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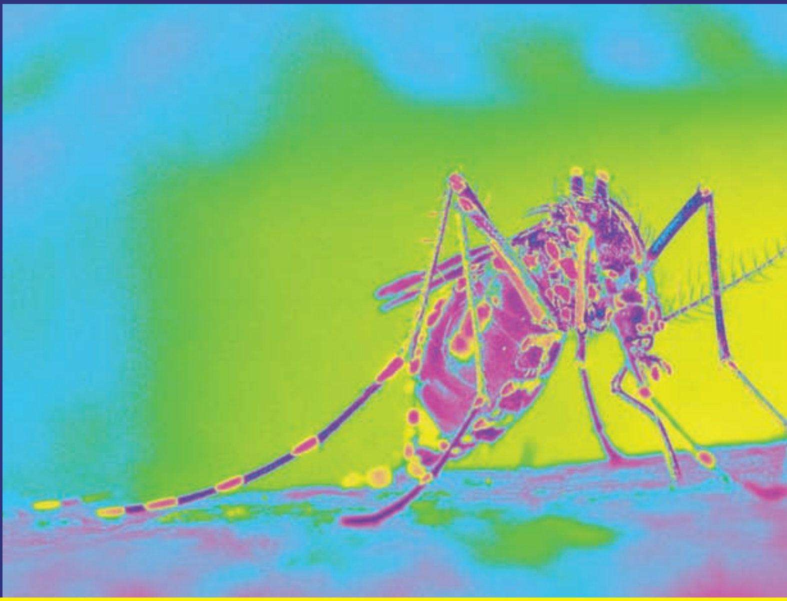
NEUE FOLGE, BAND 111, NUMMER 381

Climate Change and Infectious Diseases

Bärbel Friedrich, Jörg Hacker, Seyed E. Hasnain,
Thomas C. Mettenleiter, and Jens Schell (Eds.)



Deutsche Akademie der Naturforscher Leopoldina –
Nationale Akademie der Wissenschaften, Halle (Saale) 2010
Wissenschaftliche Verlagsgesellschaft mbH Stuttgart

Climate Change and Infectious Diseases

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Climate Change and Infectious Diseases

International Conference

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in Collaboration with
Indian National Science Academy,
Alfried Krupp Wissenschaftskolleg Greifswald, and
Friedrich-Loeffler-Institut, Federal Research Institute
for Animal Health

Alfried Krupp Wissenschaftskolleg Greifswald
May 26 to 28, 2009

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With 22 Figures and 12 Tables

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**Deutsche Akademie der Naturforscher Leopoldina –
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Nova Acta Leopoldina NF *111*, Nr. 381, 7–8 (2010)

Preface

There is no doubt that climatic changes occur at a global level which could have a serious impact on infectious diseases in humans and animals. Global warming may directly influence the distribution of arthropod and rodent vectors expanding or shifting their habitats into new areas. Extreme weather conditions, in particular the frequency and duration of rainfalls, alter seasonal patterns of emergence and expansion of diseases. Basically every infectious disease with a seasonal pattern can be influenced by changes in climate. However, direct proof for the influence of climate change on a regional, national, supranational or global level on the emergence of new or frequency of established infections is difficult to obtain.

This symposium that was jointly organized by the German Academy of Sciences Leopoldina together with the Indian National Science Academy, the *Alfried Krupp Wissenschaftskolleg* Greifswald and the *Friedrich-Loeffler-Institut*, Isle of Riems, brought together experts from climate research, biology and infectious diseases who presented data on extent and speed of climate change and its impact on vector populations or the spread of infectious diseases and their effect on human and animal health. In conclusion, the participants agreed that it is too early to identify or predict concrete consequences. The importance of long-term surveillance analyses of the different vector and reservoir populations was pointed out. However, such analyses have to be supported continuously in order to detect dynamic alterations in longer time frames.

The scientific program was completed by a visit of the *Friedrich-Loeffler-Institut* on the Isle of Riems, which is the world oldest research facility dedicated to virus research. Currently a new research facility including high containment laboratories and animal rooms up to biosafety level 4 is under construction. This new facility with an investment of 260 Mio. € will allow research on pathogens in their natural hosts that were up to now classified as ‘exotic’. Among the 120 participants of the symposium were 30 young researchers from the University of Greifswald and the *Friedrich-Loeffler-Institut*. A group of Indian students in Greifswald had the unique opportunity to meet Prof. Hasnain, the president on the Indian National Science Academy.

The organizers would like to thank the German Research Foundation (DFG) and the Alfried Krupp von Bohlen und Halbach-Stiftung for support of the symposium.

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Climate Change: Past, Present, Future

Nova Acta Leopoldina NF *111*, Nr. 381, 11–14 (2010)

Past Climate Change: Its Facts and Mysteries

Heinz Wanner (Bern, Switzerland)

With 2 Figures and 1 Table

Abstract

One of the important preconditions for understanding our future climate is a thorough diagnosis of the important processes which determined the climate of the past. In this contribution we focus on climate variability during the last 2.7 million years, that means the time period of the last series of glacial-interglacial cycles.

Zusammenfassung

Eine der entscheidenden Voraussetzungen für das Verständnis unseres zukünftigen Klimas ist eine gründliche Diagnose der bedeutenden Prozesse, die das Klima in der Vergangenheit bestimmten. In diesem Beitrag konzentrieren wir uns auf die Klimavariabilität während der letzten 2,7 Millionen Jahre, d. h. auf die Zeitperiode der letzten Serie des Glazial-Interglazial-Zyklus.

One of the important preconditions for understanding our future climate is a thorough diagnosis of the important processes which determined the climate of the past. According to Table 1 climate change and variability are determined by three groups of driving factors. Natural and anthropogenic forcings modulate the energy balance of our globe in space and time. Together with the natural (internal) variability of the climate system, caused by the complex physical and chemical interactions and feedbacks between the important subsystems ocean, atmosphere, cryosphere, land and vegetation, they form the driving factors of the observed climate.

In this contribution we focus on climate variability during the last 2.7 million years, that means the time period of the last series of glacial-interglacial cycles. We therefore do not discuss extremely long-term climate changes, for example caused by increasing solar radiation or by decreasing CO_2 concentrations during geological timescales, or by continental drift. Based on the analysis of different parameters in a 645 kyr long sequence of an Antarctic ice core, Figure 1 shows the quasi-cyclic changes between glacial and interglacial periods. Interestingly, there is evidence for longer interglacial periods between 430 and 645 kyr, but these were apparently colder than the actual interglacial, the Holocene (*IPCC* 2007). The glacial-interglacial changes were mostly driven by orbital forcing (factor 1.2 in Tab. 1), that means by changes of the precession of the equinox (periodicity: 19, 23 kyr), by the obliquity of the earth axis (periodicity: 41 kyr) and by the changing Earth-Sun distance (periodicity: 410, 95 kyr). During the last 400 kyr roughly the 95 kyr cycle dominated. Figure 1 shows that several parameters representing a temperature proxy run parallel to the CO_2 curve. Nevertheless, the explanation of glacial-interglacial CO_2 variations remains a difficult attribution problem. It appears likely that a range of mechanisms, which are possibly located in the ocean, have acted in concert (*IPCC* 2007). During both glacials and interglacials, abrupt changes between warm and cold states were observed. Best known are the Dansgaard-Oeschger (D-O) and the Heinrich events. The D-O events were likely caused by changes in the ocean thermohaline circulation. The Heinrich events are thought to have been caused by ice sheet instability and iceberg discharge with freshwater forcing in the North Atlantic Ocean (*IPCC* 2007).

Tab. 1 Driving factors of climate variability and change

Driving factor	Time scale / influence on energy balance near the ground (+/–)
1. Natural forcing	
1.1 Continental drift	10^6 to 10^7 years
1.2 Fluctuation in the Earth's orbital elements	10^4 to 10^5 years
1.3 Fluctuation in solar activity	cycles (11, 90, 210, etc. years)
1.4 Explosive volcanic eruptions	irregular (influence lasts for 2 – 3 years)
1.5 Cosmogenic nuclides	10 years
2. Anthropogenic forcing	
2.1 Greenhouse effect	+
2.2 Aerosol concentration	–
2.3 Thinning of stratospheric ozone layer and increase on boundary layer ozone concentration	+ / –
2.4 Land use changes (urbanisation, deforestation, desertification, ect.)	complex (+/–)
3. Natural variability (incl. internal modes)	
3.1 ENSO (El Niño Southern Oscillation)	3 to 7 years
3.2 NAO (North Atlantic Oscillation)	variable (2.5, 8 years)
3.3 Natural (stochastic) variability	variable

The warm period of the recent interglacial, the Holocene, started about 12 kyr ago. Due to the above mentioned orbital forcing, the solar insolation in the Northern Hemisphere (NH) decreased after about 10 kyr before present (BP). Therefore, a summer cooling was observed in the NH, and a progressive southward shift of the NH summer position of the Intertropical Convergence Zone (ITCZ), roughly called the "tropical weather systems", took place. This shift was accompanied by a pronounced weakening of the monsoon systems in Africa and Asia and increasing dryness and desertification on both continents (Wanner et al. 2008).

This slow, millennial scale change was overlapped by shorter, decadal to multi-century cooling events. The first events were likely triggered by the orbital forcing, causing freshwater fluxes from the melting ice caps in the NH and rapidly slowing the Atlantic thermohaline circulation. During the last 3000 years three coolings with remarkable glacier advances, mainly in the NH, were observed: The Iron Age Cold Epoch around 2800 yr BP, the Migration Period Cooling between about AD 450 and 800, and the Little Ice Age (LIA) between AD 1350 and 1860. The temperature reconstructions in Figure 2 show the oscillation between the temperate Medieval Climate Anomaly (MCA), the cool LIA and, finally, the Modern Warm Period

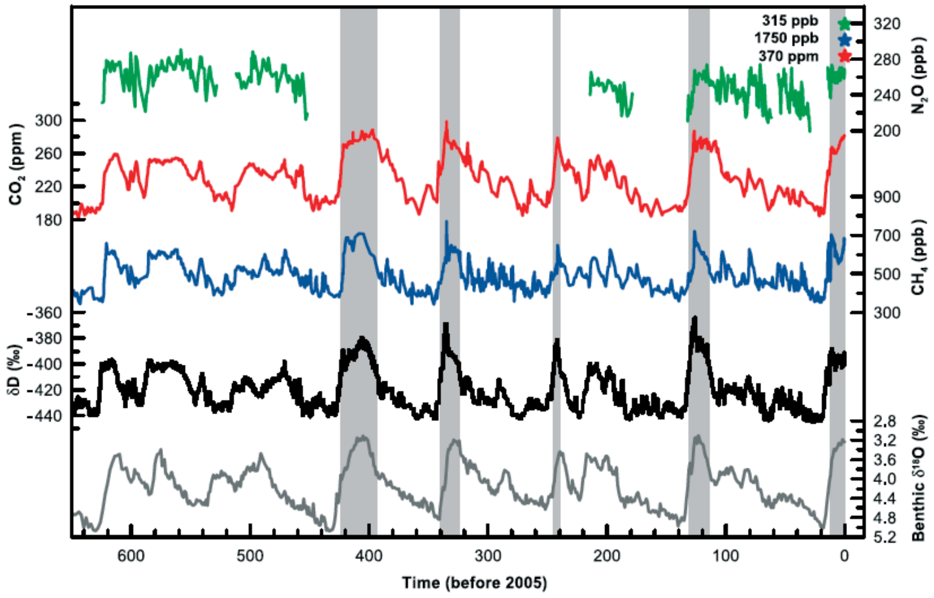

Fig. 1 Variation of nitrous oxide (NO_2), carbon dioxide (CO_2), Methane (CH_4), deuterium (δD) and the isotope $\delta^{18}O$ during the last 645 kyr, derived from air trapped in ice cores from Antarctica and from recent atmospheric measurements (*IPCC* 2007).

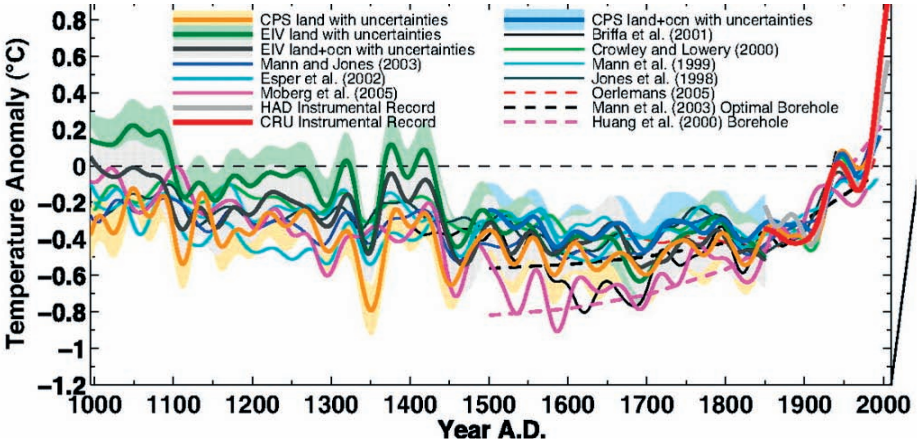

Fig. 2 Different reconstructions of the Northern Hemisphere land or land plus ocean temperature during the last 1000 years, representing the transition from the Medieval Climate Anomaly (MCA) to the Little Ice Age (LIA), and finally to the Modern Warm Period (MWP; from Mann et al. 2008); this paper also references the original papers of all represented reconstructions).

(MWP). The IPCC 4AR (2007) states that the temperature increase of the MWP since the mid-20th century is very likely due to the observed greenhouse gas concentration. The situation is not as clear for the above mentioned rapid cooling events. Probably the combination of the low NH solar irradiance (orbital forcing) with solar irradiance minima and tropical volcanic eruptions played a major role and possibly caused remarkable changes in the ocean thermohaline circulation (Wanner et al. 2008). At least some of the negative peaks in Figure 2 can likely be attributed to such events. On a regional scale the influence of internal variability through feedbacks between the different components of the climate system plays an important role.

According to the existing model simulations based on the natural forcing the Holocene interglacial will only end after about 30 kyr. There remains the question of how the anthropogenic effects will interact with these natural forcings.

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Predictions, Projections, and Perspectives of Climate Change

Manfred STOCK (Potsdam)

With 5 Figures and 1 Table

Abstract

Climate change has already exhibited many changes in physical and biological systems. Since 1970 an increasing number of observations has correlated with rising temperature due to anthropogenic greenhouse gases. There are two alternative pathways for future development: Confining global warming to 2° above preindustrial level offers the chance to handle severe impacts by adaptation. Without emission reductions, possible catastrophic impacts with uncontrollable consequences will have to be faced. According to the future path chosen, millions of people will be at risk due to water shortage and health impacts. Climate change is not a matter of prognosis but of good or bad management.

Zusammenfassung

Der Klimawandel führt bereits zu vielen Veränderungen physikalischer und biologischer Systeme. Etwa seit 1970 häufen sich die Beobachtungen und sie korrelieren mit der Temperaturerhöhung durch anthropogene Emissionen von Treibhausgasen. Für die zukünftige Entwicklung sind zwei alternative Zukunftspfade erkennbar. Bei Begrenzung der globalen Erwärmung auf 2° über dem vorindustriellen Niveau können Auswirkungen durch Anpassung beherrscht werden. Ohne Emissionsbegrenzung drohen hingegen unbeherrschbare und möglicherweise katastrophale Auswirkungen. Je nach Zukunftspfad sind unterschiedlich viele Millionen Menschen durch Wasserknappheit und Gesundheitsgefahren bedroht, Klimawandel ist daher weniger eine Frage von Prognosen als von gutem oder schlechtem Management.

Climate change has already speeded up, showing more and more consequences with a vengeance. What do we know about the probable future progress, and what kind of impacts and consequences will we have to face?

1. Predictions Are Very Difficult, Especially about the Future

In public, climate is often confused with weather, mainly because both are dealing with parameters of identical names, like temperature or precipitation. But these parameters have different meanings in both regimes. Weather takes place in the lower atmosphere, whereas climate is a state of the entire Earth system, depending on many internal and external processes. Climate defines the boundary conditions for all weather phenomena, their means, the ups and downs, and the extremes. The ups and downs of the weather are not predictable in principle. A weather forecast starting from an initial state of the weather becomes more and more uncertain the further it reaches into the future. Small uncertainties in the initial conditions grow up to an overall uncertainty. In principle this is different for climate, but in reality other circumstances prevent precise predictions.

A prediction is a statement that a particular event is going to occur in the future in more certain terms than a forecast. It is based on reasoning from observations via a scientific hypothesis to a plausible prediction. The following example concerning health is attributed to Ignaz SEMMELWEIS. He observed that women giving birth in a hospital in one building died, but in another building survived. The surviving women were attended by midwives, the others by student doctors. He proposed that a factor in the deaths must be a specific difference between the midwives and the doctors. This led to the hypothesis that corpses which the student doctors had dissected must be part of the factor. The resulting prediction: if the doctors were to wash their hands, then the factor would be avoided. This was successfully validated. After the doctors were instructed to wash their hands, all women survived.

In the case of climate change such a straight reasoning is not feasible mainly because of unpredictable future human behavior.

2. Observations and Scientific Knowledge

The possible future evolution of climate needs a fundamental scientific understanding of external radiative forcing from the solar radiation, as well as of the internal radiatively active processes by greenhouse gases, aerosols, dust, soot, and clouds. The atmospheric concentrations of those species depend on both anthropogenic emissions and the climate response to the cycles of carbon, water, and sulfur. Figure 1 shows a comparison of observations (black line) and simulations of global warming over land surface between 1906 and 2005 (*IPCC* 2007). The results of simulations with different climate models are shown with anthropogenic greenhouse gas emissions and without, including only natural forcing, mainly the variation of the solar radiation. From the early 1970s onwards, global warming can only be understood if we take the anthropogenic greenhouse gas emissions into account. In addition to the observed temperature changes since 1970, a lot of other changes in physical and biological systems are observed with significant connections to climate change (*IPCC* 2007).

In the two decades from the first IPCC report in 1990 to the fourth in 2007, our scientific knowledge about the climate system has increased tremendously. Investigating and understanding various natural changes of climate in the Earth's past has helped a lot. Figure 2 shows a rough sketch of present scientific knowledge about variation of CO_2 concentration in the atmosphere over the last 100 million years and what we might expect in the next 300 years.

After a long era of alternating warm and glacial periods, the so-called Holocene began about 10,000 years ago. Future evolutions of the concentrations of CO_2 and other relevant substances are projections of different scenarios of human development on the globe. These scenarios involve different assumptions concerning energy and land use, growth and structure of economy, and growth of population. The scenarios span emission projections from reduction through stabilization to runaway cases; nobody can predict which scenario will happen. But possibly concentrations of CO_2 will reach those of many million of years ago – an experiment of unknown outcome.

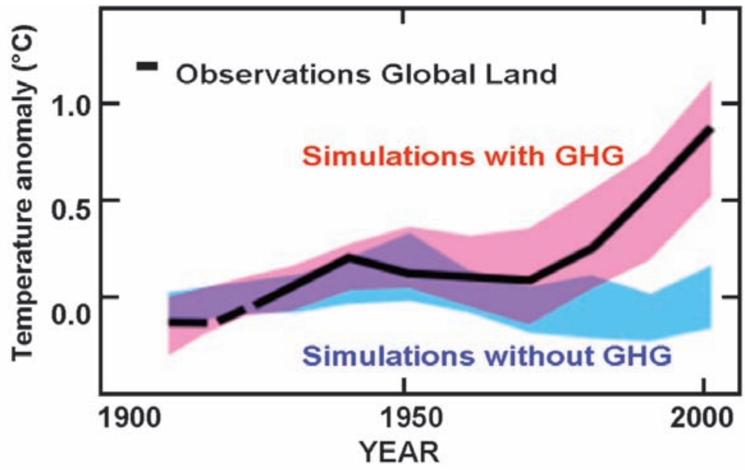

Fig. 1 Comparison of observations and simulations of global warming over land surface; black line: observations 1906–2005. Simulations with climate models, red band: with greenhouse gas emissions (GHG), and blue band: without, taking only natural forcing into account (*IPCC* 2007).

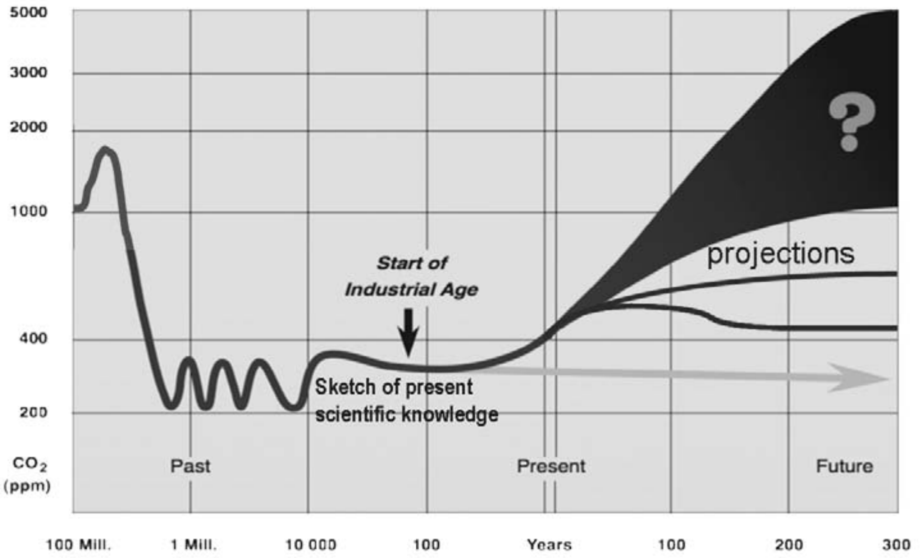

Fig. 2 Sketch of present scientific knowledge about past and possible future concentrations of carbon dioxide (CO_2) in the atmosphere (based on scientific data from *IPCC* 2007, WG1)

3. Scenarios and Projections of Future Climate

It is obvious that the present climate change – in contrast to those in Earth's history – depends highly on human decisions, as do its consequences. Therefore, it is preferable to speak of scenarios and projections instead of predictions. Figure 3 shows a diagram of the evolution of global warming between 1900 and 2100 (*IPCC* 2007). Until 2000, the averaged temperature has risen by +0.8°. At the end of the century global warming could spread from +2° for the B1 scenario up to +6° for A1FI, including ranges of uncertainty. The 2° target of the EU and a risk assessment box has been added to the diagram. What is the reason for avoiding a global warming of more than 2° above the preindustrial level? It is the realization that +1.5° is already unavoidable, whereas above +2.5° high risks will have to be avoided.

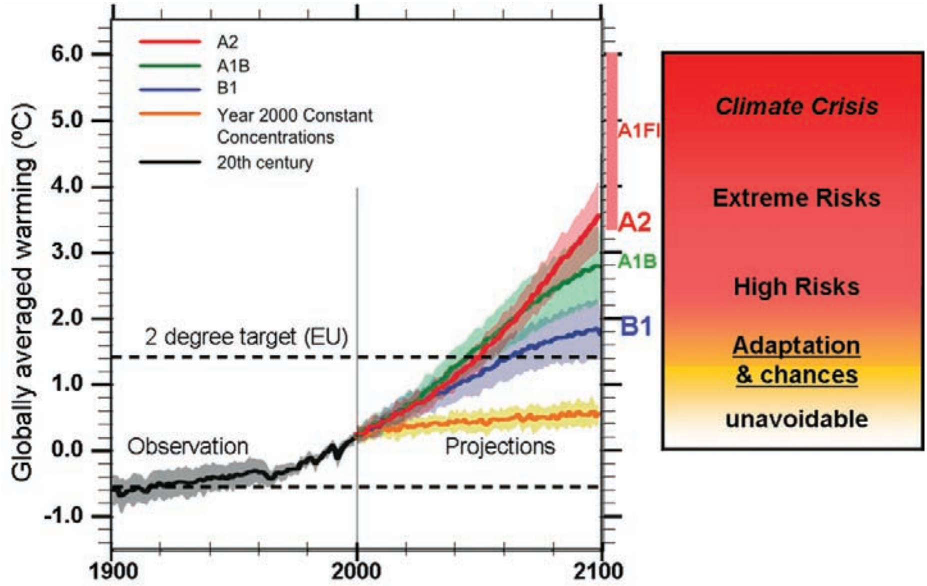

Fig. 3 Observation of global warming between 1900 and 2000 and the future projections until 2100 according to different emission scenarios B1, A1B, and A2 (diagram from *IPCC* 2007). The uppermost red uncertainty bar added to the diagram stands for the assumed worst case scenario A1FI. The 2° target of the EU is added as well as a risk assessment sketch on the right based on an evaluation of the impact assessments in the IPCC report.

The box added at the right side of the IPCC diagram links global warming to expected regimes of risks. Up to the 2° guardrail, global warming offers chances for those who can adapt. With increasing temperature, chances and possibilities to adapt will shrink whereas risks will rise rapidly. The future development of climate depends on the projections of greenhouse gas emissions and the resulting global warming, with two extreme alternative paths into future: (*i*) the 2° guardrail of global warming, allowing adaptation, and (*ii*) a "climate crisis" with probably catastrophic consequences.

4. Perspectives and Possible Consequences

Human beings are directly exposed to climate change through changing weather patterns (temperature, precipitation, sea-level rise and more frequent extreme events) and indirectly through changes in water, air and food quality and changes in ecosystems, agriculture, industry and settlements and the economy. At present, the effects are relatively small, but the future projections show progressive increase in all countries and regions.

