission is dramatically lower than previously predicted. Ecol. Lett. 16: 22–30.

Murdock CC, Paaijmans KP, Cox-Foster D, Read AF, Thomas MB, 2012. Rethinking vector immunology: The role of environmental temperature in shaping resistance. Nature Rev. Microbiol. 10: 869–876.

Mydlartz LD, McGinty ES, Harvell CD, 2010. What are the physiologcial and immunological responses of coral to climate warming and disease ? J. Exp. Biol 213: 934–945.

Okamura B, Hartikainen H, Schmidt-Posthaus H, Wahli T, 2011. Life cycle complexity, environmental change and the emerging status of salmonid proliferative kidney disease. Freshwater Biol. 56: 735–753.

Oki M, Yamamoto T, 2012. Climate change, population immunity, and hyperendemicity in the transmission threshold of dengue. PLoS One 7: e48258

Paaijmans KP, Wandago MO, Githeko AK, Takhen W, 2007. Unexpected high losses of *Anopheles gambiae* larvae due to rainfall. PLoS One e1146.

Paaiijmans KP, Blanfrod S, Chan BHK, Thomas MB, 2012.

Warmer temperatures reduce the vectorial capacity of malaria mosquitos. Biol. Lett. 8: 465–468.

Patz JA, Daszak P, Tabor GM, Aguirre A, Pearl M et al., 2004. Unhealthy landscapes: Policy recommendations on land use change and infectious disease emergence. Environ. Health Persp. 112: 1092–1098.

Paull SH, Johnson PTJ, 2011. High temperature enhances host pathology in a snail-trematode system: Possible consequences of climate change for the emergence of disease. Freshwater Biol. 56: 767–778.

Paull SH, Lafonte BE, Johnson PR, 2012. Temperature-driven shifts in host-parasite interaction drive nonlinear changes in disease risk. Global Change Biology 18:3558–3567.

Pascual M, Bouma MJ, 2009. Do rising temperatures matter? Ecology 90: 906–912.

Pfeffer M, Dobler G, 2010. Impact of climate change on Rift Valley Fever virus infections. Acta Leopoldina NF 111: 99–104.

Pickles RS, Thornton D, Feldman R, Marques A, Murray DL, 2013. Predicting shifts in parasite distribution with climate change: A multi-trophic level approach. Global Change Biology, in press.

Pounds JA, Bustamante MR, Coloma LA, Consuegra JA, Fodgen MLP et al., 2006. Widespread amphibian extinctions from epidemic disease driven by global warming. Nature 439: 161–167.

Purse BV, Mellor PS, Rogers DJ, Samuel AR, Mertens PPC et al., 2005. Climate change and the recent emergence of bluetongue in Europe. Nature Rev. Microbiol. 3:171–182.

Purse BV, Brown HE, Harrup L, Mertens PPC, Rogers DJ, 2008. Invasion of bluetongue and other orbivirus infections into Europe: the role of biological and climatic processes. Rev. Sci. Tech. 27: 427–442.

Raffel TR, Romansic JM, Halsteadt NT, McMahon TA, Venesky MD et al., 2013. Disease and thermal variation in a more variable and unpredictable climate. Nature Climate Change 3: 146–151.

Randolph SE, 2009. Perspectives on climate change impacts on infectious diseases. Ecology 90: 927–931.

Rohr JR, Raffle TR, 2010. Linking global climate and temperature variability to widespread amphibian declines putatively caused by disease. PNAS 107: 8269–8274.

Rohr JR, Schotthoefer AM, Raffel TR, Carrick HJ, Halstaedt N et al., 2008. Agrochemcials increase trematode infections in a declining amphibian species. Nature 455: 1235–1239.

Rohr JR, Dobson AP, Johnson PTJ, Kilpatrick AM, Paull SH et al., 2011. Frontiers in climate change-disease research. TREE 26: 270–277.

Roque S de la, Rioux JA, Slingenbergh J. 2008. Climate change: Effects on animal disease systems and implications for surveillance and control. Rev. Sci. Tech. 27: 339–354.

Rosenberg E, Ben-Haim Y, 2002. Microbial diseases of corals and global warming. Environ. Microbiol. 4: 318–326.

Rosenthal J, 2009. Climate change and the geographic distribution of infectious diseases. EcoHealth 6: 489–495.

Scheibling RE, Hennigar AW, 1997. Recurrent outbreaks of disease in sea urchins *Stronggylocentrotus droebachiensis* in Nova Sciotia: Evidnece for a link with large-scale meteorologic and oceanographic events. Mar. Ecol. Progr. Ser. 152:155–162.

Schöning JM, Cerny N, Prohaska S, Wittenbrink MM, Smith NH et al., 2013. Surveillance of bovine tuberculosis and risk estimation of a future reservoir formation in wildlife in Switzerland and Liechtenstein. PLoS One e54253.

Seppälä O, Jokela J, 2010. Immune defense under extreme ambient temperature. Biol. Lett. 7: 119–122.

Sorci G, Cornet S, Faivre B, 2013. Immunity and the emergence of virulent pathogens. Infect. Genet. Evol. 16: 441–446.

Trenberth KE, Jones PD, Ambenje P, Bojariu R, Easterling D et al., 2007. Observations: Surface and atmopsheric climate change. In: Solomon S, Quin D, Manning Z, Chen M, Marquis KB et al. ed. Climate Change 2007: The Physical Science Basis. Contribution of Working Group I to the 4th Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge: Cambridge University Press.

Turrell MJ, Linthicum KJ, Patrican LA, Davies FG, Kairo A et al., 2008. Vector competence of selected African mosquito (Diptera: Culicidae) species for Rift Valley Fever Virus. J. Med. Entomol. 45: 102–108.

Wahli T, Bernet D, Segner H, Schmidt-Posthaus H, 2008. Role of altitude and water temperature as regulating factors for the geographical distribution of *Tetracapsuloides bryosalmonae* infected fishes in Switzerland. J. Fish Biol. 73: 2184–2197.

Ward JR, Lafferty KD, 2004. The elusive baseline of marine disease: Are diseases in ocean ecosystems increasing ? PloS Biology 2: 524–547.

WilsonA, Mellor P, 2008. Bluetongue in Europe: Vectors, epidemiology and climate change. Parasitol. Res. 103 (suppl. 1): S69–S77.