How critical global warming could be with respect to possible resulting impacts of climate change and the number of people at risk has been assessed by M. Parry and coworkers in 2001. Figure 4 shows results for several risks concerning malaria, water shortage, famines, and coastal flooding.

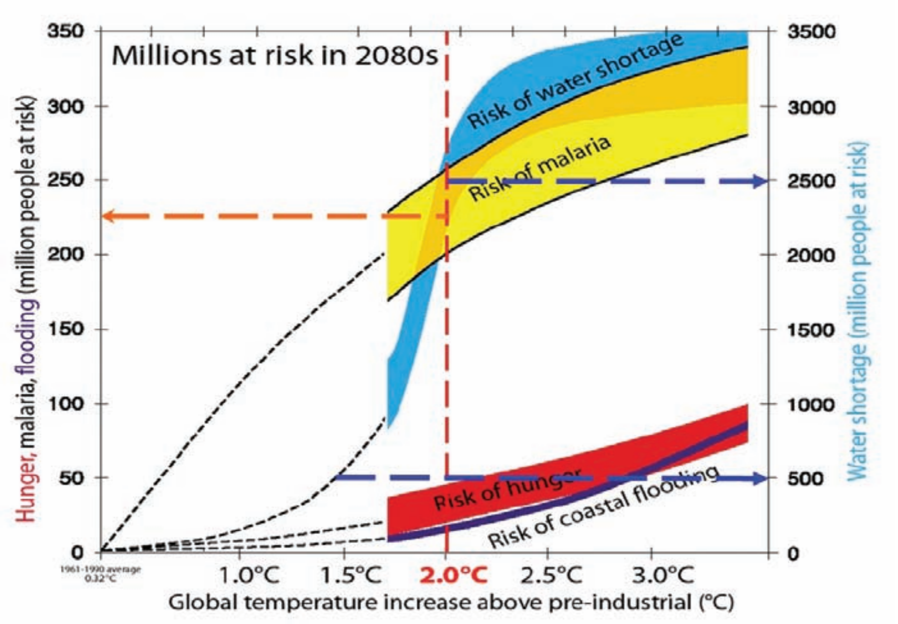

Fig. 4 Assessment of increasing risks for millions of people with global warming at 2080. Results for millions of people at risk due to malaria, hunger, and coastal flooding (left axis), and due to water shortage (right axis) are included. For the 2° guardrail of the EU the risk of malaria has risen for about 250 million people whereas the risk of water shortage lies 10 times higher at 2.5 billion people. Note that there is a highly nonlinear increase from a risk of water shortage for 500 million people at 1.5° (Parry et al. 2001).

At the 2° guardrail of the EU the risk of malaria has risen up to about 250 million people at risk. Remarkably, the risk of water shortage has risen 10 times higher to 2.5 billion people comprising a highly nonlinear increase from a risk for 500 million people at 1.5° (Parry et al. 2001). Water shortage is often associated with insanitary water conditions and therefore associated with an impact of climate change on health, e.g. through diarrheal disease.

Systematic reviews of empirical studies provide the best evidence for the relationship between health and weather or climate factors, but such formal reviews are rare. Chapter 8 of the Working Group II report of IPCC 2007 comprises the current state of knowledge of the associations between weather/climate factors and health outcomes for populations concerned. Health impacts, either direct or through multiple pathways, were assessed. Figure 5 shows in a simplified way the pathways by which health can be affected by climate change, and also shows the concurrent direct-acting and modifying (conditioning) influences of environmental, social and health system factors, which open possibilities for adaptation. Direct exposure to climate change comprises changing weather patterns (temperature, precipitation, sea-level rise and more frequent extreme events). Indirect exposure comprises changes in water, air and food quality, vector ecology and changes in ecosystems, agriculture, industry and settlements. Another indirect exposure could be caused by social and economic disruption.

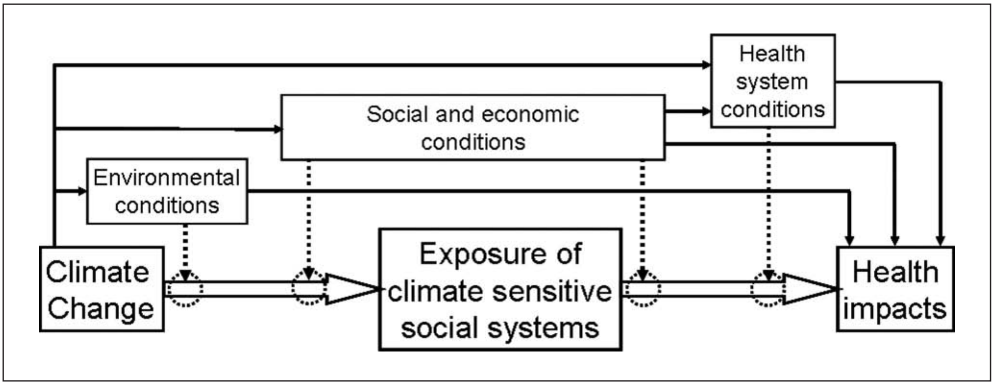

Fig. 5 Scheme of climate change impacts on health in exposed climate sensitive social systems (based on *IPCC* 2007, WG2, Fig. 8.1). The resulting health impacts are modified by environmental, social and economic as well as health system conditions (dashed lines), a possibility for adaptation.

The "Global Burden of Disease" study of the World Health Organization is a regional and global comparative risk assessment to quantify the impacts due to a range of risk factors, including climate change. In addition, it estimates the benefit of interventions to remove or reduce these risk factors. The impacts are quantified as deaths and DALYs (Disability-Adjusted Life Years). For 2000, climate change is estimated to have caused the loss of over 150,000 lives and 5,500,000 DALYs (0.3 % of deaths and 0.4 % of DALYs, respectively) (Campbell-Lendrum et al. 2003). The assessment also addresses how much of the future burden of climate change can be avoided by stabilizing greenhouse gas emissions. The health outcomes as listed in Table 1 are based on known sensitivity to climate variation, predicted future importance, and availability of quantitative global models (or feasibility of constructing them). Limited adjustments for adaptation were included in the estimates of the outcomes of:

- direct cardiovascular impacts of heat and cold;
- episodes of diarrheal disease;
- cases of *Plasmodium falciparum* malaria;
- fatal accidental injuries in coastal floods and inland floods/landslides;
- non-availability of recommended daily calorie intake (as an indicator for the prevalence of malnutrition).

Tab. 1 Health outcomes considered in Global Burden of Disease (Campbell-Lendrum et al. 2003)

Class	Mechanism	Outcome
Direct impacts of heat and cold:	Thermal stress due to higher temperatures.	Cardiovascular disease deaths
Water-washed, water-borne, and food-borne disease:	Higher temperatures encourage proliferation of bacterial pathogens.	Diarrhoea episodes
Vector-borne disease:	Rainfall and temperature affect vector abundance. Temperature affects incubation period of parasite in mosquito.	Malaria cases
	Temperature affects incubation period of virus in mosquito.	Dengue cases
Natural disasters:	Increased floods and landslides due to sea level rise and extreme rainfall.	Deaths due to unintentional injuries; other unintentional injuries (nonfatal)
Risk of malnutrition	Changes in food production and per capita food availability	Non-availability of recommended daily calorie intake

The projected relative risks attributable to climate change in 2030 vary with health outcome and region, and are largely negative, with most of the projected disease burden being due to increases in diarrheal disease and malnutrition, primarily in low-income populations already experiencing a large burden of disease (Campbell-Lendrum et al. 2003). Absolute disease burdens depend on assumptions of population growth, future baseline disease incidence and the extent of adaptation. Climate change is projected to increase, for instance, the burden of diarrheal diseases in low-income regions by approximately 2 to 5 % in 2020. Countries with an annual GDP per capita of US$ 6,000 or more are assumed to have no additional risk of diarrhea.

5. Conclusions

Climate change already is a significant cause of many observed changes in physical and biological systems. Since about 1970, the changes have to be attributed to anthropogenic greenhouse gas emissions. The future development of climate and climate impacts depends on alternative scenarios of greenhouse gas emissions, with two extreme projections of alternative paths into the future, depending on unpredictable human decisions taken today:

- the 2° guardrail of global warming, allowing adaptation,
- a possible “climate crisis” with probably catastrophic consequences.

We cannot predict the future, but we are able to prevent the worst. The future evolution of atmospheric greenhouse gas concentrations, and hence of climate change, is not a matter of prediction, it is a matter of good or bad management.

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Climate Change as a Driving Force for Evolution

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With 1 Figure

Abstract

Since there has been life on earth organisms have had to "adapt" to a changing environment driven by physiochemical exterior factors, such as geodynamic processes, cosmic radiation, the chemical composition of the sea and atmosphere, sea level, plate tectonics, volcanic activity and meteorites, which together have had an impact on the global and local climate. Environmental change can progress slowly, allowing for evolution by sequential adaptation, or rapidly, leading to drastic changes of the current flora and fauna, so called bioevents. These bioevents have often been followed by disastrous mass extinctions, which, however, paved the way for new evolutionary inventions and for significant spreading and radiation of existing organisms. Examples of bioevent-causing major global extinction events are the Precambrian/Cambrian, Ordovician/Silurian, Frasnian/Famennian, Permian/Triassic, Triassic/Jurassic and the Cretaceous/Paleogene events, in each of which more than 70 % of all living species became extinct. But these extinctions gave rise to evolutionary transitions – abruptly occurring new blueprints – and allowed the bloom of pre-adapted but until then unimportant groups. The following article is intended to give a brief and greatly condensed overview of major climate-related extinction events (Fig. 1), and current hypotheses on their origins and impacts.

Zusammenfassung

Seitdem es Leben auf der Erde gibt, musste dieses sich an eine veränderliche Umwelt „anpassen". Exogene physiochemische Faktoren, wie geodynamische Prozesse, kosmische Strahlung, chemische Zusammensetzung der Ozeane und der Atmosphäre, Meeresspiegel, Plattentektonik, Vulkanismus und Meteoriten, verändern die Umwelt und dadurch das globale und das lokale Klima. Umweltveränderungen können sich langsam vollziehen und so eine Evolution durch fortlaufende Anpassung bewirken oder sehr rasch und dann zu einem drastischen Wechsel der Flora und Fauna führen, einem sogenannten Bioevent. Die Ursache für solche Bioevents waren oft dramatische Massenaussterben, welche aber letztlich neue evolutionäre Erfindungen und die Ausbreitung und Radiation bereits existierender Organismen nach sich zogen. Beispiele für solche globalen Massenextinktionen sind das Präkambrium/Kambrium-, Ordovizium/Silur-, Frasne/Famenne-, Perm/Trias-, Trias/Jura- und das Kreide/Paläogen-Event. In all diesen sind jeweils über 70 % aller lebenden Arten ausgestorben, jedoch ermöglichten sie einerseits evolutionäre Wechsel – abrupt auftretende neue Baupläne – und andererseits das Aufblühen präadaptierter, aber bis dahin unbedeutender Gruppen. Dieser Artikel soll eine kurze und kondensierte Übersicht über die großen klimabedingten Massenaussterben und die derzeitigen Hypothesen zu deren Entstehen und deren Folgen geben.

1. Introduction

The central fundament of climate change is the carbon cycle, which itself is largely dependent on tectonic energy (Berner 2003). Today, carbon is primarily stored in the biosphere – it is the major constituent of all organic matter –, but of course also as carbon dioxide (CO_2) in

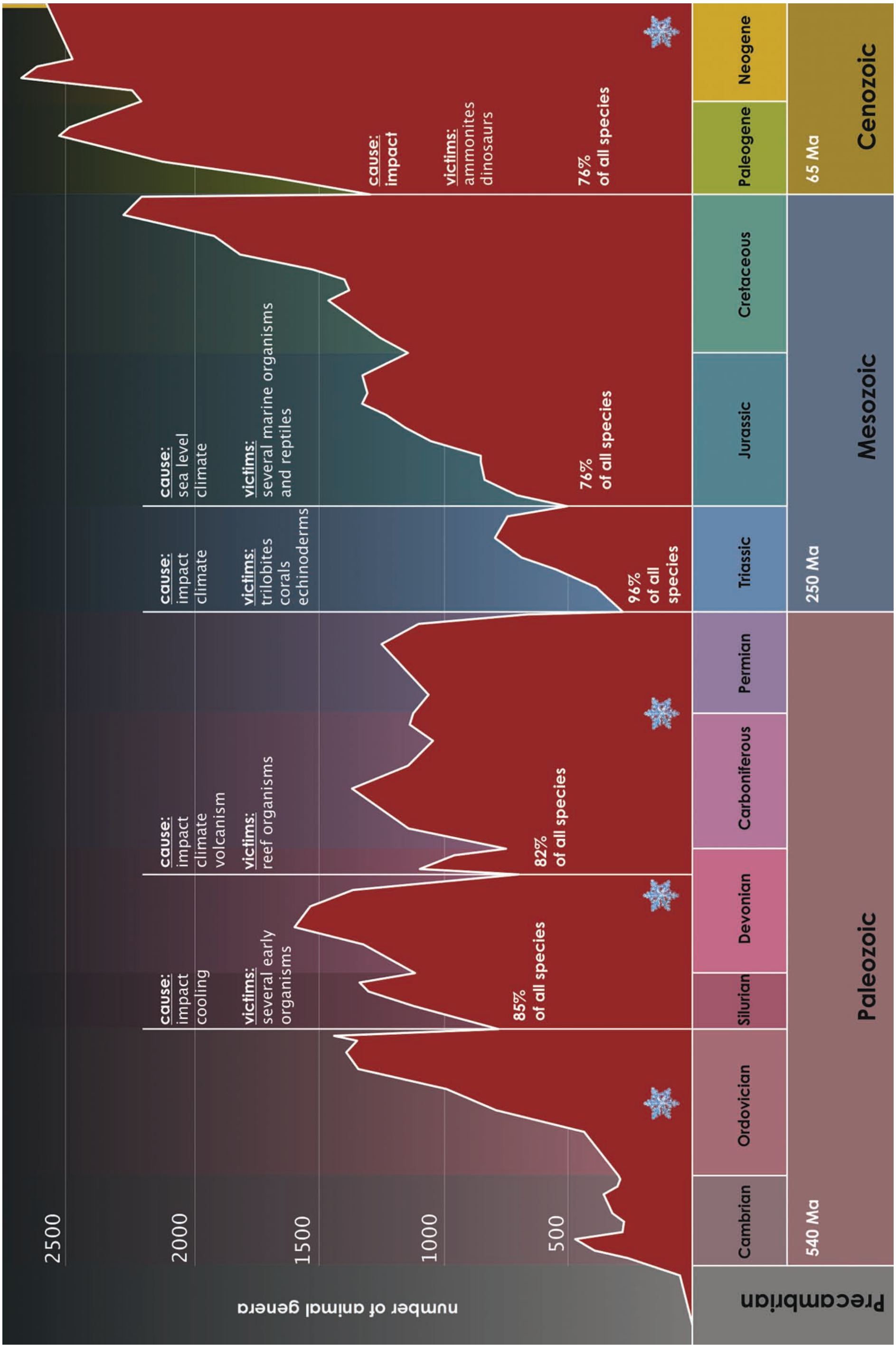

Fig. 1 Major impact events during evolution (modified after Kroh and Harzhauser 2009)

the atmosphere[1], as dissolved atmospheric CO_2 in the hydrosphere, and as fossil fuels and sedimentary rocks (limestone, chalk etc.) in the lithosphere.

Organisms gain their CO_2 mostly from the atmosphere, either directly or dissolved in water. It enters the water by simple diffusion and then resides as CO_2 and converts into carbonate (CO_3^{-2}) or bicarbonate (HCO_3^{-}), respectively. The early earth had significantly higher levels of CO_2 in the atmosphere and it was the green-house effect of this CO_2 (in combination with CH_4) that finally provided moderate temperatures (from around –18 °C to +15 °C) in spite of an approximately 30 % weaker sun compared to today (Tajika 2003, Paris et al. 2008 and references therein). This self-regulating carbon cycle has since then kept the Earth's global average temperature essentially constant, between +12 °C and +22 °C. The major driving forces for the cycle are tectonic movements leading to CO_2 release where plates drift apart and to carbonate metamorphism in the subduction zones (Berner 2003). The melted crust contains carbon in the sediments and soils. Carbonate metamorphism finally results in the accumulation of magma and eventually volcanic eruptions, these being the source of atmospheric CO_2. High CO_2 levels in the atmosphere cause climate warming, which goes along with higher decomposition rates, bringing back the CO_2 and closing the cycle.

2. Pre-Conditions for Life

Besides carbon, all life on earth is dependent on water. The very early earth, however, most probably resembled a hot volcanic ball with no liquid water (temperatures >100 °C). A steady cooling and a slowly forming atmosphere eventually set the conditions for making life possible. Four and a half billion years ago (Gya) a large meteorite, Theia[2], is assumed to have hit the earth thereby splitting off the moon (Halliday 2000, Belbruno and Gott 2005). Then, around 4.1–3.8 Gya a rapid migration of the giant planets Jupiter and Saturn, and a short phase of close encounters between Saturn, Uranus and Neptune directed numerous comets versus the earth (Gomes et al. 2005, Bottke et al. 2007). According to a widely accepted hypothesis this so-called Late Heavy Bombardment led to a significant input of cosmic water, which – in addition to "homemade" volcanogenic water vapor – lay the foundation for large connected subaerial bodies of water, the great oceans (Mottl et al. 2007, Jørgensen et al. 2009).

The early water world was a reducing environment enabling the aggregation of small structural molecules. This period is termed the RNA World. RNA is characterized not only by self-replication, but also by catalytic, metabolic and coding capabilities. These characters paved the way for the synthesis of small peptides and nucleic acids utilizing reduced nitrogen (N) compounds (e.g. ammonia). It is likely that histidine (*his*) and other imidazole-containing compounds were present in this early environment and that simple peptides containing at least two imidazole groups acted as concerted acid-base catalysts. The most stable and still most abundant amino acids are glycine (GGC) and alanine (GCC). The formation of phospholipid bilayer membranes finally led to a compartmentalization of the continuously brewing "molecule soup".

Among the early RNA, and subsequently also DNA, molecules also selfish elements soon arose, first ribozymes incorporating themselves into other molecules (group I introns), later

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[1] Presently >380 ppmv, the highest concentration for 650,000 years.

[2] In Greek mythology the goddess Theia, daughter of Gaia, gave birth to Selene, the goddess of the moon.

single strand and double strand RNA viruses, retrons and group II introns and finally DNA viruses and plasmids (Koonin et al. 2006). This period, called the Virus World, was characterized by an extensive genetic exchange, such as horizontal gene transfer, recombination, fusion, fission and spread of mobile elements, altogether finally heralding the first arms race. Defense mechanisms became necessary, RNA interference (RNAi) as an early strategy to inactivate foreign RNA, and the "erection of walls" to generally keep foreign material out – the early compartments evolved into the first cells, covered with membranes, and in the case of bacteria even with cell walls. According to one of the many possible scenarios, two spin-offs of such small compartments "filled" with organic matter were evolutionary successful leading to the Archea and the Bacteria and an endosymbiotic event of an archebacterium engulfing an eubacterium then gave rise to the first eukaryote, perhaps as soon as 2.7 Gya ago. However, the origin of life is still the subject of a most controversial debate. It is also possible – and many recent publications favor this hypothesis – that all three domains evolved at the same time, during the so called biological big bang (BBB) (Koonin 2007).

3. From Molecules to Cells

The last universal common ancestor (LUCA) is believed to have lived around 3.5 Gya and to have inhabited this system of compartments. Most probably LUCA was not the long believed hyper-thermophilic prokaryote[3], but rather a community of protoeukaryotes with a RNA genome – possibly already surrounded by a "protonucleus" – living in a relatively broad but more moderate range of temperatures (Glansdorff et al. 2008). The RNA to DNA transition could have resulted independently for Bacteria and for Archaea/Eukarya from two "viral" invasions. Then both bacteria and archaeans would have emerged by reductive evolution, the bacteria as the "non-thermophilic counterpart" to the archeans, while the first eukaryote most probably was a mesophilic cell, later adapting to the rising oxygen level by endosymbiosis (Glansdorff et al. 2008). One of the arguments corroborating the more or less synchronous evolution of Bacteria, Archaea and Eukarya is the histidine pathway. All three domains share a common gene fusion event in the *his*A and *his*F genes as the result of at least two elongation events followed by a paralogous gene duplication. However, in all three domains the *his* genes have since undergone major rearrangements in structure, organization, and order. Bacteria are assumed to have had at least two more gene fusion events, in *his*IE and *his*NB, as also eukaryotes in *his*HF and *his*IED (Fani et al. 2007).

The very oldest indications of life – by chemotrophic evidence for autotrophy – derive from ~3.8 Gya old sediments in West Greenland (Mojzsis et al. 1996). Early organisms may have lived in saline pools, and increasing oxygen toxification eventually promoted the evolution of photosynthesis, oxygenic photosynthesis evolving from anoxygenic photosynthesis (Björn and Govindjee 2008). As soon as sufficient oxygen had accumulated in the atmosphere, nitrification was outcompeted by de-nitrification, and a new stable electron "market" emerged. Photosynthesis and aerobic respiration ultimately spread via endosymbiotic events and massive lateral gene transfer to eukaryotic cells, allowing for the evolution of complex

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[3] The word prokaryote is epistemologically unsound, as the archaea and the bacteria do not seem to be a monophyletic group, and, moreover, nucleus-like structures with a double membrane and pores have been detected in representatives of the Planctomycetes (Domain: Eubacteria) (Fuerst 2005).

organisms (Falkowski and Godfrey 2008). The invention of oxygenic photosynthesis is credited to the cyanobacteria and subsequent extensive photosynthetic activity resulted in massive production of O_2. As photosynthetic organisms have a preference for light (^{12}C) over heavy carbon (^{13}C), a significant rise of ^{12}C levels in sediment layers from 2.5 Gya is one of the strongest arguments for the origin of bacteria before this period (Schidlowski 2001, Rasmussen et al. 2008). Definitive fossil records for prokaryotes exist from around 1.9 Gya, from the Gunflint formation in Ontario, Canada (Barghoorn and Tyler 1965).

The first indications of the existence of eukaryotes come from 2.8–2.5 billion years old sterane fossils found in Australia shale (Brocks et al. 2003). Sterols, a cytoskeleton and an endomembrane are characteristic for eukayotic cells. Moreover, eukaryotes "invented" an efficient intracellular transport system based on actin, myosin, tubulin, kinesin and dynein. With the further diversification of eukaryotic organisms, heterotrophy became the opposing strategy to autotrophy thereby establishing an early food chain. The permanent attack of mobile genetic elements probably quickly necessitated the development of the eukaryotic nucleus (possibly as an advancement over the "protonucleus" of LUCA) as a shelter for the genomic DNA. Early putatively fossils include the ~1.85 billion-year-old large acritarchs from the Chuanlinggou Formation, China (Peng et al. 2009), the ~2 billion-year-old coiled algae-like *Grypania spiralis* (size: >1 cm!) found in North America, China and India (Butterfield 2009), and the large colonial organisms from 2.1 Gya (El Albani et al. 2010). Fossil proof is available from 1.7 Gya and from 1.4 Gya, both genera found, *Valeria* and *Tappania* (possibly a higher fungus), were already equipped with a nucleus (Knoll et al. 2006). A recent study using continuous microfossil records inferred an early radiation of eukaryotes around 1.1 Gya (Berney and Pawlowski 2006). Among the oldest reliable identifiable eukaryotic fossil material found are the testate amoebae, referred to as vase-shaped microfossils, fossil isolates from 800–700 million years ago (Mya) being almost identical to today's isolates. Examples are the species *Nebela penardiana* Deflandre, 1936, and *Apodera vas* Certes, 1889, the later being, although obviously populating the earth for almost 1 billion years, interestingly only found in the Southern hemisphere.

4. Sexual Reproduction and Multicellularity

One of the driving forces for eukaryotic diversification was the second formation of a supercontinent, called Rodinia, and the subsequent orogeny[4] driven by tectonic movements (Li et al. 2008). Orogeny is generally followed by cooling, as weathering is increased and atmospheric CO_2 is exhausted (Goddéris et al. 2007). These events were accompanied by significant changes in ocean chemistry and a rise of the atmospheric oxygen level (Kumar et al. 2001, Donnadieu et al. 2004). Within a relatively short period of time secondary endosymbiotic events occurred – the oldest record being the genus *Paleovancheris* from 1 Gya – eventually leading to the evolution of the 6 eukaryotic supergroups around 1.7–1.2 Gya: the Opisthokonta with the animals and the fungi, the Amoebozoa, the Archaeplastida, the Chromalveolata, the Rhizaria and the Excavata. Within the photosynthetic eukaryotes, secondary and also tertiary endosymbiotic events are very common (Archibald 2005). The

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[4] Large scale orogeny was not possible until 2.7 Gya, when the strength of the Earth's mantle finally became sufficient to support high mountains.

diversification of the eukaryotes culminated in the Cambrian Explosion, the almost synchronic radiation of all 6 eukaryotic supergroups, which also implicated the invention of sexual reproduction and multicellularity. Sexual reproduction became possible with rising communication between the cells, for which cell-cell adhesion was one of the crucial steps. Multicellularity, possibly triggered by sexual reproduction, evolved in at least 7 independent events, at least once in each of the supergroups and partly probably alredy in the Proterozoic. Structures interpreted as fossils of very early multi-cellular organisms have recently been discovered from 2.1 billion-year-old black shales in Gabon. The organisms lived in an oxygenated environment and attained sizes up to 12 cm (El Albani et al. 2010). This new discovery reveals our extremely poor and patchy knowledge on early life. Proof for multicellularity comes from 1.2 Gya fossils from the Hunting Formation, Canada (Butterfield 2001). *Bangiomorpha pubescens* Butterfield, 2000, is a multicellular plastid bearing red alga with sexual reproduction and three different types of cells. Multicellular organisms, typical in the Precambrian Ediacara fauna, not only allowed for a better exploitation of the environment and gain in size – and this was not insignificant in the early arms race – but can also protect their inner cells from the environment, giving them an evolutionary advantage in a changing environment, particularly with climate extremes. Favored blueprints and organisms after the Cambrian Explosion were the bilaterian animals and the green algae. Early records for the existence of animals are dated to around 630 Mya, e. g. from the Doushantuo Formation in China (Shen et al. 2008).

5. Major Extinctions and Bioevents

One of the possible triggers for the Cambrian Explosion might have been a geodynamic crisis, maybe a Slush Ball Earth (Olcott et al. 2005, Micheels and Montenari 2008), being the result of four (perhaps even five) discrete ice ages with intermittent episodes of heat within a relatively short period of time, between 720 – 600 Mya. This interval is characterized by an enrichment of ^{13}C in carbonates and organic matter (photosynthetic organisms having a preference for the light ^{12}C carbon), intercepted by unusually low rates of $\delta^{13}C$ indicating reduced green-house capacity and glaciation (Kaufman et al. 1997).

First, the break up of Rodinia, starting around 830 Mya, and a high sea level, led to high rates of organic carbon burial, and thus reduced the atmospheric green-house capacity. Increased rainfall took CO_2 out of the atmosphere, thereby spurring the erosion of continental rocks. Massive flood-basalt eruptions between 825 –780 Mya in south China and in Canada caused a further decline of atmospheric CO_2 due to rapid and CO_2-consuming weathering (Goddéris et al. 2003, Li et al. 2008). This further reduced the CO_2 concentration in the atmosphere leading to a significant cooling and finally a glaciation, possibly covering as much as 60 % of the earth. Glaciation triggers further glaciation by the albedo effect, reflecting sun light and thus decreasing temperature, CO_2 levels then being less than 50 % of the current values. At a certain stage, however, the process tips. The cold dry air caused the formation of deserts with almost no rainfall, so CO_2 released by volcanoes remained and accumulated in the atmosphere initiating a new green-house effect that eventually increased global temperature. The resulting deglaciation and rapid precipitation of calcium carbonate led to a decreasing oceanic carbon saturation and at the same time to an increasing O_2 level in the deep ocean. These higher O_2 concentrations brought elements acting as co-enzymes (Fe, Mo etc.) into solution and thus made N_2 fixation possible[5], providing ammonium (NH_4) or nitrate (NO_3). The Cambrian explosion then, caused by significantly rising O_2 levels, resulted in an accelerated decomposition and more deposition into the ocean. At the same time the resulting arms race between the more and more diverse and specialized organisms – for the first time there was a great variety of predators – also made carapaces and shells necessary, and the exoskeleton was invented. Apparently, evolutionary rates were highly accelerated after life's first, but almost fatal, bottle neck of Slush Ball Earth.

Around 440 Mya the Ordovician/Silurian Event, preceded by the Hirnantian glaciation, a resulting fall of the sea level and a subsequent deglaciation – with the elution of large amounts of nutrients into the sea (LaPorte et al. 2009), algal bloom, reduction of O_2 levels and finally a toxification of the sea water –, caused a severe mass extinction among marine life. Jet, this mass extinction facilitated the evolution of the vertebrates and the first colonization of land. A gamma ray burst from a nearby supernova, destroying large parts of the Earth's atmosphere, is discussed as an additional trigger for this extinction event (Melott et al. 2004). The colonization of land was achieved synchronously by plants and arthropods. Early land plants were low, covered with wax as a strategy against desiccation and spread by wind (Kenrick and Crane 1997). The first trees of the Middle Devonian dispersed to large forests during the Late Devonian (Retallack 1997) coinciding with the occurrence of the first wildfires (Cressler 2001). Animal life on land could only evolve "in the shade of plants".

The Frasnian/Famennian or Kellwasser Event around 400 Mya, coinciding with a sea-level height and global warming caused by submarine volcanic activity, was one of the big extinction events in earth history (Pujol et al. 2006). It was preceded by an oceanic anoxic event[6] and followed by a significant increase of oxygen levels. The spreading of continental vascular plants and the simultaneous enormously increased continental weatherability is a further factor causing a considerable increase of the burial of organic matter (Goddéris and Joachimski 2004). The subsequent cooling caused the collapse of the forests and a shut-down of the oxygen factory. Oxygen levels declined from around 25 % during Devonian times down to 10–15 % (Ward et al. 2006). Terrestrial metazoan life was severely hampered as reflected by the so-called Romer's Gap, a lack or scarceness of terrestrial vertebrate fossils in sediments from 360–345 Mya (Ward et al. 2006). This succession of crises, however, was followed by the second colonization of land and paved the way for the invention of active flight, for which high oxygen levels are necessary. With the second colonization of land, the era of insects and amphibians came. High O_2 levels, plenty of food and a lack of predators resulted in gigantism among early land arthropods (Dudley 2000).[7] Orogeny formed the first large fresh water biotopes and these again enabled a flourishing amphibian fauna. Towards the end of this period an extremely high oxygen level (>30 %) evoked auto-ignitions causing massive forest fires (e.g. Uhl et al. 2004). This high oxygen level and a low CO_2 level, as revealed from stomata densities, allowed widespread Southern hemisphere glaciation (Beerling 2002).

The scenario, however, changed distinctly during the Permian with the ongoing clustering of the continents into Pangea, coinciding with the establishment of a widespread dry continental climate (Chumakov and Zharkov 2003). The Late Permian draught was the herald of

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[5] All organisms depend on nitrogen, as an essential component of proteins and nucleic acids, however, in the form of N_2 gas it is almost inert, due to the triple bond.

[6] Anoxia of the sea can be traced by black shale sedimentation.

[7] The size of arthropods, however, is limited by the exoskeleton and the open circulatory system with its relatively inefficient oxygen supply within the body.

the most dramatic extinction event, the Permian/Triassic Event, an extinction of > 90 % of all life and 96 % of all species. The trigger mechanisms are controversially discussed. Aside from the formation of the supercontinent, an asteroid impact (Becker et al. 2001), increased volcanism (Wignall 2009) and the release of methane hydrates (Krull and Retallack 2000) may have amplified the catastrophe. The aridity exerted massive pressure on the amphibian world in favor of amniote-egg reptiles and thus paved the way for the origination of the mammals. The large land mass, also drove vertebrate evolution by allowing for an almost endless dispersal, colonization of all possible niches, and a long and efficient food chain with large carnivorous animals at the top. The endoskeleton was a significant advantage for gaining size and the amniote egg for a much higher offspring survival rate.

One of the most famous mass extinctions is the extinction of the dinosaurs, the Cretaceous/Paleogene Event (also often referred to as Cretaceous/Tertiary or K/T Event). In this period there was extensive volcanic activity causing environmental poisoning (Grachev et al. 2005, Zhao et al. 2009) and a global warming followed by a drop of temperatures close to the Cretaceous/Paleogene boundary (Wilf et al. 2002, Ravizza and Peucker-Ehrenbrink 2003). Then, around 65 Mya, a large asteroid hit the earth resulting in the 40 km deep and 200–300 km wide Chicxulub Crater (its center lies near the coastal town of Puerto Chicxulub, Yucatan, Mexico) and a dramatic climate inter-linkage (Kring 2007). Nevertheless, the extinction of the dinosaurs was the one big chance for the warm blooded animals, birds and also mammals, which now could fill the niches for large animals. The mammals, with hair, a fatty layer under the skin, sweat glands and a four chambered heart, had significant advantages over the reptiles in times of climate change. The dramatic climate change afflicted, however, also insects and induced new directions of evolution (Aspöck 1998).

In the mid-Miocene, tectonic movements resulted in the incremental closure of Tethys coinciding with the Mid-Miocene Climate Optimum. Global mean surface water temperatures were about 3 °C warmer than present, and atmospheric CO_2 concentrations rose to 460–580 ppmv (You et al. 2009). This warming resulted in speciation of terrestrial mammals and diversification of marine environments (Barnosky et al. 2003, Harzhauser and Piller 2007). The subsequent cooling of surface waters and the expansion of the East-Antarctic ice-sheet, approximately 14.2 Mya, indicate the turning-point into the Middle Miocene Climate Transition (Shevenell et al. 2004). This trend was amplified by the uplift of Tibet between 40 and 26 Mya (DeCelles et al. 2007) which led to dramatically increased weathering rates and a drawdown of atmospheric CO_2 (Garzione 2008). Carbon fixation and water uptake is more efficient in C_4 than in C_3 plants when CO_2 levels and water supply are low, giving them an evolutionary advantage in the Late Miocene with declining rainfall. The global expansion of C_4 grasslands[8] starting around 25 Mya – and the concerted evolution of ruminants, which now specialized on grass instead of fruits – has been attributed to this decrease in atmospheric CO_2 levels. In contrast, very recent studies suggest that continental aridity, seasonality of rainfall and increasing wind strength during the Late Miocene in association with frequent and intense wildfires caused the opening of landscapes and thereby favored the expansion of C_4 grasslands (Tipple and Pagani 2007, Osborne 2008). In any case, the pre-adaptation of the digestive system coping with the changing diet was the reason for the enormous success of modern ruminants, which again, as suppliers of meat and milk have played a significant role for hominid evolution.

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[8] Most probably the C_4 pathway evolved independently in several plant groups.

6. Hominisation

Finally, in the Late Miocene, hominids first appeared on the scene, probably triggered by rainforest shrinkage and expansion of dry savannah and arid steppe – which drove groups of primates out of the forest and onto their feet. Recent data suggest a pan-African evolution of early hominids, with the oldest supposed hominid fossils from the period between 10–5 Mya (SCHRENK et al. 2004). The already bipedal australopithecines, an early lineage of the Hominini, evolved around 5 Mya. According to isotopic records this was a period of a warm interglacial climate, with a temperature peak between 4–3.4 Mya. A climate shift around 2.5 Mya then was the driving force for more robust hominids, *Australopithecus africanus* and *A. garhi* became extinct and the genus *Homo* with *Homo rudolfensis, H. habilis*, *H. ergaster* and *H. erectus* arose, co-existing with the late australopithecines, *Australopithecus robustus* and *A. boisei*. The drop of the sea level due to the Northern hemisphere glaciation during this period probably was also the trigger for the migration out of Africa, first accomplished by *H. erectus*. Early fossil records exist from Java (1.9 Mya), Georgia (1.7 Mya) and Spain (1.4 Mya) (BULYGINA and CLOLS 2000, SCHRENK et al. 2004). Another dramatic climate shift with a Northern hemisphere glaciation around 1 Mya then promoted a more progressive group of hominids, the genus *Australopithecus* became extinct and finally *H. sapiens neanderthalensis* and *H. sapiens sapiens* populated the planet. The wandering humans, of course, also brought along their parasites, and the ability of humans to cope with almost any local climate – and to explore and to fill almost any niche – is probably also the reason why *H. sapiens sapiens* is the species harboring the highest number parasites (ASPÖCK and WALOCHNIK 2007).

Altogether, one can assume a biphasic evolution; rapid evolution – usually after an extinction event – characterized by extensive genetic exchange, followed by a slow radiation of “newly invented” blueprints mostly driven by natural selection. Both phenomena are intensively linked with climate change, and most probably these lines could not be written, if climate change had not had a significant impact on human evolution.

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Fluctuations of Biodiversity in Europe in Light of Climate Change

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With 5 Figures and 4 Tables

Abstract

Climate change has always been the most important factor to explain alterations of the biodiversity in any part of the world. For an understanding of the formation and the fluctuation of the biodiversity of Europe, the development of the climate throughout the Ice Age, especially during the latest glacial period (ca. 115,000 to 12,000 BP) and of the Holocene (i.e., the past 12,000 years) is of particular significance.

During the latest glacial period, northern Europe and the northern part of Central Europe, as well as large sections of the Alps and other high mountain ranges, were covered by glaciers up to almost 3,000 metres thick. It is worth mentioning that the global average temperature during the coldest phase of the latest glacial period (ca. 25,000 BP) was only ca. 4–7 °C lower than today, and the maximum temperature differences between 25,000 BP and 6,500 BP (the Holocene optimum) in Central Europe certainly did not exceed 12 °C. The decrease in temperature and the large scale glaciations resulted in the extinction of life in large parts of these regions, whereas other parts of Central Europe, partly characterized by permafrost, were lacking in forests and thus also totally lacking in forest-linked flora and fauna. The Arboreal biome was considerably reduced, while the Oreo-Tundral biome prevailed in large parts of the continent. Forests were almost exclusively restricted to the Mediterranean and sub-Mediterranean regions. They represented important refugials centers for the biodiversity of Europe.

After the end of the latest glacial period in Europe, and as a consequence of a rise in temperature (maximum global rise: ca. 4–7 °C, in Central Europe: about 10 °C, Alpine regions: about 10 to 12 °C, Greenland: 25–30 °C), the glaciers of northern Europe (and also those of the Alps and other high mountain ranges) had largely disappeared. Northern and Central Europe became forested and a massive immigration of Mediterranean faunal elements – in variable intensity – began and continued throughout the Holocene and still proceeds today. Some Mediterranean species which extended their distribution far northwards during the Holocene optimum survived in smaller areas in ecologically favorable regions in Central Europe throughout the following millennia (e.g. sandflies). In addition, an intensive immigration from Asian refugial centers took place, particularly into northern Europe. By far the largest part of the animals were “Siberian” faunal elements, mainly Manchurian.

Moreover, a number of plants and animals which survived the latest glacial period in extra-Mediterranean European refugial centers, e.g. at the southern margins of the Alps, enlarged their distribution areas over large parts of northern Central Europe. As a consequence of the dispersal of animals – among them were hosts and vectors of pathogens, and thus also many microorganisms – their distribution expanded to the central and northern parts of the continent. There is a fundamental difference between the biodiversity in Europe of 25,000 BP and today. If one takes into consideration that this difference is the result of a rise of the global temperature of only 4–7 °C, and that it is absolutely realistic that the global temperature in this century will increase by another 3 °C, one can easily understand that fundamental changes in the biodiversity in Europe are to be expected in the course of the coming decades.

Zusammenfassung

Klimawandel war stets und in allen Ökosystemen und in jedem Teil der Welt die wichtigste und nachhaltigste Ursache für Veränderungen der Biodiversität. Für ein Verständnis der Entwicklung und der Fluktuationen der Biodiversität in Europa ist vor allem die Entwicklung des Klimas in den Eiszeiten, besonders in der jüngsten Eiszeit (Würm-

Weichsel-Eiszeit, ca. 115 000 bis 12 000 vor der Gegenwart) und im Holozän (das sind die letzten 12 000 Jahre) von entscheidender Bedeutung.

Während der letzten Eiszeit waren große Teile Nordeuropas ebenso wie die Alpen und andere hohe Gebirge von Gletschern bis fast 3000 m Dicke bedeckt. In diesem Zusammenhang verdient die Tatsache Beachtung, dass die globale Durchschnittstemperatur während der kältesten Phasen der letzten Eiszeit (vor ca. 25 000 Jahren) nur ca. 4 – 7 °C niedriger war als heute und dass die maximalen Temperaturunterschiede zwischen 25 000 (stärkste Vereisung) und 6 500 (holozänes Optimum) vor der Gegenwart in Mitteleuropa 12 °C sicher nicht überschritten. Das Absinken der Temperatur und die großräumigen Vergletscherungen führten im Wesentlichen zur Auslöschung des Lebens in großen Teilen dieser Gebiete, während andere große Teile von Mitteleuropa, zum Teil durch Permafrost gekennzeichnet, waldlos waren und daher keine Existenzmöglichkeiten für an Wald gebundene Organismen boten. Das Arboreal-Biom war entscheidend reduziert, während das Oreo-Tundral in vielen Teilen des Kontinents vorherrschend war. Wälder waren fast ausschließlich auf die mediterranen und submediterranen Teile Europas beschränkt. Sie stellten wichtige Refugialzentren für die Biodiversität Europas dar.

Nach dem Ende der letzten Eiszeit und in Folge des Anstiegs der Temperatur (maximaler globaler Anstieg: 4 – 7 °C, in Mitteleuropa: ca. 10 °C, in den Alpen: ca. 10 – 12 °C, in Grönland: 25 – 30 °C) verschwanden die Gletscher in Nordeuropa und zum größten Teil auch in den Alpen. In Mittel- und Nordeuropa entstanden Wälder, und eine massive Einwanderung von mediterranen Faunenelementen nach Norden setzte ein und hielt – in wechselnder Intensität – durch das gesamte Holozän hindurch bis heute an. Manche im holozänen Optimum weit nach Norden vorgedrungene Arten haben in später wieder geschrumpften kleinen Arealen die folgenden Jahrtausende in Mitteleuropa überdauert und werden häufig erst jetzt entdeckt (Beispiel: Sandmücken). Außerdem fand eine massive Einwanderung, besonders nach Nord- und Mitteleuropa, aus asiatischen Refugialzentren statt; beim größten Teil davon handelt es sich um „sibirische“, vorwiegend mandschurische Faunenelemente.

Darüber hinaus erweiterte eine nicht unbeträchtliche Zahl von Pflanzen und Tieren, die die letzte Eiszeit in extramediterranen europäischen Refugien, z. B. am Südrand der Alpen, überdauert hatten, ihre Verbreitungsareale über große Teile von Mittel- und Nordeuropa. Dieser Prozess ist nach wie vor – und durch globale Erwärmung verstärkt – im Gange und umfasst selbstverständlich auch Wirte und Vektoren von Parasiten und pathogenen Mikroorganismen.

Es besteht ein fundamentaler Unterschied zwischen der Biodiversität in Europa von vor 25 000 Jahren und von heute. Wenn man bedenkt, dass diese gravierenden Unterschiede das Ergebnis von nur 4 – 7 °C globaler Erwärmung sind und dass die Annahme einer weiteren Erwärmung um 3 °C in diesem Jahrhundert absolut realistisch ist, lässt sich leicht ermessen, welche fundamentalen Veränderungen der Biodiversität in Europa in den nächsten Jahrzehnten zu erwarten sind.

1. Introduction

In the “Haus der Natur” (“House of Nature”) in Salzburg, Austria, a large oil painting by Adrian Leitl can be seen which is divided horizontally into two parts (Fig. 1). The lower part depicts Salzburg as we know it today with its numerous towers, the castle, the many old houses, the green, partly forested hills and the tall mountains surrounding the famous town of Wolfgang Amadeus Mozart. The upper part shows a reconstruction of exactly the same region – but 15,000 years earlier – that is based on the results of geological, glaciological and climatological research. With considerable attention to detail, Adrian Leitl painted a view which one could have had at the end of the last glacial period. We see a huge melting glacier covering the largest part of that region where the city of Salzburg is today. In another scenario of the last glacial period, during the maximum glaciation of the last glacial period, the Inn valley, where the city of Innsbruck lies today, was covered by a glacier more than one and a half kilometers thick extending to the peaks of the high mountains surrounding Innsbruck today.

These two examples impressively demonstrate how deeply the fauna and flora must have changed during this comparatively short period in which the global average temperature increased by 4 to 7 °C (*IPCC* 2007), and the average temperature in the Alps by 10 to 12 °C. In certain northern parts of the world this rise in temperature was even markedly higher, e.g. in Greenland by 25 to 30 °C.

Fig. 1 Area of Salzburg, Austria, present (below) and 15,000 years ago (above). Oil painting by Adrian Leitl, House of Nature (*Haus der Natur*), Salzburg. Reproduced with the kind permission of Dr. Norbert Winding.

If we look at a graph showing a reconstruction of the global average temperature throughout the past, it becomes obvious that fluctuations of biodiversity have actually occurred on a permanent basis. This has been the case throughout the past 3 billion years. With respect to an understanding of the present biodiversity of Europe, the fluctuations of temperature throughout the whole Ice Age – roughly in the past two million years – have been of tremendous effect. Climate change means not only a change in temperature, however, temperature along with precipitation are the key factors for the development of a particular fauna and flora in a given geographic area. The climate correlates typically and markedly with the animals, plants, fungi, but also with microorganisms – particularly those dependent on other organisms (i.e., pathogens transmitted by arthropods).

2. Main Biomes in Europe

At present, Europe is composed of several biomes of which the Arboreal is by far the most extensive (Tab. 1), while the Oreal, the Tundral and the Oreo-Tundral biomes are represented only in the northern-most parts of the continent and in high mountain areas above the timberline.

The biodiversity of Europe (regardless of the palaeogeographic condition) has undergone significant fluctuations throughout all geological periods. To better understand the forma-

Tab. 1 Main biomes in Europe

Arboreal:	Areas in which temperature and precipitation are high enough for development of forests (presently > 90 % of the land).
Oreal, Tundral, Oreotundral:	Areas with enough precipitation, but temperature is too low for development of forests (presently < 10 %).
Eremial:	Areas with high temperature, but precipitation is too low for development of forests (presently < 0.01 %).
In addition, several other types (e.g. Xeromontane, Dinodal).	

tion of the present fauna, however, the last (better one should say, the latest) glacial period (= Würm period = Weichsel period), which lasted from about 115,000 to 12,000 BP, and the Holocene, i.e. the past 12,000 years, are of particular significance.

Eremial parts of Europe are found only in very small areas in the southeast of the Iberian peninsula, where precipitation is so low that forests are unable to develop. Extremely arid and semi-desert biozoenoses resulted.

The climatic conditions in all previous interglacial periods were very similar with temperatures comparable to the present. However, during the glacial periods, huge glaciers (up to almost 3,000 m, Ruddiman 2008)covered the north of Europe, as well as the higher mountain ranges (not only the Alps), and large parts of the continent, e.g. the area between the northern and the Alpine glaciers (i.e. almost the entirety of Central Europe), were characterized by a lack of trees due to the low temperature, thus representing the Tundral biome. The Arboreal biome was more or less restricted to the southern European peninsulas and thus was much smaller than it is today (Fig. 2).

Each biome has its specific fauna and flora, including the microorganisms. Everybody knows that a mountain, and particularly that part above the timberline, harbors totally different animals and plants than those in a lowland forest in Central Europe or in arid areas of southwest Europe. Thus it is obvious that, in the course of the altered distribution of the biomes following the climate change in the glacial and inter-glacial, the biodiversity of Europe changed permanently, and that this process continues today.

3. Mechanisms of Dispersal of Organisms

Table 2 shows the most important mechanisms of dispersal of organisms. All of these – with the exception of the last which is a result of human activities – have always played an important role. They were, they are and they will be the fundamental causes of fluctuations of biodiversity. On the one hand, animals, plants and microorganisms may invade areas previously not inhabited by them and become established. On the other hand, they may disappear – gradually or sometimes suddenly. Table 3 gives an overview of the mechanisms responsible for these phenomena.

4. Survival of Organisms during Periods of Climate Change

One of the gravest and, at least for long periods, most irreversible factors resulting in considerable depletion of biodiversity is climate change. It often leads to a total extinction of

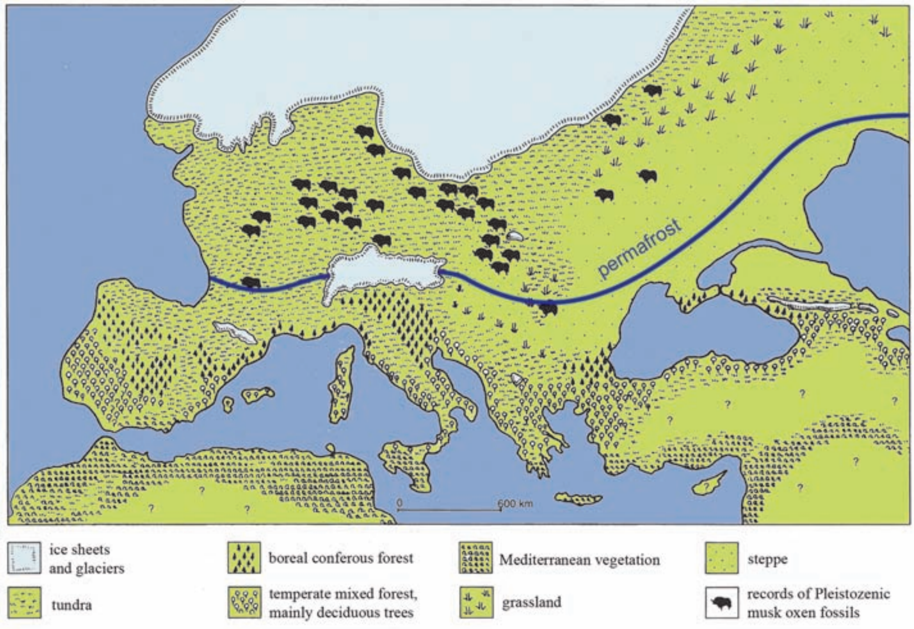

Fig. 2 Europe about 21,000 years ago during the coldest phase of the latest glacial period. Large parts of the continent were covered by huge glaciers: Scandinavia, the British Isles, the northern parts of Germany, the Alps and Pyrenees. The remaining permafrost region (Central and Eastern Europe) had a Tundra-like character with poor biodiversity. (Modified after SUDHAUS et al. 1997, from ASPÖCK and WALOCHNIK 2009.)

Tab. 2 Mechanisms of dispersal of organisms

Active expansion of distribution by migration dependent on suitable ecological conditions and degree of expansion capacity

Passive dissemination by:
– wind
– water
– other organisms
  – directly (e.g. parasites s.l.)
  – exchange of goods and services including transportation in vehicles (various forms of globalization)

Tab. 3 Mechanisms responsible for the disappearance of organisms

Loss of suitable ecological conditions – due to climate change – due to interference with other invasive organisms – due to human-made alterations of ecological conditions Extinction by predators or pathogens
Eradication by humans

species. However, there are also mechanisms of survival (Tab. 4). The third factor mentioned is undoubtedly the most influential, and it is often combined with the second factor. A typical example: species occurring in large parts of the lowlands of Central Europe, as well as in higher altitudes in southern parts of Europe, will, in the case of a decrease in temperature, disappear in Central Europe but may survive in lower altitudes in the south.

Tab. 4 Survival of Organisms during Periods of Climate Change

– Adaptation by selection
– Shift of vertical distribution by migration
– Downsizing of distribution and survival in refugial areas (refugial centres) with suitable orographic structure

5. Areas Representing Refugial Centers for the Survival of Biodiversity of Europe

Each glacial period led to a fundamental depletion of biodiversity in Europe, particularly in the northern, north-western, north-eastern and central parts of the continent. However, if the species from there also existed in the southern parts of Europe, in particular in the southern peninsulas, they would have had a high chance of survival. These parts of the continent are referred to as refugial centers (De Lattin 1967, Varga 1977, Aspöck et al. 1991, Aspöck 2008). By far the majority of them for European fauna are situated in the Mediterranean parts of Europe (Fig. 3). Besides these, there are also a few extra-Mediterranean centers. Those situated in regions to the south of the Alps prevailed during the maximum of glaciation, at least in a reduced form of the Arboreal biome with smaller forests or scattered trees and bushes. These refugial centers were only identified a few decades ago (Aspöck 1978, 1979, Malicky et al. 1983, Aspöck und Aspöck 2005). They probably assured the survival, particularly, of species of Asian origin, namely Siberian faunal elements, which immigrated into Europe from Manchurian or Mongolian refugial centers in a previous inter-glacial period.

During the glacial periods, the summits of the highest mountains, e.g. in the Alps, projected out of the glaciers (so-called nunataks) and were therefore free of ice and snow for a short period in summer. They had a modest to low vegetation and thus represented refugials for a few organisms, also some insects, on and above the glaciers. With respect to human pathogens, they were of no significance.

6. Post-Glacial Re-Colonization of Europe

About 15,000 years BP, a global warming began which led to the end of the latest glacial period. By 10,000 BP, the glaciers had largely disappeared, not only those in the north of Europe, but large parts of them in the mountain ranges in Central Europe, e.g. the Alps.

Thus, the ecological conditions in Europe fundamentally changed, and an intensive re-colonization began in the regions which were previously covered by glaciers or characterized by an absence of trees, thus representing biozoenoses of the Oreo-Tundral biome. From both the Mediterranean and the European extra-Mediterranean centers, and the large Asian centers, thousands of species of plants and animals invaded these newly emerging, mainly Arboreal habitats carrying with them numerous microorganisms including pathogens (Fig. 4).

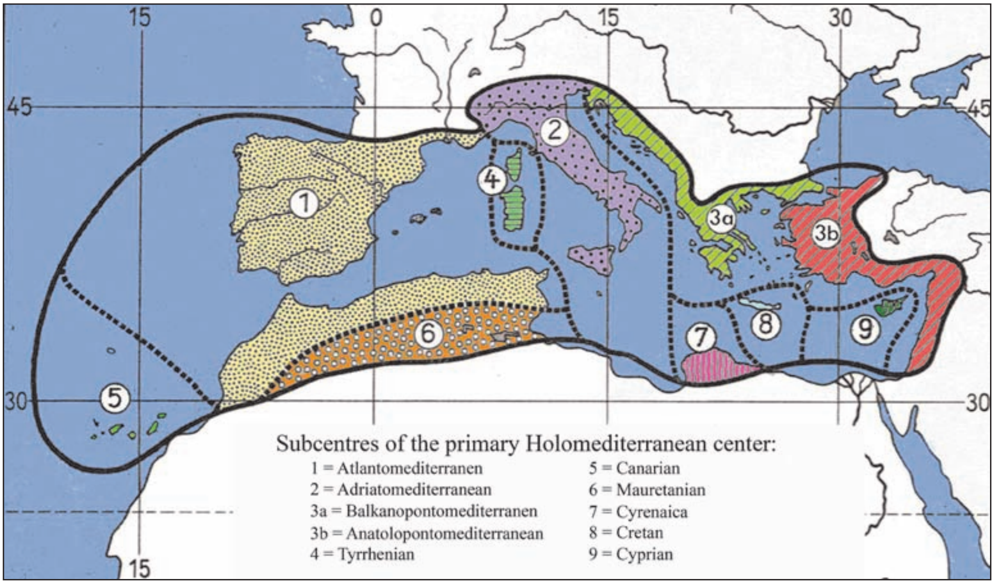

Fig. 3 The large Mediterranean refugial center and its subcenters. (Modified after De Lattin 1967 and Aspöck 2008.)

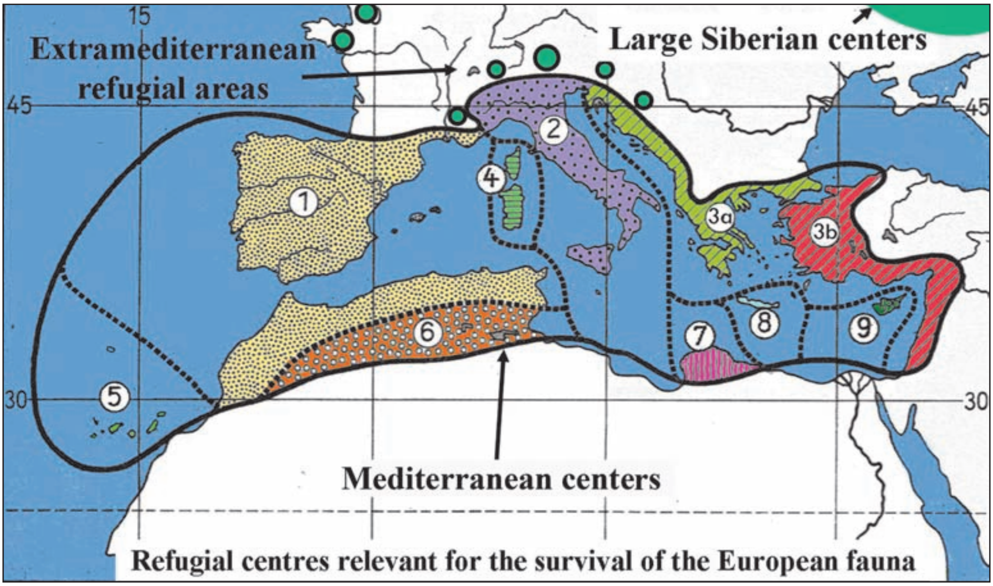

Fig. 4 Re-colonization of Europe north of the Mediterranean from Mediterranean, extra-Mediterranean and Asian refugial centers.

7. Recent and Future Fluctuations of the Biodiversity of Europe due to Climate Change

The end of the latest glacial period, and thus the beginning of the Holocene, marks a fundamental change in the biodiversity of Europe. However, this was not an event which happened abruptly and within a short period. It is a process which has been continuing with variable intensity and with fluctuations for more than 10,000 years – and which will continue into the future. If one examines the curve of the average temperature within the Holocene (Fig. 5), one recognizes a continuous change of increases and decreases with several extreme periods. At about 6,500 BP and 4,500 BP, there were periods of marked global warming (the Holocene climatic optimum) during which a particularly intensive flow of species immigrating from the Mediterranean centers occurred. One may assume that at those times Central Europe had an even higher level of biodiversity than it does today. When the temperatures began to drop again, in particular in the course of the first millennium BC, some of these newly immigrated species disappeared totally or could survive only in very restricted areas with outstandingly favorable climatic conditions throughout the following millennia. This explains why in some small areas with exceptionally favorable ecological conditions in northern parts of Europe, e.g. northern Germany, species of southern origin occur which cannot be found in most other parts of Central Europe. Some of these Mediterranean species were known to exist by the 19th century (e.g. HAGEN 1854), others were detected much later, and those which were found only in recent years were first interpreted in the light of the present climate change. An im-

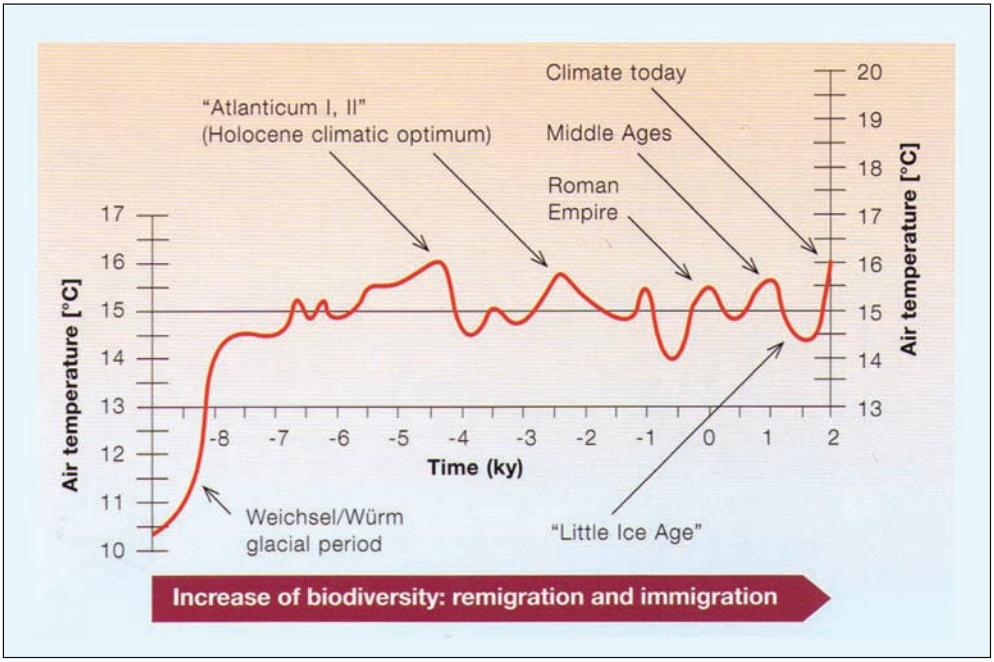

Fig. 5 Course of average temperature during the past 12,000 years in Europe. (Modified after KINZELBACH 2007, from ASPÖCK and WALOCHNIK 2009, with the kind permission of Dr. Gerhard HESSE, Bayer Environmental Science).

pressive example is the detection of sandflies in Germany a few years ago (Naucke and Pesson 2000). At first glance, it seems obvious that they are new immigrants due to global warming. However, an analysis of the distribution of Phlebotominae in other parts of Europe convincingly revealed that they have existed here for a long time, most likely since the Holocene climatic optimum (Aspöck et al. 2008, Aspöck and Walochnik 2009).

The present increase of the global average temperature (global warming) which will continue at least for the following few decades and most probably for the entire century, if not for longer, with an increase of temperature by about 3 °C (Kromp-Kolb and Formayer 2005, *IPCC* 2007, Böhm 2008, Schmidt et al. 2009) will undoubtedly lead to both a further dispersal of the Mediterranean faunal elements, which presently have restricted occurrences in Central Europe, and to new immigrations of elements from Mediterranean refugial centers. Recently, a remarkable book (Settele et al. 2008) appeared which deals with the predicted changes for the distribution of European butterflies and which contains hundreds of maps with predicted distributions in the course of this century. Such maps would be highly desirable for the arthropods and other animals of medical importance.

Moreover, it is likely that organisms – among them pathogens introduced by humans as a result of globalization – may become established due to the altered favorable climatic conditions.

The biodiversity of Europe has always been effected by climate change. However, presently we live in a period in which considerable changes in the biodiversity due to the altered climatic conditions must be expected, including the emergence of new vectors and new pathogens. To deny these dangers would be irresponsible. A continual surveillance, including extensive research, is an inevitable consequence of this situation.

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Temperature-Induced Bacterial Bleaching of Corals

Eugene Rosenberg[1], Gil Sharon[1] and Ilana Zilber-Rosenberg[2]
(Ramat Aviv, Israel)

With 1 Figure

Abstract

In recent years there has been extensive deterioration of coral reefs through direct human activities and indirect global warming. Part of the coral damage has resulted from newly emerging diseases. The most serious disease is bleaching, the loss of the endosymbiotic zooxanthallae. In two cases, it has been shown that the causative agent of coral bleaching is a *Vibrio* sp. High temperature plays a key role in bleaching. Several critical *Vibrio* virulence factors are produced only at warm temperatures, suggesting that the primary effect of temperature is on the pathogen, not the host. The ability of corals to adapt to environmental stresses, including elevated temperature conditions and infection by specific pathogens, has led to the development of the coral probiotic hypothesis. A generalization of this hypothesis, the hologenome theory of evolution, considers the holobiont as a unit of natural selection. The hologenome theory posits that all animals and plants harbor abundant and diverse microorganisms and that these microbial symbionts affect the fitness of the holobiont. Variation in the hologenome can be brought about by changes in either the host genome or the microbial population genomes, and these variations, including those of the microbiota, can be transmitted from one generation to the next with fidelity.

Zusammenfassung

In den letzten Jahren gibt es einen ausgedehnten Rückgang der Korallenriffe durch direkte menschliche Aktivitäten und indirekte globale Erwärmung. Ein Teil der Schäden an den Korallenriffen ist auf neu auftretende Erkrankungen zurückzuführen. Die schwerwiegendste Krankheit ist das Bleichen, der Verlust der endosymbiontischen Zooxanthellen. In zwei Fällen konnte gezeigt werden, dass das verursachende Agens des Korallenbleichens *Vibrio* spec. ist. Hohe Temperaturen spielen für das Bleichen eine Schlüsselrolle. Verschiedene entscheidende *Vibrio*-Virulenzfaktoren werden nur bei höheren Temperaturen gebildet, sodass der primäre Temperatureffekt eher auf das Pathogen als auf den Wirt wirkt. Die Fähigkeit der Korallen, sich an Umweltstress, einschließlich erhöhte Temperaturen und Infektion durch spezifische Pathogene, anzupassen, hat zur Entwicklung der Korallen-Probionten-Hypothese geführt. Die Verallgemeinerung dieser Hypothese, die Hologenom-Theorie der Evolution, betrachtet den Holobionten als Einheit der natürlichen Selektion. Die Hologenom-Theorie postuliert, dass alle Tiere und Pflanzen zahlreiche verschiedenartige Mikroorganismen beherbergen und dass diese Mikrosymbionten die Fitness des Holobionten beeinflussen. Die Variation in den Hologenomen kann entweder durch Änderungen im Wirtsgenom oder im Populationsgenom der Mikroorganismen erbracht werden. Diese Veränderungen, einschließlich jener der Mikroorganismen, können mit Genauigkeit von einer Generation auf die nächste übertragen werden.

Coral reefs harbor a reservoir of enormous biodiversity and are of major economic importance to many countries. During the last few decades there has been extensive deterioration

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of coral reefs through direct human activities and indirect global warming. A large part of the coral deterioration has resulted from newly emerging diseases, such as black band, white plague, white pox, aspergillosis, yellow blotch and bacterial bleaching. Most of these diseases are affected by seawater temperature: the higher the temperature, the more prevalent and severe the disease. On the global scale, the most serious disease is bleaching, the loss of the endosymbiotic algae, referred to as zooxanthallae. In two cases, it has been shown that the causative agent of coral bleaching is a *Vibrio* sp.: bleaching of *Oculina patagonica* in the Mediterreanean Sea by *Vibrio shiloi* and bleaching of *Pocillopora damicornis* by *Vibrio coralliilyticus*.

As seen in Figure 1, bleaching of *O. patagonica* in the sea occurs at elevated seawater temperatures. High temperature also plays a key role in bleaching by *V. shiloi* in laboratory aquaria experiments (Kushmaro et al. 1996). At 29 ºC bleaching is rapid and complete, at 25 ºC it is slower and incomplete, and below 20 ºC no bleaching occurred, even with a very high inoculum size of *V. shiloi*. In principle, the inability of *V. shiloi* to bleach *O. patagonica* at the winter temperatures could be due to increased resistance of the coral or decreased virulence of the pathogen. The data summarized below indicate that several critical *V. shiloi* virulence factors are produced only at the elevated summer water temperatures, suggesting that the primary effect of temperature is on the pathogen, not the host.

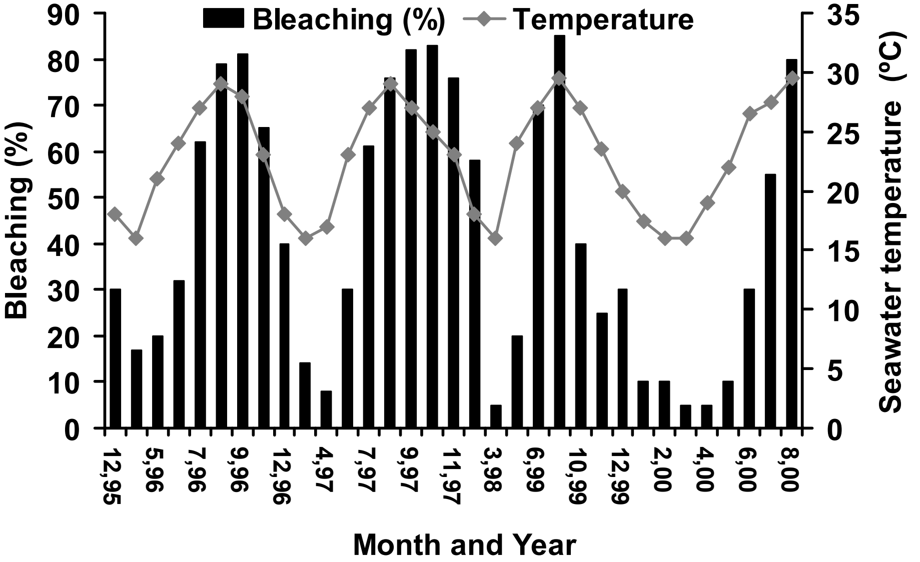

Fig. 1 Bleaching of the coral *Oculina patagonica* as a function of seawater temperature. Adapted from Rosenberg and Falkovitz 2004.

As noted above, expression of crucial bacterial virulence genes is temperature dependent. At warm temperatures, *V. shiloi* expresses a cell-surface adhesin that is required for bacterial adhesion to the coral surface (Toren et al. 1998). At elevated temperatures, the microorganism also expresses Toxin P, which inhibits photosynthesis of the endosymbiotic algae (Banin et al. 2001), and superoxide dismutase, which is required for survival inside the coral (Banin et al. 2003). In the case of infection by *V. coralliilyticus*, synthesis of an extracellular proteinase, an important virulence factor, is temperature dependent (Ben-Haim et al. 2003).

From 1994 to 2002, bacterial bleaching of the coral *O. patagonica* in the eastern Mediterranean occurred every summer. During that time period, *V. shiloi* was repeatedly isolated from bleached corals and shown to cause bleaching of healthy corals in controlled aquaria experiments. However, since 2003 all attempts to isolate *V. shiloi* from bleached or healthy corals have been unsuccessful, and inoculation of fresh healthy corals (taken directly from the sea) with *V. shiloi* does not result in coral bleaching.

The ability of corals to adapt to environmental stresses, including elevated temperature conditions and infection by specific pathogens, has led to the development of the coral probiotic hypothesis (Reshef et al. 2006). This hypothesis posits that a dynamic relationship exists between symbiotic microorganisms and corals at different environmental conditions that selects for the most advantageous coral holobiont in the context of the prevailing conditions. By altering the structure of its resident microbial community, the holobiont can adapt to changing environmental conditions more rapidly and with greater versatility than a process that is dependent on genetic mutation and selection of the coral host. The following data support the coral probiotic hypothesis: first, corals contain a large and diverse microbial population associated with their mucus and tissues; second, coral-associated microorganisms can benefit their host by various mechanisms, including photosynthesis, nitrogen fixation and the production of antimicrobials; third, the coral-associated microbial population undergoes rapid changes when environmental conditions are altered; and fourth, although lacking an adaptive immune system, corals can develop resistance to pathogens. The coral probiotic hypothesis could help explain the evolutionary success of corals and moderate predictions of their demise.

Many of the arguments presented to support this hypothesis of adaptation and evolution are relevant to other invertebrates, and to higher animals and plants. Indeed, extrapolating from this hypothesis led us to propose a higher order of postulation, namely, the hologenome theory of evolution. The hologenome theory of evolution considers the holobiont with its hologenome, acting in consortium, as a unit of natural selection in evolution. The holobiont is defined as the host organism together with all of its symbiotic microbiota (Rohwer et al. 2002). The hologenome is the sum of the genetic information of the host and its microbiota (Zilber-Rosenberg and Rosenberg 2008). The hologenome theory posits that all animals and plants harbor abundant and diverse microorganisms and that these microbial symbionts affect the fitness of the holobiont. Furthermore, variation in the hologenome can be brought about by changes in either the host genome or the microbial population genomes, and these variations, including those of the microbiota, can be transmitted from one generation to the next with fidelity.

As a result of the development of molecular non-culturing techniques for enumerating microbial communities in the last few decades, it is now clear that all animals and plants harbor diverse population of microbes. For example, the human colon: In the 1970s it was estimated that the number of bacterial species that inhabit the human colon was a few hundred. This value was based on isolation and characterization of colony formers; in recent years, using 16S rRNA gene sequences, the number of species was estimated to be 1000–2000; most recently, Frank and Pace (2008) reported a minimum of 40,000 species in the human colon, using metagenomic techniques. Assuming this latter value, the number of unique microbial genes in the human colon can be calculated to be 200 times that of the host.

Variation is one of the key driving forces in essentially all science-based theories of evolution. When considering the holobiont as a unit of natural selection, variation can arise from changes in either the host or the symbiont genomes. Genetic variation in the host as well as in individual microorganisms can be generated by the well-recognized mechanisms of sexual recombination, chromosome rearrangement and mutation. Stochastically generated variants followed by selection of the fittest are the essence of neo-Darwinian evolution. It must be born in mind that "fittest" in the case of a holobiont must include interactions between the host and its symbionts as well as symbionts with other symbionts in addition to interactions of the holobiont with other holobionts.

Consideration of the hologenome, namely, the host genome combined with that of its microbiota, brings forth two additional modes of variation which are specific to the holobiont: The first is microbial amplification, the increase of one group of symbionts relative to others which can occur when conditions change. The holobiont is a dynamic entity with certain microorganisms multiplying and others decreasing in number as a function of local conditions within the holobiont. An increase in the number of a particular microbe is equivalent to gene amplification. Considering the large amount of genetic information encoded in the diverse microbial population of holobionts, microbial amplification can be a powerful mechanism for adapting to changing conditions. Examples of environmental factors that can lead to changes in symbiont populations and thereby to variation in the hologenome include temperature, nutrient availability, antibiotics and newly acquired symbionts.

The second mechanism for introducing variation into holobionts is the acquisition of new symbionts from the environment. Animals and plants come in contact with billions of microorganisms during their lifetime. It is reasonable to assume that occasionally, as a random event, some of these microbes will find niches and become established in the host. Under the appropriate conditions, the novel symbionts may become more abundant and affect the phenotype of the holobiont. Unlike microbial amplification, acquiring new symbionts can introduce entirely new genes into the holobiont.

For symbiotic microbes to play a role in the evolution of higher organisms they must be transmitted with fidelity. In recent years, it has become clear that microbial symbionts can be transmitted from parent to offspring hosts by a variety of methods (McFall-Ngai 2002, Zilber-Rosenberg and Rosenberg 2008). The most conserved model of transmission of symbionts is when the microorganisms are in or on the reproductive cells, exemplified by mitochondria and chloroplasts which can be considered extreme symbionts (Margulis 1993), and *Buchnera* which are situated in bacteriocytes of its host aphid and are transmitted to and then via the eggs (Baumann et al. 1995). Direct contact is another slightly less direct mode of transmission demonstrated in mammals in which many of the symbionts are derived during passage through the birth canal or subsequently by close physical contact with parent or family and community members. It also should be noted that some animals and most plants can develop from cells other than gametes: during vegetative reproduction the offspring will still contain some of the symbionts of the parent. Thus, regardless of the mechanism, there is now abundant evidence that the microbial component of the hologenome is transferred from generation to generation.

In conclusion, microbes play a key role on the adaption and evolution of animals and plants.

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Continents under Climate Change

Konferenz aus Anlass des 200. Gründungsjubiläums der Humboldt-Universität zu Berlin

in Zusammenarbeit mit dem Potsdam-Institut für Klimafolgenforschung (PIK) und der Deutschen Akademie der Naturforscher Leopoldina
Unter der Schirmherrschaft des Auswärtigen Amtes der Bundesrepublik Deutschland

vom 21. bis 23. April 2010 in Berlin

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Der Klimawandel gehört zu den drängendsten globalen Problemen unserer Zeit. Die Menschheit steht vor besonderen Herausforderungen, um insbesondere den CO_2-Ausstoß zu senken. Führende Wissenschaftler aus der Klimaforschung betrachten die Auswirkungen des Klimawandels auf die Kontinente Europa, Asien, Afrika, Amerika und Australien sowie die Polarregionen. Dabei werden neueste Klimadaten unter globalen und regionalen Gesichtspunkten ausgewertet und Simulationsmodelle für zukünftige Entwicklungen diskutiert. Die Ausführungen bieten ein gut fundiertes Bild der Klimaänderungen, die sich weltweit bereits vollziehen bzw. in Zukunft ereignen werden, und untersuchen kritisch die Folgen für Natur, Gesellschaft und Wirtschaft. Der Kongress „Continents under Climate Change" wurde im Rahmen der 200. Jahrfeier der Humboldt-Universität zu Berlin vom Potsdam-Institut für Klimaforschung und der Deutschen Akademie der Naturforscher Leopoldina – Nationale Akademie der Wissenschaften veranstaltet. Alle Beiträge sind in englischer Sprache verfasst.

Wissenschaftliche Verlagsgesellschaft mbH Stuttgart

Impact of Climate Change on Vector-borne Infections of Humans

Nova Acta Leopoldina NF *111*, Nr. 381, 53–56 (2010)

Arboviral Disease Emergence: What is the Role of Climate Change?

Lyle R. Petersen (Atlanta, GA, USA)

With 1 Figure and 1 Table

Abstract

The arthropod-borne viruses (arboviruses) cause considerable morbidity and mortality worldwide in animals. Weather and climate greatly influence the population size, temporal variation, and geographic distribution of arthropod vectors and vertebrate hosts, as well as the nature and extent of interaction between humans and infected arthropod vectors. In addition, increasing ambient temperature shortens arthropod vector extrinsic incubation period as well as affects arthropod survival. Both increased daily survival and decreased extrinsic incubation period increase in a logarithmic relationship the likelihood that an infected mosquito will infect a human.

Zusammenfassung

Die insektenübertragenen Viren (Arboviren) verursachen in Tieren weltweit eine beträchtliche Morbidität und Mortalität. Wetter und Klima beeinflussen außerordentlich die Populationsgröße, das zeitliche Auftreten und die geographische Verbreitung der Arthropoden als Vektoren bzw. der Wirbeltiere als Wirten sowie das Ausmaß der Kontakte zwischen Menschen und infizierten Arthropoden. Eine steigende Außentemperatur verkürzt die extrinsische Inkubationsperiode der Vektorarthropoden und beeinflusst das Insektenüberleben. Sowohl das wachsende Überleben als auch die verringerte extrinsische Inkubationsperiode erhöhen in logarithmischer Weise die Wahrscheinlichkeit, dass ein infiziertes Insekt einen Menschen infiziert.

The arthropod-borne viruses (arboviruses) cause considerable morbidity and mortality worldwide in animals. At least 130 of the more than 500 known arboviruses cause human disease, which manifests as three main clinical syndromes: neuroinvasive disease (encephalitis, meningitis, and acute flaccid paralysis), fever/arthralgia, and hemorrhagic fever. The arboviruses exist in amplification cycles involving primary vertebrate hosts and arthropod vectors, often with high vector and host specificity (Fig. 1). Mosquitoes and ticks comprise the most medically significant vectors. With a few exceptions, such as the dengue and chikungunya viruses, humans develop insufficient viremia to infect arthropods, and thus do not contribute to the amplification cycle.

Weather and climate greatly influence the population size, temporal variation, and geographic distribution of arthropod vectors and vertebrate hosts, as well as the nature and extent of interaction between humans and infected arthropod vectors. In addition, increasing ambient temperature shortens arthropod vector extrinsic incubation period (the time from when an arthropod vector ingests an infected blood meal to the time its bite becomes infectious) as well as affects arthropod survival. Both increased daily survival and decreased extrinsic incu-

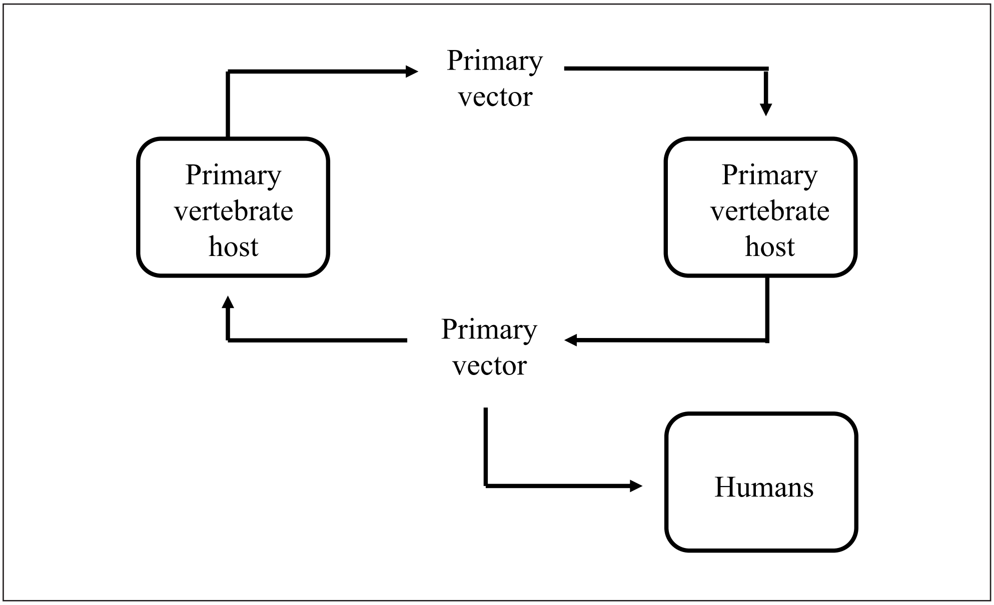

Fig. 1 Simplified arbovirus amplification cycle.

bation period increase in a logarithmic relationship the likelihood that an infected mosquito will infect a human. For example, the 30-day extrinsic incubation period at 17 ºC for *Culex tarsalis*, a vector for West Nile virus, nearly prohibits viral amplification in nature; however, the 5-day extrinsic incubation period at 30 ºC greatly augments transmission and the possibility of outbreaks.

In temperate climates, arbovirus amplification begins with increasing springtime vector and vertebrate host populations. As summer approaches, higher ambient temperatures increase viral amplification, as noted by the rapid rise in human West Nile virus infections in late July each year in the United States. Higher than normal summer temperatures often promote arboviral disease outbreaks, as exemplified by the association of West Nile virus outbreaks with above average July temperatures in the northern hemisphere. However, such a relationship is not apparent in warmer climates of the southern United States.

In Puerto Rico, a small Caribbean tropical island with marked climate variability, modeling of more than 20 years of dengue incidence data using natural adaptive cubic splines to minimize seasonal confounding demonstrated that increases in monthly temperature and rainfall augmented dengue incidence up to two months later. Temperature increase was most correlated with increased dengue incidence in municipalities with the coolest climate. Correspondingly, increase in monthly rainfall was most correlated with dengue in municipalities with the driest climate; whereas, rainfall had no effect or was even negatively associated with dengue incidence in municipalities with the wettest climate. Thus, weather has differential effects based on underlying climate.

The influence of weather and climate to vector-borne disease incidence has fueled concern that climate change is driving the recent emergence of many vector-borne diseases globally. Interannual climate variation has been studied by examining the impact of the El Niño Southern Oscillation (ENSO). ENSO relates to increased rainfall in East Africa, which by flooding "dambos" greatly increases production of floodwater vector mosquitoes. However, little correlation could be found between Rift Valley fever and ENSO in West Africa. Attempts to correlate historical yellow fever outbreaks in North America to ENSO have been inconclusive most likely because yellow fever was never enzootic in that region and outbreaks resulted from chance importations. In another study using wavelet analysis, little or no coherence was observed between ENSO and dengue in Puerto Rico, Mexico, and Thailand. The relationships between ENSO and arboviral disease incidence may have been obscured by other factors affecting incidence or that the areas investigated were too large and climatically varied.

Globally, multiple anthropogenic factors, especially globalization, have influenced arbovirus incidence trends (Tab. 1). Climate change appears to have had no or comparatively little influence on incidence trends to date. The best evidence for the influence of climate change exists perhaps for tick-borne encephalitis (TBE). In Scandinavia, fewer very cold days and extended spring and autumn periods have apparently resulted in a northward spread and increased prevalence of *Ixodes ricinus* ticks, the main vector of TBE. However, increases in TBE may have preceded observed temperature increases. In the Czech Republic over a 30-year period, TBE cases have increasingly occurred at higher altitudes, coincident with climate warming. However, overall increases in TBE in the Czech Republic were attributed mostly to other factors such as increased deer populations. In other countries, TBE incidence increases in some countries were attributed to increased recreation in endemic areas while in other countries decreased incidence was attributed to TBE vaccination.

Tab. 1 Trends in some medically important arboviruses and underlying causes.

Virus	Trend	Causes
Chikungunya	Increasing incidence and geographic distribution.	Susceptible human populations, travel, globalization of *Aedes albopictus* from used tires, viral adaption.
Dengue	Increasing incidence and geographic. distribution.	Population growth, urban slums, "container societies", ineffective or absent control, global travel.
Japanese encephalitis	Decreasing incidence in many Asian countries. Expansion into parts of South Asia	Vaccination, urbanization away from pig growing areas.
St. Louis encephalitis	Decreasing incidence.	Replacement by West Nile virus?
Tick-borne encephalitis	Increasing in some areas, decreasing in others.	Warmer temperatures, land use, vaccination, recreational travel, host population changes.
Venezuelan equine encephalitis	No long-term trend.	
Western equine encephalitis	Almost disappeared.	Unknown.
West Nile	Emergence in Americas. Strain of apparent increased pathogenicity.	Importation to New York City.
Yellow fever	No long-term trend.	

Predictions of the future impact of climate change on arboviral disease incidence must take into account myriad drivers of incidence besides predicted vector and host distributions. Multiple dengue outbreaks in adjacent cities along the United States' border with Mexico illustrate this point. While considerable concern exists that dengue could emerge in the United States, outbreak investigations consistently reveal ample vector populations on both sides of the border, yet differences in living conditions, such as the use of air conditioning, result in substantially lower incidence in the United States.

In conclusion, climate change so far has had little demonstrable impact on arboviral disease emergence. However, a strong biologic basis exists that further climate change will influence arboviral disease incidence and distribution. These changes will depend on underlying climate as well as multiple anthropogenic and other factors. Sorting out the role of climate change will require greater understanding of the ecology of the arboviruses as well as long-term surveillance, particularly in areas bordering current endemic zones.

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Human Viral Diseases Imported to Europe

Matthias NIEDRIG (Berlin)

With 1 Figure and 3 Tables

Abstract

The transmission and the passage of diseases between countries or continents is a rather complex process that involves several factors (climate-, environmental-factors, movement of travelers and goods, etc.) which influence each other and are not well understood. In general there are two major routes for the importation of infectious agents from one country to another. One possibility is the direct import of infected vectors like rodents, mosquitoes or sand flies by containers or airplanes. The second, more common, route for importation of infectious agents is the import by tourists/migrants. The paper discusses cases of rabies, Yellow Fever, Dengue, Chikungunya Fever infections. The close connections of globalization and climate changes will be the most important factors to facilitate the distribution of new and emerging pathogens. Although some human viruses are on the list for eradication due to worldwide vaccination campaigns (polio, measles, mumps) travelers have to be aware that these viruses are still present in some remote areas in Africa where the vaccination management fails due to political unstable conditions. Better education and communication of protective measures for travelers seems the only option to minimize the overall risk.

Zusammenfassung

Die Verbreitung und Ausbreitung von Krankheiten zwischen Ländern und Kontinenten ist ein sehr komplexes Geschehen, das durch verschiedenste Faktoren (Klima, Umwelt, Bewegung von Reisenden und Waren, etc.), die miteinander interagieren, beeinflusst wird. Diese Zusammenhänge sind derzeit nur unzureichend aufgeklärt. Im Wesentlichen existieren zwei Wege, auf denen Infektionserreger nach Europa eingeschleppt werden können. Eine Möglichkeit ist der direkte Import von Nagern, Moskitos und Sandfliegen in Containern oder Flugzeugen. Der zweite Weg ist der Import von infektiösen Erregern durch Touristen oder Migranten, die die Infektion während ihres Aufenthaltes in den jeweiligen Endemiegebieten erworben haben. Verschiedene Faktoren begünstigen die Übertragung von viralen Erregern während einer Reise. Einige Touristen verfügen nicht über die empfohlenen Impfungen und sind über geeignete Schutzmaßnahmen nicht informiert. Viele sind auch nicht vertraut mit den Infektionsrisiken im Reiseland, so dass sie sich schnell eine Krankheit zuziehen können. Gerade die respiratorischen Krankheiten haben ein großes Potential, sich schnell und effizient auszubreiten. Dies hat sich gerade an dem Beispiel von SARS und der neuen Grippe H1N1 eindrucksvoll gezeigt. Hingegen stellen sowohl sexuell übertragene Krankheiten als auch durch Lebensmittel übertragene Krankheiten ein konstantes Risiko für Reisende in Ländern mit hoher Bevölkerungsdichte und unzureichenden Hygienebedingungen dar. Spektakuläre Infektionen wie hämorrhagische Fieber stellen zwar ein erhebliches Risiko für die unmittelbaren Kontaktpersonen der Patienten dar, sind aber auf Grund ihres akuten Krankheitsverlaufs keine Ursache von zahlenmäßig großen Ausbrüchen. Eine verbesserte Aufklärung von Reisenden und eine Anpassung der medizinischen Ausbildung bezüglich der Erkennung und Behandlung von seltenen und neuen Infektionskrankheiten wären geeignete Maßnahmen, sich adäquat auf die sich verändernden Bedingungen vorzubereiten.

The transmission and the passage of diseases between countries or continents is a rather complex process that involves several factors (climate-, environmental-factors, movement of travelers and goods, etc.) which influence each other and are not well understood.

In general there are two major routes for the importation of infectious agents from one country to another. One possibility is the direct import of infected vectors like rodents, mosquitoes or sand flies by containers or airplanes. From time to time this proven way results in cases of malaria in European citizens without any history of travel to tropical countries (Rodger et al. 2008). This phenomenon, known as airport malaria, requires a clever physician who considers the unexpected infection and introduces the proper treatment for the patient.

The second, more common, route for importation of infectious agents is the import by tourists/migrants which contract the infections during their travel abroad. There are several factors contributing to the circumstances for transmission of viral pathogens during a journey. Some tourists are inadequately prepared by neglecting vaccination or other health measures. Many are unfamiliar with the risk of getting infected with unknown pathogens in foreign countries where it is sometimes very easy to contract new diseases (Tab. 1). Sometimes vacations expose the travelers to infected vectors or animal hosts they never were exposed to before. Recent cases of tourists infected via a bat scratch with rabies, or by bat contact with Marburg virus resulted in fatal outcomes for the tourists after they returned home (Timen et al. 2009, van Thiel et al. 2009). These are tragic and unexpected cases while infections caused by neglected vaccination measures for Yellow Fever also often result in an avoidable fatal outcome (Bae et al. 2005). Additionally, a great number of imported Dengue infections are diagnosed since the four Dengue serotypes are widely distributed in nearly all tropical areas (Jelinek 2009). Fortunately, no or only insufficient numbers of susceptible mosquitoes are living in most regions of Europe, so the risk of local transmission and subsequent local outbreaks is rather low at the moment.

Tab. 1 Selected most frequent diagnoses from 27,069 travelers (excludes immigrants and expatriates) reported from European sites between 04/97 – 05/09. Source: GeoSentinal database

Position	Disease	Fraction
1	Diarrhoea, acute unspecified	10.0 %
2	Diarrhoea, chronic	8.6 %
4	Viral syndrome (no rash)	6.8 %
5	Respiratory infection, acute	6.8 %
6	Diarrhoea, acute bacterial	5.1 %
7	Diarrhoea, acute parasitic	4.9 %
8	Malaria (all species)	3.1 %
11	Dengue, uncomplicated	2.0 %
17	AIDS, HIV, Syphilis, Gonorrhoea	1.3 %
22	Rabies, post exposure prophylaxis	1.0 %

However, an alarming event was the outbreak of Chikungunya Fever (CHIK) in the region of Emilia Romagna in Italy in summer 2007. The most contributing factor for this outbreak was the increase of the susceptible *Aedes albopictus* mosquitoes in the region over the preceeding years which created the conditions for a successful transmission of the CHIK imported by an infected Indian man arriving from a region with an ongoing CHIK epidemic. This importation resulted in 292 suspected and 125 laboratory confirmed CHIK cases including one death of an 81 year old patient with pre-existing conditions (Rezza et al. 2007, Casolari et al. 2008, Straetemans 2008).

The patterns of imported viral diseases in travelers and in immigrants are quite different (Tab. 1 and 2). While diarrhoea is the disease most frequently reported by returning travelers, most immigrants coming to Europe suffer from chronic infections such as Malaria, sexual transmitted diseases (STD), Tuberculosis or Hepatitis which are much more serious for the public. Even the faecal-oral transmission of some viral pathogens is very efficient, further transmission is mostly self-limiting due to the acute cause of disease and the introduction of appropriate hygiene measures.

Tab. 2 Selected most frequent diagnoses from 1041 immigrants (arriving < 6 month before clinical visit date) reported from European sites between 04/97 – 05/09. Source: GeoSentinal database

Position	Disease	Fraction
1	Malaria (all species)	12.3 %
2	AIDS, HIV, Syphilis, Gonorrhoea	10.8 %
3	*Mycobacterium tuberculosis*	8.3 %
4	Hepatitis (viral – chronic)	6.3 %
8	Respiratory infections, acute	4.1 %
9	Diarrhoea, acute parasitic	3.3 %
20	Viral syndrome (no rash)	1.0 %
21	Diarrhoea, acute unspecified	0.9 %
25	Rabies	0.8 %

Another important group of imported diseases can be subsumed as respiratory diseases which comprises also Severe Acute Respiratory Syndrome (SARS) and the recently emerged "new influenza" A H1/N1. The extremely fast global distribution of both diseases gives an impression how much these pathogens profit from globalization.

These close connections of globalization and climate changes will be the most important factors to facilitate the distribution of new and emerging pathogens. Since in both subtropical and temperate regions climate factors have multiple effects on the environment, food supply, animal host, transmission vectors, etc., the role and importance of the different factors in this open loop are still not understood (Fig. 1).

It will be one major task to find out if and how these factors can be changed or influenced by intervention measures to avoid future outbreaks caused by newly introduced pathogens.

In survey studies (2003–2007) on mosquitoes no specimen of *Aedes aegypti* – a very potent vector for Dengue and Yellow Fever – was reported in mainland Europe (Reiter et al. 2010). However, in recent sentinel investigation *Aedes aegypti* was found on the island of Madeira which operates daily ferry connections with the mother country. It is a matter of time until the mosquitoes successfully use this or other efficient routes of transport for conquering Europe. Once present in Europe this new vector can change the requirements for introduction of new and other pathogens as described previously. In the meantime it is very important to get an idea of which mosquitoes are present in Europe at the moment and which competence they have for those pathogens at risk for importation to Europe. One obstacle to a comprehensive answer to this question is the limited number of experienced entomologists working on these tasks due to the limited funding invested in this area in recent years. As we have learned from the recent introduction of bluetongue virus into Germany and other European countries, the

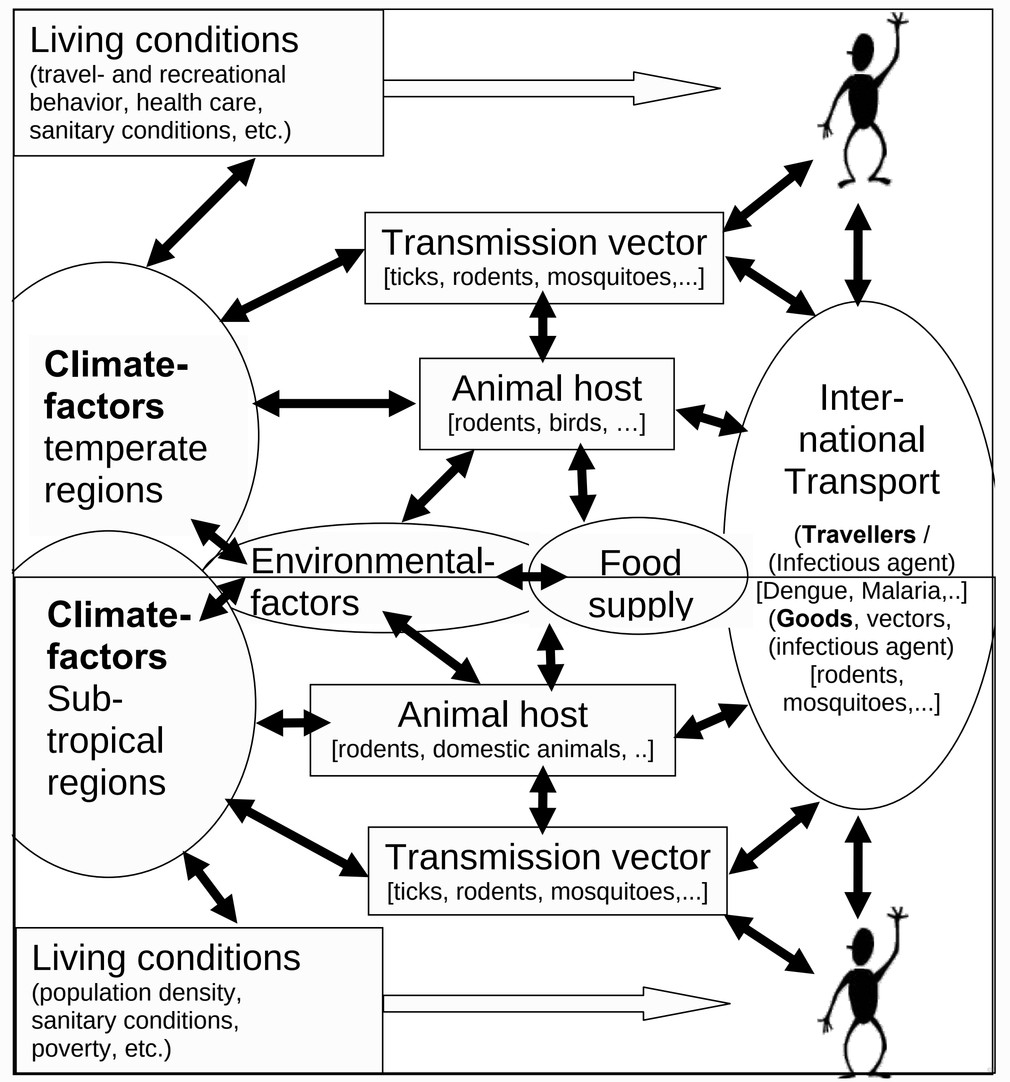

Fig. 1 Climate factors and Globalization. Overview of the impact of different factors contributing to the global exchange of infectious agents and vectors. The multilayer interaction of climate factors for the northern hemisphere with developed countries (upper part) and the countries in tropical areas (lower part) is quite obvious.

intervention strategies after the introduction of a new pathogen based on a widely distributed vector are rather limited and can cause major financial damage and losses.

There are several viral pathogens that are at risk to be imported to European countries which have a different risk of further distribution and causing outbreaks in the human population (Tab. 3). Some pathogens, such as Tick-borne Encephalitis and Hantavirus, already present in some regions might also expand their area of distribution due to the changing climate conditions. Others have been detected locally, but did not spread further for several years such as the West Nile Fever virus which is present in the Rhone delta region, Northern Italy and the Balkans.

Tab. 3 Overview of human viral pathogens at risk to be imported to Europe considering changing climate conditions and newly introduced vectors. * Human vaccine available.

Infectious agent	Vector	Present distribution	Presence of competent vector in Europe	Imported, infectious agent vector or vehicle	Risk estimation regarding distribution and out-breaks
Tick-borne Encephalitis Virus*	ticks (*Ixodes* ssp, *I. ricinus*)	Middle- and North Europe, Russia, North Asia, North America	existing	infected domestic and wild animals	possible
Hantavirus	rodents	Middle-, North Europe, Russia, America, Asia	existing	infected domestic and wild animal	possible
Rabies Virus*	domestic-, wild animals	Europe, Asia, Americas	existing	infected domestic and wild animals	minor
Sandflyfever virus	Sand flies	South Europe, Mediterranean countries	regional existing, upper Rhine valley	infected individuals, infected birds	possible
West Nile Virus	mosquitoes (*Culex* and *Aedes* ssp.)	South France, North Italy, Balkan region	existing	infected individuals	possible
Lymphocytic Choriomeningitis Virus	rodents, hamster	Europe	existing	infected individuals	possible
Crimean Congo Hemorrhagic Fever Virus	ticks (*Hyalomma* ssp.)	Africa, Middle East, Balkan region, Turkey	regional existing	infected individuals	minor
Chikungunya-Virus	mosquitoes (*Aedes* ssp.)	Africa, Asia, Upper Italy	regional existing	infected individuals	possible
Dengue Virus	mosquitoes (*Aedes* ssp., *A. aegypti*)	Asia, South America, Africa	regional existing	infected individuals, import of goods	possible
Yellow Fever Virus*	mosquitoes (*Aedes* ssp.)	Africa, South America	regional existing	import of goods, infected individuals	possible
Japan Encephalitis Virus*	mosquitoes (*Culex* ssp.)	Asia	regional existing	import of goods, infected individuals	minor
Rift Valley Fever Virus	mosquitoes (*Culex* and *Aedes* ssp.)	Africa, Middle East	regional existing	import of goods, infected individuals	minor

It is not clear if higher numbers of cases are always related to a broader distribution of the pathogen, or sometimes caused by more serious analysis and improved diagnostic detection assays. Based on the existing knowledge it is possible to evolve rough risk estimation for some of these pathogens. Most of the knowledge we are lacking concerns the distribution and competence of vectors and the routes for possible importation of pathogens via infected individuals, animals or as passengers with imported goods.

From experiences of the last couple of years we can point to some tasks which are important for future scenarios of major public health issues.

Zoonotic viral diseases will emerge, and they will require more effort to combat as we have seen with the bluetongue outbreak. Other diseases like Rift Valley Fever have conquered the Arabian Peninsula recently and are a real risk for countries like Turkey with very similar environmental habitat. In recent outbreaks of Rift Valley Fever in Africa several human cases occurred, some with a fatal outcome.

A closer and improved cross link between the veterinary and human disease surveillance and diagnosis will help to foster the preparedness regarding new and unexpected diseases. A quick exchange of information will facilitate the timely introduction of suitable health measures as we have learned from the avian flu outbreaks several years ago.

Although some human viruses are on the list for eradication due to worldwide vaccination campaigns (polio, measles, mumps) travelers have to be aware that these viruses are still present in some remote areas in Africa where the vaccination management fails due to political unstable conditions.

This means that these viruses will be a constant risk for unvaccinated travelers as well as for the unvaccinated contacts after returning home. A clear risk analysis and a proper check of the vaccination certificate before traveling will be the only way to avoid such problems.

This also applies to two other disease risks for travelers. Especially in developing countries, sexual transmitted diseases and food- and water-borne virus infections (Noro-, Astro- and Hepatitis A viruses) will persist, and cause an endemic situation with a clear risk of infection for travelers.

Better education and communication of protective measures for travelers seems the only option to minimize the overall risk. This and the improved training of medical students becoming familiar with the new and even unexpected diseases is another prerequisite to facilitate a quick and improved detection of rare and new exotic diseases in Europe. This means that the education curriculum for physicians must be expanded for the new and upcoming health threats caused by travel activities and health threats expected from climate changes. The expertise of the physician along with the skills of the diagnostic laboratory will determine if new and or unexpected diseases will be detected in time to introduce health measures. How many cases will be necessary to attract the attention of the public health institutions depends on the proficiency of the surveillance system in the respective country. The Chikungunya outbreak as non fatal disease in Italy taught us that roughly one hundred cases within approximately one month are required to detect the introduction of a new and unexpected emerging disease in a restricted area. One can hope that a more severe disease will provoke a quicker and more efficient response from all partners involved to allow timely measures from the public health institutions.

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Medicine at the Interface between Science and Ethics

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Naturwissenschaft und Theologie/Ethik versuchen mit unterschiedlichen Konzepten, ein Weltbild zu erfassen, das die *conditio humana* besser zu verstehen erlaubt. Die Fragen sind weit gefasst; endgültige Antworten wird man nicht leicht finden. Gemeinsame Diskussionen über diese Probleme könnten beiden Gebieten Anregungen geben und der Biomedizin im Umgang mit der sehr kritischen Öffentlichkeit helfen. Voraussetzung ist Offenheit gegenüber der anderen Denkweise. Der vorliegende Band behandelt daher aus der Perspektive von Naturwissenschaftlern und Ethikern so verschiedene Themen wie die neuen Herausforderungen an Moral- und Ethikdiskurse durch die jüngsten Fortschritte der Biowissenschaften, die Grenzen der ethischen Reflexion bei den neueren Entwicklungen der Molekularbiologie, die Geschichte der Auffassungen vom „Gen“ und seiner Bedeutung in der Humanbiologie, aber auch die Missverständnisse zwischen den beiden Kulturen der Naturwissenschaften und der Geisteswissenschaften in der Forschung über Lebensprozesse. Dazu kommen Beiträge zur Stammzellproblematik, der Verwendung von Tiermodellen in der Translationsmedizin, über Würde von Zellen in Kultur, Fragen der Pluripotenz von Zellen und der Reprogrammierung von Zellkernen sowie der Bedeutung von Methylierungsmustern für die Epigenetik. Die Beiträge sind in englischer oder deutscher Sprache verfasst.

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Helicobacter pylori – From Pre-History to Industrialization: Acquisition, Adaptation, and Endangerment of a Celebrated Bacterial Parasite

Niyaz Ahmed (Hyderabad, India)

Abstract

In the last two decades, several researchers have predicted mass migrations as a consequence of climate change. Some of the enteric pathogens which chronically inhabit human niches also co-migrate with their human host. Population dynamics and disease potentials of these pathogens are likely to change with the change in history, geography and ecology of their hosts. Pathogens such as *Helicobacter pylori* have been shown to work as past-witnesses of human history as well as reliable markers to dissect population migration.

Zusammenfassung

In den letzten zwei Jahrzehnten haben einige Forscher Massenwanderungen als Konsequenz des Klimawandels vorausgesagt. Einige der Darmpathogene, die chronisch im menschlichen Darm vorkommen, wandern mit ihren Wirten mit. Die Populationsdynamik und die Krankheitspotentiale dieser Pathogene werden sich wahrscheinlich mit den Veränderungen in Geschichte, Geographie und Ökologie ihrer Wirte wandeln. Pathogene wie *Helicobacter pylori* haben sich als Zeugen für die Menschheitsgeschichte und als verlässliche Marker für die Analyse der Populationswanderungen erwiesen.

In the last two decades, several researchers have predicted mass migrations as a consequence of climate change. They have foreseen millions of people fleeing from rising sea levels, floods, disease outbreaks and drought, leading to serious consequences for both migrants and the receiving societies. Some of the enteric pathogens which chronically inhabit human niches also co-migrate with their human host. Population dynamics and disease potentials of these pathogens are likely to change with the change in history, geography and ecology of their hosts. Some of the enteric pathogens are prominent candidates whose epidemiology and evolution within different stationary and migratory communities have been of interest since quite some time as the impact of climate change on enteric infection has emerged as a concern in recent years. Apart from this, pathogens such as *Helicobacter pylori* have been shown to work as past-witnesses of human history as well as reliable markers to dissect population migration.

Population genetic structure of many of the parasites supposedly co-evolved with humans juxtaposes to genetic distribution patterns of their host. Human DNA analysis in the recent past has revealed that along the major land routes out of Africa, human populations become genetically isolated – the farther from eastern Africa a population is, the more genetically diverse it is compared to other human populations. Other observations have revealed gradual differences in European populations, analogous to the migration of Neolithic farmers moving northwards. Comprehensive genetic analysis of *H. pylori* found almost exactly the same genetic distribution patterns for this bacterial parasite. Genetic analyses incorporating human and bacterial data sets lend support to the contention that *H. pylori* may have migrated from eastern Africa at almost exactly the same time as early humans, approximately 60,000 years ago. This ultimately conveys that humans and this bacterium have been intimately linked for at least the last 60,000 years (Linz et al. 2007). However, the question that has not been answered clearly until now is whether this 60,000 year old *H. pylori* was as virulent as today's *H. pylori*? In other words, it is not clear if *H. pylori* harbored its virulence genes since the beginning or if it acquired them later as a result of gradual change in human history and ecology.

The beginning of agriculture and the domestication of farm animals (which seem to have occurred hand in hand, but across multiple domestication events in a continent specific manner) suggests a scenario that can be linked to the acquisition of virulence by *H. pylori*. It can be hypothesized that early bacterial communities, originating from crop plants, animals or rodent pests etc., rampant in the vicinity of early human societies may have served as donors of some of the virulence gene cassettes. Such genetic elements may have been acquired by *H. pylori* either bit by bit or en-bloc, at some point in time through horizontal gene transfer events. There is indirect evidence to this effect in the form of sequence and structural similarities of some of the *H. pylori*'s virulence genes to their homologues in plant pathogens and environmental bacteria. Also, we believe that the extraneous virulence genes may have conferred some survival advantage upon *H. pylori* with respect to fitness in different human and animal hosts and, as a result, the pathogen may have spread selectively in a geographically compartmentalized manner. To date, the genetic structure of *H. pylori* is highly geographically oriented, both with respect to the core and the flexible genome components. Many of the genetic elements supposedly of foreign origin in *H. pylori* have been described to be virulence linked in a strain specific manner. That means, for some strains, enhanced pathogenic and proinflammatory potentials are imparted by novel elements which may not be universally conserved (Rizwan et al. 2008; see also Ahmed et al. 2008, 2009, Akhter et al. 2007, Carrol et al. 2004, Devi et al. 2006, 2007, Prouzet-Mauléon et al. 2005).

H. pylori induced chronic gastritis is a definitive risk factor for the development of gastric cancer. However, it was found that statuses of some of the chief virulence factors (CagA and VacA) do not always correlate with particular outcomes of infection. To understand this dilemma we hypothesized a complex interplay of many different virulence factors. We focused initially on a few of the functionally unknown members of the genomic plasticity region, a putative type IV secretion cluster believed to be acquired horizontally. Two members of this cluster (JH940 and HP986) potentially appeared to be interacting with the human immune system.

In view of this, it appears that the virulence of *H. pylori* is a complex phenomenon which has to be seen as a strategy for survival and adaptation. However, it is not clear how the bacterium maintains its niches for almost the entire life span of its host without being cleared. Perhaps some biological interaction operates between the host and the pathogen. Further experiments with the HP986 experimentally proved that it is a proinflammatory and proapoptotic agent. Most persistent microbes seemingly evolve strategies to avenge innate responses to gain niche and to maintain growth fitness. For example, *H. pylori* traditionally harnesses its cardinal virulence factors to downregulate T-cell responses (through the VacA mediated cell cycle arrest) and upregulates mucosal proinflammatory pathways (by CagA). Surprisingly, in our studies HP986 appears to be able to perform both the immune stimulatory and immune evasion tasks single handedly. Thus we believe that HP986 probably functions as a persistence factor which awaits validation using appropriate animal models (ALVI et al., unpublished).

If we discuss survival advantage to the pathogen, we should also see if there is any protective advantage for the host? Although there is no direct evidence in this direction, recent studies point to the possibilities that *H. pylori* infection protects against childhood diarrhoea, gastro-oesophagial reflux disease, oesophageal cancers and asthma. Eradication of *H. pylori* by antibiotic therapy has shown augmented incidence of some of these diseases in different populations. Also, due to eradication, *H. pylori* is in steep decline in the west and has been rightly dubbed an 'endangered species' in the stomach (BLASER 2005).

Do we need to save and conserve *H. pylori* as an important beneficial organism and a marker of human history; or should we eradicate it completely? Is eradication that simple? In most developing countries, it is not achievable because of rampant drug resistance among local strains. Also, even if eradicated using future effective drugs, re-colonization is almost unavoidable due to poor water hygiene and frequent contamination. Apart from the need for future functional studies to link *H. pylori* to human disease (with certainty), or to promulgate it as a commensal or a mutualist, epidemiological approaches are also required to ascertain need for eradication or otherwise for different populations and societies.

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Individuelle und globale Ernährungssituation – gibt es (noch) eine Lösung?

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Der Anteil der Menschen, die übergewichtig bis fettleibig sind, ist heute ebenso groß wie der Anteil derjenigen, die an Hunger leiden – jeweils fast eine Milliarde! Die Beiträge hinterfragen, welche Handlungsalternativen wir im Hinblick auf unsere individuelle und globale Ernährungssituation haben. Sie zeigen auf, was wir tun können, um den globalen Hunger zu bekämpfen, und was wir tun müssen, um die individuelle Ernährungssituation in den Griff zu bekommen.

Zurzeit sehen wir mit der Umnutzung von Ackerböden für den *Non-Food*-Bereich Entwicklungen, die die globale Nahrungsmittelverfügbarkeit weiter verschärfen. Dazu werden Fragen der Nahrungsmittelproduktion und Verteilung – bis hin zum Einsatz von Gentechnik – behandelt, um eine ausreichende Versorgung der Weltbevölkerung zu erreichen. Der Band diskutiert Ursachen und Folgen von Über- und Mangelernährung und hebt besonders die gesundheitspolitische Relevanz der Ernährungsfrage hervor.

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Impact of Climate Change on Infectious Diseases of Humans

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Impact of Climate Change on *Dirofilaria* Infections in Animals and Humans

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Abstract

A temperature-based model, a threshold of 14 °C and 130 cumulative *Dirofilaria* Development Units (DDUs) reached in 30 consecutive days was assumed for extrinsic *Dirofilaria* larval development to infective stage into mosquitoes. The model was used to predict the occurrence and seasonality of *Dirofilaria* in Europe, and the data was interpolated utilizing the Linear Kriging function of a Geographical Information System to calculate the number of *Dirofilaria* generations in Europe. The output showed that temperatures can theoretically allow the extrinsic development of worms in most European countries and that *Dirofilaria* transmission is markedly seasonal in Europe, with peaks in summer from June to September. In many cases, the predictions have been confirmed by empirical data. The role of *D. repens* as zoonotic agent is stressed.

Zusammenfassung

Ein temperaturbasiertes Modell, ein Schwellenwert von 14 °C und 130 kumulative *Dirofilaria*-Entwicklungseinheiten (*Dirofilaria* Development Units – DDUs), in 30 aufeinander folgenden Tagen erreicht, wurden für die extrinsische Dirofilarien-Larvenentwicklung zu infektiösen Stadien in Moskitos angenommen. Das Modell wurde eingesetzt, das Auftreten und die Saisonbewegungen von *Dirofliaria* in Europa vorauszusagen, und die Daten wurden unter Verwendung der Linearen Kriging-Funktion eines Geographischen Informationssystems interpoliert, um die Anzahl von *Dirofilaria*-Generationen in Europa zu kalkulieren. Die Ergebnisse zeigten, dass die Temperaturen theoretisch in den meisten europäischen Ländern eine extrinsische Entwicklung des Wurms gestatten und dass die Dirofilaria-Übertragung ausgesprochen saisonabhängig ist und einen deutlichen Höhepunkt in den Sommermonaten von Juni bis September aufweist. In vielen Fällen bestätigen empirische Daten diese Voraussagen. Die Rolle von *D. repens* als zoonotischer Erreger wird betont.

1. Introduction

Global warming is defined as an average increase in the temperature of the atmosphere near the Earth's surface and in the troposphere, which can contribute to changes in global climate patterns. There is now strong scientific consensus that: (*i*) global warming is occurring, (*ii*) it is largely attributable to human emission of greenhouse gases, (*iii*) the effects are now observable, (*iv*) further warming will occur and (*v*) that climate change has a potentially serious

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impact on human and animal health (Blashki et al. 2007). A recent report by the Intergovernmental Panel on Climate Change estimates current global warming to be almost 0.8 °C above pre-industrial levels and project a further rise of 1.1–6.4 °C by 2100 (*IPCC* 2007). By altering the global environment, climate change has significant potential to intensify certain diseases, particularly those transmitted by vectors (Khasnis and Nettleman 2005). Global climate change can affect disease vector behavior, which in turn may alter the current patterns of vector-borne diseases transmitted by the bite of haematophagous arthropods (Rogers and Randolph 2006). For instance, in Italy canine leishmaniosis and dirofilariosis have changed distribution patterns; *Leishmania infantum* was endemic in southern areas of the country until late 1990's, but is now more frequently diagnosed in northern areas. Dirofilariosis, which was endemic in canine populations in northern Italy, is now spreading all over the country (Otranto et al. 2009).

Arthropod vectors are cold-blooded animals, meaning that their internal temperature is affected by the temperature of their environment. Thus, for many terrestrial arthropod species, a northward range expansion can be expected in response to projected climate change. Furthermore, vector-borne pathogens are particularly sensitive to climate, and there is some evidence that anthropogenic climate change can play a role increasing their incidence and intensity (Purse et al. 2005). However, it is interesting to note that the effects of climate change can also influence gastrointestinal worms which have free-living developmental stages, such as trichostrongylid nematodes of ruminants. Recently, van Dijk et al. (2008) observed a consistent increase of trichostrongylid infections over the last 5–10 years in small ruminants in Great Britain. The authors argue that alternative explanations such as anthelmintic resistance or changes in production methods cannot account for changes in seasonality of recorded disease, while all these fit expectations based on the effects of temperature on infective larvae availability. This suggests that climate change could also influence the epidemiology of diseases caused by parasites whose development outside the host is sensitive to temperature.

2. *Dirofilaria* Worms Life Cycle

Dirofilaria diseases are vector-borne parasitic infections of mainly dogs and cats (and wild carnivores) that in Europe are caused by *D. immitis* and *D. repens*. The life cycle of both parasites consists of five larval stages developing into both an intermediate host (embryo-infective L_3 larva) that also acts as vector and into a definitive vertebrate host (L_3-adult stage). Adult *D. immitis* worms occur in the pulmonary arteries and right heart chambers while *D. repens* is found mainly in subcutaneous tissues. Adult female worms release embryos (microfilariae) into the blood. The intermediate hosts are mosquitoes of the family Culicidae that become infected when feeding on blood from a microfilaraemic host. *Culex pipiens* and *Aedes albopictus* are mostly implicated as natural vectors of *Dirofilaria* in Italy (Genchi et al. 1992, Cancrini et al. 2007). *Ae. albopictus*, which was mainly considered a problem of a serious biting nuisance for humans at the beginning of its introduction into Europe, has currently changed its behavioral patterns from mainly exophylic to partially endophylic. Furthermore, its generalistic feeding-behavior and urbanization (Valerio et al. 2008) has increased the probability of transmission of canine, feline and human dirofilariosis in the urban environment (Pietrobelli 2008).

3. *Dirofilaria* Epidemiology and Zoonotic Impact

Many southern European countries are endemic for *Dirofilaria* infections. Until recently, the interest concerning dirofilariosis has been focused mostly on *D. immitis* because of its pathogenicity (for a review see McCall et al. 2008). However, the increasing spread of *D. repens* towards eastern and northern European countries (Svobodova et al. 2006, Fok 2007, Overgaauw and van Dijk 2009) and its role as a zoonotic agent (Pampiglione et al. 2001, Szénási et al. 2008) have renewed the interest for this species. Both *Dirofilaria* species are zoonotic, and the human infections caused by *D. repens* are increasing in Europe (Raccurt 1999, Pampiglione and Rivasi 2000). Usually, the parasites do not develop to adult stage in humans, although at least three cases of microfilaraemic zoonotic infections have been reported in Europe (Nozais et al. 1994, Petrocheilou et al. 1998, Kucsera 2008, personal communication) and one in Iran (Negahban et al. 2007).

Transmission of dirofilariosis is dependent on the presence of: (*i*) sufficient numbers microfilaraemic dogs (microfilaraemia is usually absent in cats and their role as reservoirs is not relevant), (*ii*) susceptible mosquitoes, and (*iii*) a suitable climate to permit extrinsic incubation of *Dirofilaria* in the mosquito intermediate host. Although infected mosquitoes might be limited in their range and movement, the movement of dogs is not similarly constrained and the easing of restrictions on the movement of pets throughout Europe may increase the risk of spreading filarial infections (Trotz-Williams and Trees 2003). Thus, the movement of dogs across Europe, together with climatic changes, have caused an increase in the geographical range of *Dirofilaria* infections.

Temperature, precipitation, and relative humidity are the main factors that determine the abundance of mosquitoes and the prevalence of mosquito-borne diseases such as *Dirofilaria* infection. The optimum temperature for mosquito development of tropical/temperate species is 25–27 °C (Monteiro et al. 2007, Swain et al. 2008), and there is a strong temperature dependence for the development of the parasites within the mosquito vectors (Kalluri et al. 2007). Climate-based forecast systems usually employ the concept of growing degree days, i.e. 1 degree day occurs when the mean temperature for the day is 1 °C above the threshold temperature. For *Dirofilaria* infections, climate-based models that determine the effect of temperature on the extrinsic incubation of larval stages are based on the study of Fortin and Slocombe (1981). The rationale of this model is that climate dictates the seasonal occurrence of *Dirofilaria* transmission, and there is a threshold of about 14 °C below which development will not proceed. The authors demonstrated that at 30 °C, development of *D. immitis* microfilariae to infective L3 larvae was completed in 8–9 days in the mosquitoes. This increased to 10–14 days at 26 °C, 17 days at 22 °C, and 29 days at 18 °C. For *D. repens*, the development times of microfilariae to the infective stage at the different temperatures are quite similar: 8–13 days at 28–30 °C, 10–11 days at 26 °C, 16–20 days at 22 °C (Webber and Hawking 1955, Coluzzi 1964, Bain 1978, Cancrini et al. 1988). In *Ae. albopictus* the development from the microfilaria stage to infective larvae takes 14–18 days at 26 °C for *D. immitis* and 16–18 days for *D. repens* (Cancrini et al. 1995). The seasonal transmission model (Slocombe et al. 1989, Lok and Knight 1998) assumes a requirement of 130 *Dirofilaria* Development Units (DDUs) for larvae to reach infectivity and a maximum life expectancy of 30 days for a vector mosquito. Based on these assumptions, climate-based models have been used in order to predict the occurrence and seasonality of *Dirofilaria* in Europe (Genchi et al. 2005), in UK (Medlock et al. 2007) and Argentina (Vezzani and

Carbajo 2006). In a recent study (Genchi et al. 2009), a threshold value of 130 cumulative DDUs was accepted only if it was reached in 30 consecutive days, and the data was interpolated utilizing the Linear Kriging function of a Geographical Information System to calculate the number of *Dirofilaria* generations. The input of the model was based on the average temperature of the last 15 years, for a total 5,475 temperature measures per station and over 19,000,000 values processed. The output of this model was predictive maps which assessed the duration of the *Dirofilaria* transmission risk period and monthly maps showing the stations that reached 130 DDUs. Most stations located in south, central and eastern Europe have reached 130 DDUs at least once in the studied years (Genchi et al. 2009). To note, previously this model (Genchi et al. 2005) had correctly predicted the spreading of *Dirofilaria* infections in some eastern European countries. Indeed, studies from Hungary (Fok 2007), the Czech Republic (Svobodova et al. 2006), Slovakia (Miterpáva et al. 2008) and northern Serbia (Tasi et al. 2008) confirmed that areas formerly free of *Dirofilaria* infection are now endemic. However, there is still an open question: why *D. repens* is spreading more rapidly than *D. immitis*? Actually, the most recent studies have reported *D. repens* in animals and humans mainly from northern European countries (i.e.: northeastern Austria: Deplazes, P., 2009, personal communication; southern Germany: Hermosilla et al. 2006, Sassnau et al. 2009, the Netherlands: Overgaauw and van Dijk 2009) and even when *D. immitis* was found, *D. repens* showed a higher prevalence (i.e.: northern Serbia: Tasi et al. 2008). It is important to note that human *D. repens* infections clearly show the same trend: the more recent and severe cases have been reported in northeastern countries such as Hungary (Szénási et al. 2008), the Slovak Republic (Babal et al. 2008), Polonia (Zarnowska-Prymek et al. 2008) and Russia (Kramer et al. 2007). In Europe, zoonotic *Dirofilaria* infections are caused by *D. repens* and a critical analysis of 28 human cases attributed to *D. immitis* diagnosed in Europe (compared to more than 450 cases of *D. repens* infection) have recently been critically revised by Pampiglione et al. (2009). The authors concluded that "there is no proof demonstrating with certainty that Old World-*D. immitis* plays a pathogenic role in humans". However, *D. immitis* has an important role in zoonotic infections in the Americas, where *D. repens* is absent. Pampiglione's hypothesis was that "perhaps twin *D. immitis* populations exist with different genotypes". However, this hypothesis is likely not valid, as it has been demonstrated that genetic identity exists among *D. immitis* worms from different geographical locations around the world (Bazzocchi et al. 2000, Huang et al. 2009). Even though *D. repens* is able to grow in the same mosquito species at the same temperature and humidity as *D. immitis* under laboratory conditions, and has the same developmental time from the microfilarial stage to the infective larva, factors inherent to vectors in the field can likely influence the complex mechanisms of the mosquito-parasite relationship, affecting larval survival and transmission.

4. Conclusion

While nobody would deny the sensitivity of mosquitoes and mosquito-borne disease systems to climatic factors that largely determine their geographical distributions, other significant factors are probably driving the recent temporal patterns in the epidemiology of a mosquito-borne disease such as dirofilariosis. Identifying the causal factors correctly will allow appropriate action and more reliable predictions in the future. Because of the high risk of *D. repens* human infections in Europe, human and veterinary health authorities should advise for an appropriate prevention of the infection in companion animals.

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Festakt zur Ernennung der Deutschen Akademie der Naturforscher Leopoldina zur Nationalen Akademie der Wissenschaften

Ceremony to Mark the Nomination of the German Academy of Sciences Leopoldina to the National Academy of Sciences

Nova Acta Leopoldina N. F., Bd. *98*, Nr. 362
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Die Deutsche Akademie der Naturforscher Leopoldina wurde am 14. Juli 2008 im Rahmen eines Festaktes in Halle zur Nationalen Akademie der Wissenschaften ernannt. Damit erhielt Deutschland – wie andere europäische Länder oder die USA – eine Institution, die Politik und Gesellschaft wissenschaftsbasiert berät und die deutsche Wissenschaft in internationalen Gremien repräsentiert. Der Band dokumentiert den Festakt mit der Übergabe der Ernennungsurkunde durch die Vorsitzende der Gemeinsamen Wissenschaftskonferenz und Bundesministerin für Bildung und Forschung Annette SCHAVAN. Er enthält die Reden von Bundespräsident Horst KÖHLER, Sachsens-Anhalts Ministerpräsident Wolfgang BÖHMER und Leopoldina-Präsident Volker TER MEULEN sowie den Festvortrag „Rolle und Verantwortung nationaler Akademien der Wissenschaften“ von Jules A. HOFFMANN, Präsident der *Académie des sciences*, Paris. Der Aufbau einer Nationalen Akademie ist ein richtungsweisender Schritt für die deutsche Forschungslandschaft, da für den kontinuierlichen Dialog von Wissenschaft und Politik eine solche Einrichtung erforderlich wurde. Der Publikation ist eine DVD mit dem Mitschnitt der Festveranstaltung beigefügt.

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Climate Change, Ticks and Tick-borne Diseases with Special Emphasis on Europe, *Ixodes ricinus*, *I. persulcatus* and Tick-borne Encephalitis (TBE)

Jochen Süss (Jena)

With 1 Table

Abstract

By nature, there is a close association between alterations in climate and the biology and ecology of ticks – and, thus, the spread and incidence of tick-borne diseases. The quality and quantity of these highly complex processes and their manifold interactions are largely unknown, although there are many examples reflecting these interrelations. The northward spread of ticks in Europe, the expansion of tick habitats to higher altitudes accompanied by the development of natural foci of these zoonotic diseases in so far pathogen-free zones are examples of these developments. Since direct and indirect anthropogenic influences affect these developments, intensive research is required to gain enough insight into these interactions to establish concepts for the control of tick-borne diseases.

Zusammenfassung

Klimaveränderungen, Biologie und Ökologie von Zecken und damit auch die Verbreitung und die Inzidenz von durch Zecken übertragenen Krankheiten stehen naturgemäß in einem sehr engen Verhältnis. Die vielfältigen Interaktionen sind dabei weitgehend unbekannt. In den letzten Jahren waren in Europa eine Nordausbreitung von Zeckenbiotopen und ein Vordringen von Zecken in größere Höhen in den Gebirgen, begleitet von der Entwicklung von Naturherden zoonotischer Erkrankungen in bisher erregerfreie Zonen, festzustellen. Da direkte und indirekte anthropogene Einflüsse dieses Geschehen erheblich beeinflussen, besteht ein erheblicher Forschungsbedarf zur Erkennung dieser Zusammenhänge und zur Entwicklung von Konzepten zur Zurückdrängung der durch Zecken übertragenen Erkrankungen auf wissenschaftlicher Basis.

The existence of climate change and global warming has become accepted scientific knowledge (Gerstengarbe and Werner 2008). The causes, however, are still discussed.

Intensive research is conducted on the influence of climate change on infectious, especially vector-borne diseases, and results have been presented, e.g. at the IXth International Jena Symposium on Tick-borne Diseases “Climate Change and Tick-borne Diseases”, Jena 2007 (Süss and Kahl 2008), the conference “Vector-borne Diseases: Impact of Climate Change on Vectors and Rodent Reservoirs”, Berlin 2007 (Habedank et al. 2008), and the conference “Climate Change and Infectious Diseases”, Greifswald 2009. The controversial discussions demonstrate that no final conclusions are to be expected in the near future.

This also applies to the spread of tick populations and the increase in tick-borne diseases (Lindgren and Jaenson 2006). There are sufficient data which provide evidence for the increase in disease cases and the spread of tick populations (Lindgren et al. 2000, Jääskeläinen et al. 2006, Süss 2008). However, it is still debated whether there is a direct or indirect relationship between these two phenomena. For certain regions (e.g. Russia, the Baltic states) Sumilo et al. (2007) and Randolph (2008), as well as Korenberg (2009), identify anthropogenic influences as the main cause for the increasing incidence of TBE, whereas others rather see climate change as the crucial factor (Gray et al. 2009). Critical analysis of the available literature, as well as our own results shows that, in addition to other factors, climate and anthropogenic changes are responsible for the increase in the incidence of tick-borne diseases (Lindgren and Jaenson 2006). Alterations in climate are responsible for changes in the geographic occurrence as well as the local density of tick populations, and for differences in the development of the individual stages. However, the extent to which the individual factors are responsible is unknown and so are possible co-factors.

Definition of the influence of individual effects of climatic factors on ticks, pathogens, vectors and hosts is crucial, but far from being achieved. In addition, there are the direct and indirect anthropogenic factors which influence incidence and prevalence of tick-borne diseases. These may be of political, economic, social or ecological origin.

Here, we present some results which support an association between global warming, the spread of vectors and the occurrence of tick-borne diseases.

The impact of climate change (global warming, increased precipitation) is stronger in the Northern hemisphere, i.e. in those regions where the *Ixodidae* (*I. pacificus*, *I. scapularis*, *I. ricinus*, *I. persulcatus*, *I. ovatus*) which are of special importance for pathogen transmission to humans and animals, have their habitats. In Europe, more than 90 % of tick-borne diseases are transmitted by hard ticks, in Central Europe the most important is *Ixodes ricinus*, the castor bean tick, in Eastern Europe and the Far East *I. persulcatus*, the Taiga tick. In Europe, the most common diseases following tick bites are Lyme Disease (LD) and TBE. Although epidemiological data are not fully reliable and many disease cases are not registered or even noticed, 100,000 to 150,000 clinical cases of LD per year are estimated to occur in Europe. In contrast to TBE, LD is also endemic in the New World.

Much more information is available on the epidemiology of TBE. At present, TBE is endemic in 27 European countries. In 16 countries – among them 13 EU member states – the disease is notifiable. For 19 European countries, more or less reliable data are available starting from the mid-1970s. Between 1990 and 2009, 169,937 TBE cases were documented in Europe, i.e. an average of 8,497 cases per year. Omitting Russia, there were 56,301 TBE cases, i.e. an average of 2,815 cases per year (Süss 2008). Furthermore, TBE virus circulates in China, Mongolia, Korea, Kazakhstan, Kyrgyzstan, and Japan.

However, the number of unreported cases is assumed to be high, and case definition and reporting conditions differ between individual countries. Therefore, the introduction of a uniform TBE case definition as a basis for comparable epidemiological data and databases. Thus, the following definition is proposed:

- Clinical picture: Typically a biphasic course with flu-like symptoms during the first phase, and signs of meningitis, encephalitis or radiculitis or mixed forms of these symptoms after an asymptomatic period without fever.
- Antibody-detection: Detection of TBEV-specific antibodies (specific IgM and IgG antibodies) in the serum; detection of TBEV-specific antibodies in the cerebrospinal fluid (CSF) – increased CSF serum index, detection of specific IgM and IgG in the CSF.
- Cross reactive antibodies against other flaviviruses (to which the patient might have been exposed) or vaccinations – verification: ELISA test versus neutralization test.
- Moderate pleocytosis.

- Epidemiology: history, vaccination status, tick bite, exposure in known risk areas, raw milk in risk areas.

Moreover, the definition of risk areas (risk districts) currently applied in Germany (*RKI* 2007) based on the number of confirmed TBE cases from 2002 to 2006 in the district or in the district region (the given district plus all the adjacent districts) (significantly) higher than the number of expected cases when the incidence is 1 to 100,000 should be replaced by a uniform definition on a European level for a TBEV endemic area defined as an area with TBEV circulation between ticks and vertebrate hosts based on the detection of TBEV or the detection of autochthonous infections in animals or humans within the last 20 years (Tab. 1) (Süss et al. 2010). Knowledge of TBEV endemic areas and risk factors should be the basis for a recommendation regarding TBE vaccination.

Tab. 1 Definition of Risk Areas

Risk areas are TBEV endemic areas.
The risk of being infected in such an area depends on many factors, including seasonal and outdoor activities.
A TBEV endemic area is an area with TBEV circulation.
It has been defined as an area with TBEV circulation between ticks and vertebrate hosts inferred by the detection of TBEV or the detection of autochthonous infections in animals or humans within the last 20 years. Knowledge of TBEV endemic areas and risk factors should form the basis for a recommendation with regard to TBE vaccination.

Risk maps are not 100 % accurate due to the technical difficulties of proper identification of the site of a documented infection, e.g. because of mobility of humans and other hosts (e.g. birds, deer) and endemic foci can shift within a given area. However, the proposed definition takes into account relevant factors, such as e.g. the vaccination rate in the population and the structure of natural foci.

Factors which determine the life and development of *I. ricinus* are weather conditions and the availability of (competent) hosts. *I. ricinus* can use virtually any vertebrate host for its blood meal, whereas for persistence of the pathogen in a natural focus the availability of competent hosts is decisive. Important factors are humidity, which for *I. ricinus* should be > 85 %, temperature and microclimate. This is not surprising, as ticks spend almost their entire life within the habitat. In comparison, the time spent on the blood meal, as a rule 3 times for females and 2 times for males, is extremely short.

For the coming decades an increase of the average temperatures in the Northern temperate climate zone of Europe by 1.5 to 2.5 °C has been predicted, a value which has been corrected upwards repeatedly over the past few years (Gerstengarbe and Werner 2008). In combination with increased summer precipitations this may be advantageous for the development of ticks permitting a northward spread of *I. ricinus* and *I. persulcatus*.

As far as survival at cold temperatures is concerned, *I. ricinus* is not unsusceptible, especially to solid blankets of snow in the winter. After an adaptation phase in the winter, this tick species can survive temperatures of –14.4 °C to –18.9 °C for a day; the longer these cold spells last, however, the more ticks will die (Gray et al. 2009). Further crucial factors are humidity and the chance to retreat to more humid places to escape fatal dehydration. Unfed nymphs and diapausing engorged larvae and nymphs are especially sensitive.

Besides their ability to survive extreme conditions within the upper and lower range of tolerance, more emphasis is placed on the temperature profile over a longer time period of the year which permits the development of the individual stages (as a matter of course only if the other conditions are fulfilled, e.g. availability of hosts, humidity etc.).

Many observations made over the past few years with regard to the spread of tick populations and/or the development of natural foci of TBE easily fit into this picture.

- Spread of tick populations in Northern and Central Sweden, recorded between 1980 and 1995 (Lindgren et al. 2000, Lindquist and Vapalahti 2008). Lindgren et al. (2000) show an association with climatic conditions, as there was a significant increase in the number of days with favorable weather for the development of *I. ricinus* within this area and time period. Of special importance was the decrease in the number of days with temperatures of –12 °C and below.
- The long-term investigations of Bormane et al. (2004) in Latvia demonstrated a significant increase of the population density of *I. ricinus* and *I. persulcatus* from 1991 to 2002 within a time period of increasing average temperatures. This development can hardly be explained by anthropogenic influences.
- The almost classical establishment of a TBE risk area at the southern tip of Norway from 1998 to present in an area where TBE had not been detected prior to 1998 with an increasing number of cases (1998–2008: 40 autochthonous TBE cases) (Skarpaas et al. 2004). In Germany, such a focus has developed e.g. in the Odenwald since 1992.
- The westward spread of TBE risk areas along the Alpine valleys in Austria (Heinz, personal communication), two new TBE risk areas were identified recently, 100 km south of the Arctic circle, so far the northern most TBE risk areas (Jääskeläinen et al. 2010).
- The northernmost detection of *I. persulcatus* in Finland, approx. 300 km south of the polar circle (Jääskeläinen et al. 2006).
- The northward spread of *Dermacentor reticulatus* in Germany which has also caused a northward spread of canine babesiosis (Dautel et al. 2006). Comparable developments have been observed in Hungary, Switzerland and the Netherlands. Comparable observations at higher average temperatures were made by Eisen (2008) in Colorado, USA, with *D. andersoni* as study object.
- The northward spread of TBE risk areas and individual cases of disease in Germany. The TBE risk districts in Germany have continued to spread. In 1998, 63 of the 440 urban and rural districts were considered to be TBE risk areas, in 2009 as many as 136 (*RKI* 2010). However, there is also evidence for extinction of TBE risk areas (Klaus et al. 2009).
- It could be shown that in mild winters a year-long host search activity of *I. ricinus* is possible (Dautel et al. 2008).

Similar conclusions can be drawn with regard to the detection of *I. ricinus* at higher altitudes in the mountains:

- Until 1979/80 there was scientific consensus that *I. ricinus* occurred up to an altitude of 700 to 800 m above sea level and that it was also able to complete its developmental cycle and contain pathogens at these altitudes.
- Czech scientists were able to prove that e.g. in the Krkonoše Mountains *I. ricinus* carrying TBE virus has spread to altitudes of up to 1200 m above sea level (Daniel et al. 2003, Materna et al. 2005, 2008).

- Recent investigations in Austria demonstrated *I. ricinus* at over 1500 m above sea level in the Alps, in the Vorarlberg region, with concurrent TBE disease at these altitudes (Holzmann et al. 2009).

Other factors besides climate change can also cause changes in the epidemiology of tick-borne diseases. First, the awareness of physicians and patients, media and public in general has been raised by research, publications and education measures which also results in an increase of reported cases. Second, a more profound knowledge and improved diagnostics, the availability of reporting systems and their gradual improvement also lead to increased incidences.

A significant factor is the increased use of natural areas by man for a multiplicity of activities which *per se* increases the risk of exposure to ticks (Süss 2008a, b, Süss et al. 2008). In the developed industrial countries of Europe the reduction of work hours has increased leisure time which is often spent in natural areas with hiking, sports activities, mushroom forays, etc. The same effects are caused by the high unemployment rate in some countries where part of the available leisure time is spent in natural areas to improve food supply and/or economic situation. The increased life expectancy of the population, often in combination with a good health status, causes a significant prolongation of the active life span which to a considerable extent is spent traveling and engaging in outdoor activities. In the comparatively wealthy industrial countries other factors are of importance, however, the result is the same. While the costs for gas and oil are increasing significantly, many people are no longer willing or able to pay for these and thus return to the classical fuels, e.g. wood. Gathering wood can also lead to a higher exposure rate to tick bites.

In countries with lower economic standards, people gather mushrooms, berries and fire wood to improve their economic situation. This also leads to a higher exposure to ticks. Political factors also play a role. After the collapse of the communist governments and the withdrawal of the Russian troops from the Eastern European and Baltic states, large military off-limits areas have become accessible, which in some cases are strongly contaminated with infected ticks. These natural areas were attractive due to the resources they offered. This too caused an increase in the number of disease cases after tick bites.

The drastic changes in agricultural production also led to higher exposure rates. An increase in grazing and other forms of nature-oriented animal husbandry and a decrease of indoor animal production has been observed. Agrotourism and the consumption of non-pasteurized milk in TBE risk areas may cause alimentary TBE via oral ingestion of the virus.

EU subsidies for set-aside land leads to the formation of fallow land which subsequently overgrows with weeds and bushes. These areas provide more favorable living conditions for mice, the main host of ticks, which as a consequence can lead to an invasion or reproduction of these vectors. In Central Europe, pesticides are used more reluctantly or with more caution, which improves the ecological situation but also living conditions of ticks. The emission of pollutants from industrial facilities is being further reduced in Central Europe which also creates more favorable ecological conditions for ticks. Pesticides, which are less toxic or permit a more specialized and targeted use, have been developed and produced.

Korenberg (2009) showed that from 1950 to 2008 in Russia two peaks of TBE incidence occurred, namely in the years 1955–1965 (incidence approx. 3 to 4/100,000 inhabitants) and 1993–2002 (incidence approx. 5 to 7/100,000 inhabitants). These were interrupted by strongly reduced values (1970–1990, incidence approx. 1 to 2/100,000 inhabitants and approx. 2005 to 2008, incidence 2 to 3/100,000 inhabitants). Similar epidemiological data are available for Germany. Peaks of the reported number of disease cases were registered in the years 1994/1995 and 2005/2006. These were followed by a strong reduction in the years 2007 to 2009. Comparable tendencies were observed in the Czech Republic, Lithuania, Poland, Slovakia, Slovenia, and Switzerland. Considering that the ecological, economic and political situation in these countries is very different, this is an astonishing situation which shows that neither climate changes nor anthropogenic influences alone can be responsible.

A metaanalysis of the causes of the global increase of emerging infectious diseases from 1940 to 2004 (Jones et al. 2008) demonstrates that this increase is definite. The emergence of these diseases is thought to be driven largely by socio-economic, environmental and ecological factors and the majority of these diseases are zoonoses, mainly vector-borne diseases (*WHO* 2004) (60.3 %). This metaanalysis again is not able to determine individual factors for this tendency. In the future it will become more and more important to focus on very detailed individual analyses to gradually clarify this complex issue.

Intensive research will be required over the coming years to obtain data on the influence of climate change on ticks and tick-borne diseases. This will be decisive for the development of scientifically founded control strategies and for the successful control of tick-borne diseases.

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Gedenken an die Leopoldina-Mitglieder, die in Konzentrationslagern des nationalsozialistischen Regimes zu Tode kamen

Einweihung einer Gedenkstele am 1. Oktober 2009 in Halle (Saale)

Nova Acta Leopoldina N. F. Supplementum Nr. *22*
Herausgegeben vom Präsidium der Deutschen Akademie der Naturforscher Leopoldina
(2010, 24 Seiten, 16 Abbildungen, 5,00 Euro, ISBN: 978-3-8047-2808-0)

Zum Andenken der Mitglieder der Deutschen Akademie der Naturforscher Leopoldina, die in nationalsozialistischen Konzentrationslagern oder an den Folgen der Lagerhaft zwischen 1942 und 1945 ums Leben kamen, wurde in Halle im Oktober 2009 eine Gedenkstele enthüllt. Der vorliegende Band dokumentiert die Veranstaltung und setzt damit auch das Bestreben der Akademie fort, in Publikationen und Vorträgen die Geschichte der Leopoldina in den Jahren zwischen 1933 und 1945 aufzuarbeiten. Dem kulturellen Gedächtnis der Leopoldina wird mit der Gedenkstele ein weiterer Mosaikstein hinzugesetzt, weil die Entstehung, die Entwicklung und die Bewahrung einer Erinnerungskultur zu den Grundlagen unserer Freiheit und damit zu den Grundlagen der Demokratie in Deutschland gehören. Die Beiträge sind in deutscher und englischer Sprache verfasst.

Wissenschaftliche Verlagsgesellschaft mbH Stuttgart

Nova Acta Leopoldina NF *111*, Nr. 381, 87–89 (2010)

Impact of Climate Change on Leishmaniasis

Paul D. Ready (London, UK)

Abstract

Leishmaniasis (or "leishmaniosis") is a mammalian disease caused by infections of the parasitic protozoan *Leishmania* (Kinetoplastida, Trypanosomatidae) (vector: sand flies). Most natural transmission is by the bite of sand flies (Diptera, Phlebotominae), specifically of *Phlebotomus* species (Old World) and *Lutzomyia* species (New World). At least 20 *Leishmania* species cause cutaneous and/or visceral human leishmaniasis, mostly in the tropics or subtropics. In recent decades, endemic regions have spread and prevalence has increased.

Zusammenfassung

Die Leishmaniose ist eine Säugetiererkrankung, die durch die Infektion mit dem parasitischen Protozoon *Leishmania* (Kinetoplastida, Trypanosomatidae) hervorgerufen wird (Vektor: Sandmücken). Der überwiegende Anteil der Übertragungen erfolgt durch den Biss der Sandmücken (Diptera, Phlebotominae), besonders von *Phlebotomus*-Arten (Alte Welt) und *Lutzomyia*-Arten (Neue Welt.). Mindestens 20 *Leishmania*-Arten verursachen kutane und/oder viszerale Leishmaniose, meist in den Tropen und Subtropen. In den letzten Jahrzehnten haben sich die Endemiegebiete ausgeweitet und die Verbreitung vergrößert.

Spatio-temporal modeling of the distribution of the leishmaniases and their sand fly vectors has been reviewed recently in relation to climate change (Ready 2008). Leishmaniasis is endemic in the Mediterranean region of Europe, and its risk of spreading to adjoining and nearby temperate areas has also been reviewed recently (Ready 2010).

Leishmaniasis (or "leishmaniosis") is a mammalian disease caused by infections of the parasitic protozoan *Leishmania* (Kinetoplastida, Trypanosomatidae). Most natural transmission is by the bite of sand flies (Diptera, Phlebotominae), specifically of *Phlebotomus* species (Old World) and *Lutzomyia* species (New World). *Leishmania* are ingested by blood-feeding female sand flies, which then transmit the infective promastigote stages (often "metacyclics") at a subsequent blood meal (Bates 2007). These are phagocytozed by the mammalian host's macrophages or related cells, within which they transform to amastigotes and often provoke a cutaneous ulcer and lesion at the site of the bite ("cutaneous leishmaniasis"). The infection can spread to produce other lesions in the skin (including "diffuse cutaneous leishmaniasis"), the mucosa ("muco-cutaneous leishmaniasis") and the spleen, liver and bone marrow ("visceral leishmaniasis", which is usually fatal if untreated). Fewer than 50 of the ca. 1000 species of sand flies are vectors of leishmaniasis worldwide (Killick-Kendrick 1990, Ready 2008), and this is explained by the inability of some sand fly species to support the development of infective stages in their guts, and/or a lack of ecological contact with reservoir hosts. At least 20 *Leishmania* species cause cutaneous and/or visceral human leishmaniasis, mostly in the tropics or subtropics. In recent decades, endemic regions have spread and prevalence has increased (Desjeux 2004, *WHO* 2009). Declaration is compulsory in only 32 of the 88 countries where 350 million people are at risk, and the disability-adjusted life years (Dalys) are estimated at 2.4 million (Desjeux 2004).

Many transmission cycles are rural zoonoses, so the earlier ecological studies of leishmaniasis were often based on "landscape epidemiology". More recently, fluctuations in the annual incidence of visceral leishmaniasis in Brazil (Franke et al. 2002) and of American Cutaneous Leishmaniasis (ACL) in Costa Rica (Chaves et al. 2008) have been linked statistically to the El Niño Southern Oscillation Cycle, with the latter authors demonstrating the importance of social factors and land cover. Ecological niche models have also been explored for ACL (Peterson and Shaw 2003), but they pose difficulties because of the number of assumptions. Recent statistical modeling has not always produced novel conclusions, exemplifying the difficulty of applying spatial models outside the original geographical region (Ready 2008). More basic research is needed before tackling other climate-change scenarios, including the emergence in northern Europe of leishmaniasis caused mainly by *Leishmania infantum*. This is a task of the leishmaniasis sub-project of the EU FP6 project "Emerging Diseases in a changing European eNvironment" (Eden: http://www.eden-fp6project.net/), as outlined in the presentation at Greifswald.

Dogs are widespread reservoir hosts of veterinary importance, and the economic and public health significance of canine leishmaniasis (CanL) caused by *L. infantum* is well established in both the Mediterranean region of Europe and in many of the drier parts of the neotropical region of Latin America. There is a published analysis of the northern range extension of CanL and their vectors in Italy (Maroli et al. 2008), but an association with climate change was not demonstrated. After 1945, socio-economic changes at first favored a reduction in "infantile visceral leishmaniasis" (caused by *L. infantum*) in southern Europe, including better nutrition, better housing and a reduction in the rural population. Then there were changes that increased contact with Mediterranean vectors, including more holidays and second homes for northern Europeans, and fundamental assumptions about leishmaniasis epidemiology were challenged (Ready 2008, 2010). Firstly, HIV/*Leishmania* co-infections were recorded worldwide and widespread needle transmission of *L. infantum* was inferred in southwest Europe. Secondly, leishmaniasis became more apparent in northern latitudes where sand fly vectors are either absent or present in very low densities, such as in eastern North America (Duprey et al. 2006) and Germany (Harms et al. 2003, Mettler et al. 2005). Most infections involve CanL, and this is most likely explained by dog importation from, or travel to, endemic regions, followed by vertical transmission from bitch to pup or horizontal transmission by biting dogs. Increasing dog travel in the Mediterranean region and non-vector transmission probably explains autochthonous cases of CanL in Germany (Ready 2008). Vector transmission in Germany should be investigated by experimentally testing the vectorial competence of *Phlebotomus* (*Transphlebotomus*) *mascittii*, because this sand fly is now widespread in northern France, Belgium and Germany (Naucke and Schmitt 2004, Depaquit et al. 2005). However, low human-biting rates and autogeny (Ready 2010) do not suggest that it has any epidemiological importance.

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Neue Bilder vom Alter(n)
Wettbewerb und Ausstellung

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Die Menschen leben länger, und der Anteil alter Menschen in der Gesellschaft nimmt zu – das macht den demographischen Wandel zu einem brisanten gesellschaftlichen Thema, denn „Altern“ berührt in besonderer Weise das Leben jedes Einzelnen und unsere Gesellschaft, ihren Wohlstand und ihre Verfasstheit. Die Leopoldina hat sich daher über einen längeren Zeitraum mit dem „Altern in Deutschland“ beschäftigt. Das Altersbild und die verfügbaren Alternsrollen sind vielfach noch durch eine traditionelle Sichtweise geprägt. Die anstehenden Veränderungen erfordern jedoch einen veränderten Blickwinkel. Der Katalog zeigt Bilder des Alterns, die sich den neuen Herausforderungen und Potentialen des Älterwerdens des Einzelnen und der Gesellschaft auf verschiedene Weise stellen. Er ergänzt damit im Dialog mit der Gesellschaft die wissenschaftlichen Veröffentlichungen der Akademie zur Alternsproblematik um einen künstlerischen Bezug.

Wissenschaftliche Verlagsgesellschaft mbH Stuttgart

Impact of Climate Change on Infectious Diseases of Animals (incl. Zoonoses)

Nova Acta Leopoldina NF *111*, Nr. 381, 93–98 (2010)

Impact of Climate Change on Orbivirus Infection

Franz Josef Conraths, Jörn Martin Gethmann, Bernd Hoffmann, Martin Beer, Matthias Kramer, and Christoph Staubach (Wusterhausen and Greifswald-Insel Riems)

With 1 Figure

Abstract

Important orbiviruses include Bluetongue Disease Virus and African Horse Sickness Virus. Bluetongue disease can affect all ruminants, including sheep, cattle, deer, goats, and camelids (camels, llamas, alpacas, guanaco and vicuña). Cattle are believed to be the main mammalian reservoir of the virus, although sheep are most severely affected with case-fatality rates of up to 100 % in some flocks. To date, 24 distinct serotypes of Bluetongue Disease Virus (BTV) have been described. The main vector of BTV in Africa is *Culicoides imicola*, which has spread from North Africa to large regions of the European part of the Mediterranean basin. Climate change might have facilitated this spread. However, in 2006 an outbreak of BT disease, serotype 8, occurred simultaneously in Belgium, the Netherlands and Germany in the absence of *C. imicola*. Detailed epidemiological analysis revealed that other Palaearctic biting midges, in particular *C. obsoletus* sensu stricto, serve as vectors for Bluetongue disease in Germany. The warm summer in 2006 may have helped BTV to spread after the initial introduction. In 2007, there was no evidence that temperature had an effect on the spread of BT. These findings suggest that, after initial introduction of an orbivirus, increased temperature may trigger an epidemic and lead to lasting, perhaps irreversible establishment of a disease.

Zusammenfassung

Das Virus der Blauzungenkrankheit (BTV) und das Virus der Afrikanischen Pferdepest sind bedeutende Vertreter der Gattung Orbivirus. BTV kann sowohl Wiederkäuer wie Schafe, Rinder, Hirsche und Ziegen als auch Kamele (Trampeltiere, Dromedare, Lamas, Alpacas, Guanakos und Vikunjas) infizieren. Rinder gelten als Hauptsäugetierreservoir, wobei Schafe mit einer Letalität von bis zu 100 %, die in einigen Herden beobachtet wurde, schwerer betroffen sind. Bisher sind 24 BTV-Serotypen bekannt. BTV wird durch Mücken (Gnitzen der Gattung *Culicoides*) übertragen. Der Hauptvektor in Afrika, *Culicoides imicola,* hat sich mittlerweile über große Bereiche des europäischen Mittelmeerraums verbreitet. Es wird vermutet, dass klimatische Veränderungen bei dieser Ausbreitung eine wichtige Rolle gespielt haben. 2006 kam es erstmals zu einem Ausbruch der Blauzungenkrankheit, verursacht durch den BTV-Serotyp 8, nördlich der Alpen. BTV-8 wurde gleichzeitig in Belgien, den Niederlanden und Deutschland diagnostiziert, und zwar in Abwesenheit des aus dem Mittelmeerraum bekannten Vektors *C. imicola*. Eine genaue Analyse der epidemiologischen Situation zeigte, dass andere, paläarktisch verbreitete Gnitzen, insbesondere *C. obsoletus* sensu stricto, in Deutschland als Vektoren für BTV fungierten. Der heiße Sommer im Jahr 2006 könnte bei der Verbreitung von BTV nach der initialen Einschleppung eine Rolle gespielt haben. 2007 konnten allerdings keine Temperatureinflüsse auf die Ausbreitung der Blauzungenkrankheit beobachtet werden. Die Ergebnisse der Analysen erlauben den Schluss, dass erhöhte Temperaturen eine Orbivirus-Epidemie nach erfolgtem Ersteintrag auslösen und zu einer dauerhaften, eventuell irreversiblen Etablierung der Seuche führen können.

1. Introduction

Orbiviruses belong to the family *Reoviridae*. They possess segmented genomes of double-stranded RNA, characteristic virion morphology and structure, and are pathogens of vertebrate hosts transmitted by arthropod vectors. Important species of the genus Orbivirus include Bluetongue Disease Virus (BTV) and African Horse Sickness Virus (AHSV). Bluetongue disease can affect all ruminants, including sheep, cattle, deer, goats, and camelids (camels, llamas, alpacas, guanaco and vicuña). Cattle are believed to be the main mammalian reservoir of the virus, although sheep are most severely affected with case-fatality rates of up to 100 % in some flocks (Elbers et al. 2008a, b). To date, 24 distinct serotypes of BTV have been described. A closely related virus recently discovered in goats in Switzerland (Toggenburg Virus) may represent a new serotype of BTV (Hofmann et al. 2008) Bluetongue disease is characterized by changes to the mucous linings of the mouth and nose and the coronary band of the foot. Clinical signs include fever, excessive salivation, swelling of the lips, face and tongue, nasal discharge, lacrimation, haemorrhages, udder lesions, coronitis and lameness and cyanosis of the tongue (Erasmus 1975, Elbers et al. 2008a, b). In particular in cattle and goats, the symptoms can be mild; the infection may even remain clinically inapparent.

The main vectors of the virus are various species of *Culicoides* biting midges (Du Toit 1944). *Culicoides* (Diptera: Ceratopogonidae) are small insects, 1–3 mm in size. More than 1,300 species are known worldwide. Several are obligate haemotaphagous; they attack mammals (including humans), birds, reptiles and even other insects. Approximately 120 species are known to exist in Europe (*Anonymus* 2007)

Bluetongue disease was first described in South Africa but has since been detected in most countries in the tropics and sub-tropics. Since 1998 there have been outbreaks of Bluetongue (mainly serotypes 1, 2, 4, 9, 16) in the Balearic Islands, Bulgaria, Corsica, Croatia, Greece, Italy, Kosovo, Macedonia and other regions of the former Yugoslavia (Mellor and Wittmann 2002, Mertens and Mellor 2003, Purse et al. 2005, Mellor et al. 2008). These outbreaks occurred far north and west of the previous distribution of Bluetongue disease. It appears that the virus has spread from both Turkey and North Africa. At the same time, the main vector of Bluetongue disease in Africa, *Culicoides imicola*, has apparently spread from North Africa to large areas of the European part of the Mediterranean basin. It has been argued that climate change may have facilitated the spread of *C. imicola* (Purse et al. 2005).

Bluetongue outbreaks in central, western and northern Europe: Bluetongue disease was never reported in Europe north of the Alps before August 2006, when outbreaks were almost simultaneously discovered in Belgium, France, Germany and the Netherlands. Serotype 8, which caused the epidemic, had not been detected in Europe and the Mediterranean basin before then. Isolates of the virus were obtained from several animals across the affected region. Sequence analyses of Seg-2 from a Dutch isolate showed that the virus is from a western lineage from sub-Saharan Africa, but is distinct from the BTV-8 vaccine strain (*Anonymus* 2007).

In Germany, the disease was diagnosed in 571 cattle holdings, 309 sheep flocks, 3 other bovines, 6 red deer, 3 mouflons and 1 roe deer in the Federal States of North Rhine-Westphalia, Rhineland-Palatinate, Hesse, Lower Saxony and Saarland in 2006. The core region of the epidemic in Germany was situated in North Rhine-Westphalia, adjacent to the affected areas in Belgium, the Netherlands and Luxembourg. The disease was first detected in calendar week 34 with 37 cases, reached a peak in calendar week 42 with 154 cases, and decreased slowly until the end of the year (Fig. 1). The infection overwintered in the region and flared up again in 2007 to spread over most of Germany during the summer and autumn 2007, resulting in 20,624 new outbreaks. The first case was detected in calendar week 23. The number of new cases started to rise constantly from week 30 onwards, reached a maximum of 3,001 new cases/outbreaks in week 37, and subsequently decreased slowly until the end of year. The proportion of affected sheep was higher in the first months of the BT season in 2007, while affected cattle dominated the late phase.

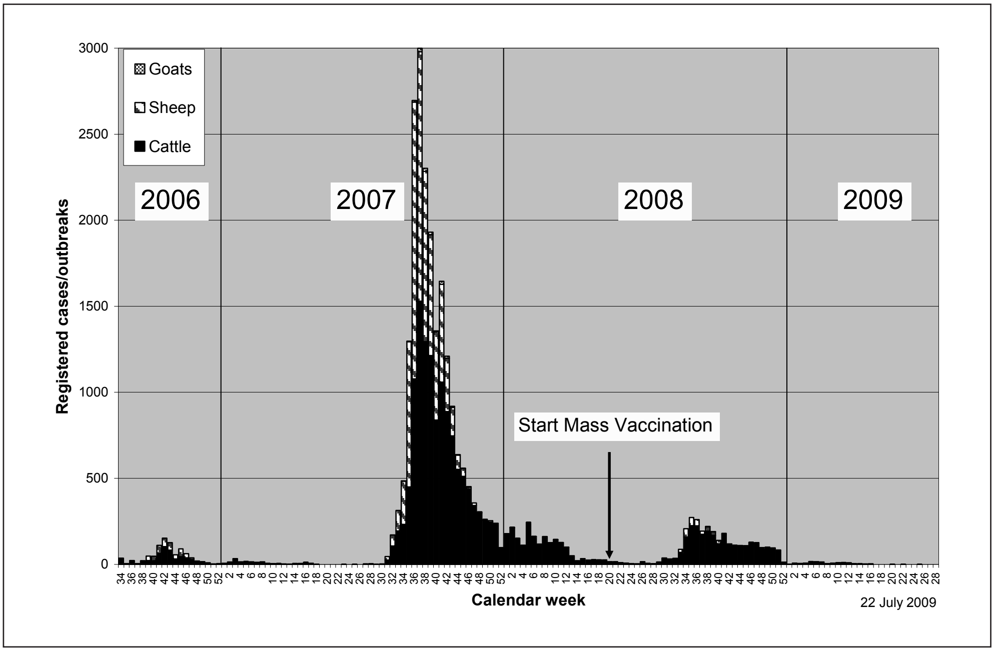

Fig. 1 Bluetongue disease in Germany 2006–2009. Epidemic curve

In 2006, at least 48,364 cattle, 9,781 sheep and 56 goats were exposed to BTV on affected premises. Of these animals, 1,131 cattle (2.34 %) and 590 sheep (6.03 %) were found to be infected. Seventy-two cattle and 221 sheep died. The case-fatality rate was much higher in sheep (37.5 %) as compared to cattle (6.4 %). These calculations are based on the assumption that all BT cases were reported. Since the infections caused only mild disease or remained even clinically inapparent in some animals, in particular in cattle, it is likely that there was a certain level of underreporting. As a consequence, the case fatality rate in cattle may be slightly overestimated.

Due to the enlargement of the affected territory in 2007, the exposed population rose to at least 1,317,111 cattle, 503,282 sheep and 3,346 goats kept on affected farms. The numbers of diseased animals on these farms amounted to 26,772 cattle, 32,116 sheep and 209 goats in 20,624 new outbreaks. While mortality remained at relatively low levels as in 2006, the case fatality proportion rose to 13.1 % in cattle and 41.5 % in sheep. In 2008, the incidence decreased considerably under the influence of a mass vaccination campaign that started in May/June 2008. In 2008, a total of 1,070 new cases (PCR-positive, sampled after 1 May 2008; i.e. infection acquired in the current transmission season) were reported. They were mainly found in two regions in the north-west of Lower Saxony and western parts of Baden-Württemberg. These cases can be explained by the relatively late onset of the immunization campaign because of initially limited supply of BTV-8-vaccine.

2. Identification of New Vectors for BTV

Since the main vector of Bluetongue disease in the Mediterranean, *C. imicola*, has so far not been detected north of the Alps, a comprehensive study was undertaken to determine the abundance of haematophagous *Culicoides* spp. and to identify putative vectors of BTV in Germany (Hoffmann et al. 2009). Biting midges were caught from April 2007 until May 2008 using 89 blacklight traps (BG-Sentinel™ Midge trap, Biogents, Regensburg, Germany) distributed mostly over the German BT restriction zone of January 2007. Traps (n = 85) were placed in the vicinity of cow sheds, either adjacent to the barns or in their entrance area, or (n = 4) on cattle pastures when the animals were kept outdoors all day. Batches of a maximum of 50 female biting midges were tested for BTV by real-time RT-PCR.

The overall number of caught biting midges started at a moderate level (11,577) in April 2007, peaked in October (246,882), decreased to low levels between December 2007 and March 2008, and started to rise again (462) in April 2008. Small numbers (66–81) of *Culicoides* spp. were also detected in some traps between January and March. Members of the *C. obsoletus* Complex (including *C. dewulfi*) were most frequently trapped, followed by the *C. pulicaris* Complex. Biting midges of the *C. pulicaris* Complex were more often collected during spring and summer 2007 in discrete locations. *C. imicola* was not detected at any time during the monitoring.

From a total of 24,513 batches analyzed by rRT-PCR, 16,206 batches (66.1 %) belonged to the *C. obsoletus* Complex, 5,796 (23.6 %) to the *C. pulicaris* Complex and 2,511 represented other *Culicoides* spp. A total of 585 batches (2.4 %) tested positive for BTV by rRT-PCR, 562 (96.1 %) of which belonged to the *C. obsoletus* Complex, 16 (2.7 %) to the *C. pulicaris* Complex, 6 (1.0 %) to other *Culicoides* spp., and one was identified as *C. achrayi*. The number of positive pools varied considerably between different months. All batches that were positive in the BTV-rRT-PCR analysis with a Ct-value of less than 37 (n = 464) were confirmed as BTV positive.

BTV-infected biting midges (*C. pulicaris* Complex) were first detected in June 2007, a few weeks after the first new infection with BTV-8 had been discovered in that year (5). The number of BTV-positive *Culicoides* batches reached a maximum (n = 401) in October 2007 which coincided with the peak of midge abundance. Between December 2007 and May 2008 no BTV-positive batches were detected.

540 batches of biting midges carried a low (Ct values > 30–40), and 45 a high (Ct values < 30) BTV genome load. Batches with a high virus genome load showed Ct values which were similar to those of highly positive, undiluted blood samples from cattle or sheep. The findings therefore provide strong evidence for virus replication in the biting midges present in the highly positive pools. Most batches with a high virus genome load consisted of midges of the *C. obsoletus* Complex. Only two batches with Ct values < 30 were of the *C. pulicaris* Complex. These data clearly support the role of species of the *C. obsoletus* Complex as competent vectors for BTV.

When the species composition of batches of the *C. obsoletus* and *pulicaris* Complexes with a high viral genome load was further determined, it became obvious that *C. obsoletus* sensu stricto was present in all investigated batches of the *C. obsoletus* Complex. Furthermore, a large number of BTV-positive batches morphologically classified as *C. obsoletus* Complex consisted exclusively of *C. obsoletus* sensu stricto. These findings indicate that *C. obsoletus* sensu stricto is involved in the transmission of BTV in Germany, but a role of other members of the *C. obsoletus* Complex and the *C. pulicaris* Comlex in the transmission of BTV cannot be ruled out. In conclusion, in absence of the main vector for Bluetongue disease in Africa and the Mediterranean, indigenous, Palaearctic biting midges, in particular *C. obsoletus* sensu stricto*,* serve as vectors for Bluetongue disease in Germany.

The distribution of *Culicoides* spp. underlies environmental influences. It has been shown that biting midges travel by wind, and it is assumed that Bluetongue disease has been introduced into new locations (e.g. Cyprus, Turkey, Portugal, the Balearic Islands, Greece and Bulgaria) by infected *Culicoides* travelling in the air (Sellers et al. 1978, Sellers and Pedgley 1985, Alba et al. 2004, Ducheyne et al. 2007). It has also been proposed that the major vector for Bluetongue disease in Africa, *C. imicola*, has spread to Europe, carrying six BTV serotypes which have spread across 12 countries and 800 km further north in Europe than has previously been reported (Purse et al. 2005). The authors suggest that these events were driven by recent changes in the European climate that have allowed increased virus persistence during winter, the northward expansion of *C. imicola*, and, beyond the range of this vector, transmission by indigenous European *Culicoides* spp. – thereby expanding the risk of transmission over larger geographical regions. In addition, the introduction of infected biting midges via trade with animals or plants cannot be ruled out.

3. The Impact of Climate Change

The potential impact of climatic (temperature, precipitation, wind), ecological (land use), geographical (elevation), and agricultural (animal density) data on the Bluetongue disease epidemic which started in Belgium, Germany and The Netherlands in August 2006 was studied by an international group of veterinary epidemiologists. It was concluded that the extremely high temperature in the summer and autumn of 2006 may have been favorable for the establishment of Bluetongue disease after initial introduction into the affected area. When an intrinsic incubation period of 4 weeks was taken into account, a statistically significant association between the mean temperature (corrected to sea level) and the number of new cases/outbreaks of Bluetongue disease per week was observed. Calculating backward, wind trajectories provided no evidence for an introduction of BTV serotype 8 by the wind, while calculation of forward wind trajectories matched the spatial distribution of Bluetongue disease in 2006. Cattle and sheep density were also associated with the spatial distribution of the cases/outbreaks, i.e. the incidence of Bluetongue disease was increased in areas with a high ruminant density. The disease was mainly found in the lowlands where the cattle density was high. In 2007, Bluetongue disease spread in all directions. An influence of temperature, wind and elevation could no longer be detected. Only the association between animal (cattle, sheep) density and the occurrence of the disease was still obvious.

In conclusion, the available data suggests that *C. imicola* has not (yet) arrived in Central Europe. In the region affected by BTV8, the virus has been transmitted by indigenous *Culicoides* spp., mainly of the *C. obsoletus* Complex, as vectors. It is likely that *C. obsoletus* sensu stricto plays a major role in the transmission of Bluetongue disease in Germany.

The warm summer in 2006 may have helped BTV to spread after the initial introduction. In 2007, there was no evidence that temperature had an effect on the spread of BT. These findings suggest that, after initial introduction of an orbivirus, increased temperature may trigger an epidemic and lead to lasting, perhaps irreversible establishment of a disease.

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Impact of Climate Change on Rift Valley Fever Virus Infections

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With 1 Figure

Abstract

Rift Valley fever (RVF) is a serious disease in livestock animals in Africa and the Arabian peninsula. Enzootically maintained and transmitted by various mosquito species, it irregularly causes large epidemics with enormous economic losses in the affected areas. All major epidemics thus far have been associated with extensive flooding and massive vector mosquito population increases. Hence, heavy rainfall and favorable climate conditions have been studied in depth in order to relate RVFV epidemics to weather and to subsequently develop predictive risk maps. These forecasts have been shown to allow an early warning system and corresponding prevention strategies for East Africa. However, when applying similar models of risk analyses for West Africa or Madagascar, the predictive risk maps and actual RVFV outbreaks did not overlap. Different ecology of the main vector mosquito species and local rainfall dynamics may be responsible for these differences. Because many mosquito species have been shown to be capable to transmit RVFV, and because the mosquito life cycle is strongly influenced by the availability of water and its temperature, climate change will have a strong impact on Rift Valley fever occurrence in the near future.

Zusammenfassung

Das Rifttal-Fieber (RVF) ist eine gefürchtete Erkrankung der landwirtschaftlichen Nutztiere in Afrika und der Saudi-Arabischen Halbinsel. Das gleichnamige Virus wird durch verschiedene Stechmückenarten enzootisch und epizootisch auf Mensch und Tier übertragen. Alle bekannten, großen Epidemien bisher waren mit großen Überflutungen und einer massiven Vermehrung der Vektorpopulationen verbunden. Starke Regenfälle und andere begünstigende Faktoren für RVF-Epidemien wurden analysiert, um entsprechende Korrelationen zu finden und daraus Risikogebiete ableiten zu können. Für Ostafrika haben sich derartige Analysen bereits bewährt, und entsprechende Frühwarnsysteme wurden etabliert. Diese Modelle ließen sich jedoch nicht auf Westafrika und Madagaskar mit dem gleichen Erfolg anwenden. Die unterschiedliche Ökologie der hauptsächlich übertragenden Stechmückenarten sowie die Dynamik der lokalen Regenfälle könnten hierfür die Ursache sein. Viele Stechmückenarten sind als kompetente Vektoren für das RVF-Virus bekannt. Zudem ist der Entwicklungszyklus der Stechmücken stark von der Verfügbarkeit von Brutgewässern und deren Temperatur abhängig. Im Zusammenhang mit der globalen Erwärmung ist daher ein direkter Einfluss auf die Verbreitung und die Häufigkeit von RVF zu erwarten.

1. Aetiology

Rift Valley fever virus (RVFV) is a member of the Genus *Phlebovirus* within the family *Bunyaviridae*. This genus currently compromises 52 viruses which are partially grouped together based on a certain level of serological cross-reaction, geographic occurrence or sharing related arthropod vector species. As suggested by the genus name, most of these viruses are transmitted by phlebotomine sandflies. Although RVFV has occasionally been found in sandflies in nature, and vector competence has been demonstrated in the laboratory, the virus is usually transmitted by mosquitoes (Turell 1993, Turell and Perkins 1990, Turell et al. 1984, 1990, 2008). As with all bunyaviruses, RVFV is characterized by a tripartite RNA genome of negative polarity. The small (S) genome segment of about 1.7 kb encodes the nucleocapsid (N) protein that is associated as multimer with the viral RNA genome and an additional non-structural protein (NSs) in ambisense orientation. The medium (M) segment of about 3.9 kb encodes a glycoprotein precursor that is co-translationally cleaved into NSm, the M segment-derived non-structural protein with yet unknown function, as well as G1 and G2 envelope glycoproteins. The latter two proteins form oligomers which mediate the interaction of the virus with the cellular receptor. The large (L) segment of about 6.4 kb encodes the RNA-dependent RNA polymerase that functions as transcriptase and replicase (Flick and Bouloy 2005).

2. The Public Health Impact of Rift Valley Fever

By far the most important animal pathogen within the Genus *Phlebovirus* is the type species RVFV. It was first isolated during an epizootic involving sheep, cattle and humans near Lake Naivasha in the (name-giving) Rift Valley in Kenya in 1930 (Daubney and Hudson 1931). Since then epidemics were reported at irregular intervals affecting livestock animals (“abortion storms”) and humans in sub-Saharan Africa (summarized in Martin et al. 2008) until October 1977 when about 18,000 people were sickened – with almost 600 fatalities – in Egypt due to RVFV infections (El-Akkad 1978). Trade movement of infected livestock animals into southern Egypt has been claimed as the source of introduction of RVFV. This alone, however, may not explain the magnitude of this outbreak. Extensive flooding due to the construction of the Aswan Dam at that time may have facilitated an enormous abundance of mosquitoes capable of transmitting RVFV. A similar phenomenon was observed (and predicted) in Mauretania when the Diama dam was built and the waters of the Senegal River caused subsequent flooding of the riverbanks in the valley two years after the dam was completed. As a consequence, millions of floodwater mosquitoes hatched and almost 200 people died due to a fatal RVFV infection (Digoutte and Peters, 1989). The next large RVFV outbreak again occurred after severe flooding due to heavy rainfall in 1997 in Kenya. During this epidemic 27,500 people became infected of which about 170 succumbed (Woods et al. 2002). The next step of the geographic expansion of RVFV was in the year 2000 when livestock animals were diagnosed with Rift Valley fever in parts of Yemen and Saudi Arabia on the Arabian peninsula, outside of Africa (Shoemaker et al. 2002). The most recent reported and well documented big outbreak again occurred in Kenya in December 2006 after two months of heavy rainfall and lasted until May 2007 during which it spread to Tanzania and Somalia (Anyamba et al. 2009). Out of the livestock species, sheep are most susceptible to a RVFV infection, followed by goats, cattle, camels and water buffalos. Human illness is thought to be an uncomplicated, flu-like illness in the majority of cases. However, disease manifestation may lead to either haemorrhagic fever with liver involvement, or encephalitis with confusion, coma, sequelae and sometimes death, or an ocular involvement with a loss of vision due to retinal haemorrhages and macular oedema and sometime residual damage in the form of permanent blindness (Peters and Meegan 1994).

3. Epidemiology of Rift Valley Fever

It becomes obvious from the previous paragraph that all RVFV epidemic episodes were related to unusually severe flooding, either man made or due to heavy rainfall. The additional water bodies created increased opportunities for various mosquito species to multiply which resulted in their paramount abundance. As for other arboviruses, RVFV circulates between vertebrate hosts and mosquitoes, but it does not need such a transmission cycle continuously or a vertebrate reservoir host for maintenance. Transovarial transmission of RVFV seems to be the mode of how the virus endures dry seasons and long interepizootic periods. Infected eggs of floodwater mosquitoes are laid close to or within landscape depressions (so-called Dambos). They hatch in very high numbers when they get wet, and after completing their aquatic developmental stages, the mosquitoes feed on the animals that come to these places to drink (Fig. 1). Herdsman can also become infected on such occasions, but the majority of human cases are thought to result from handling diseased animals. This is mainly while dealing with the aborted foetuses or while trying to "save" the milk or the meat of the dying livestock. Many human infections are

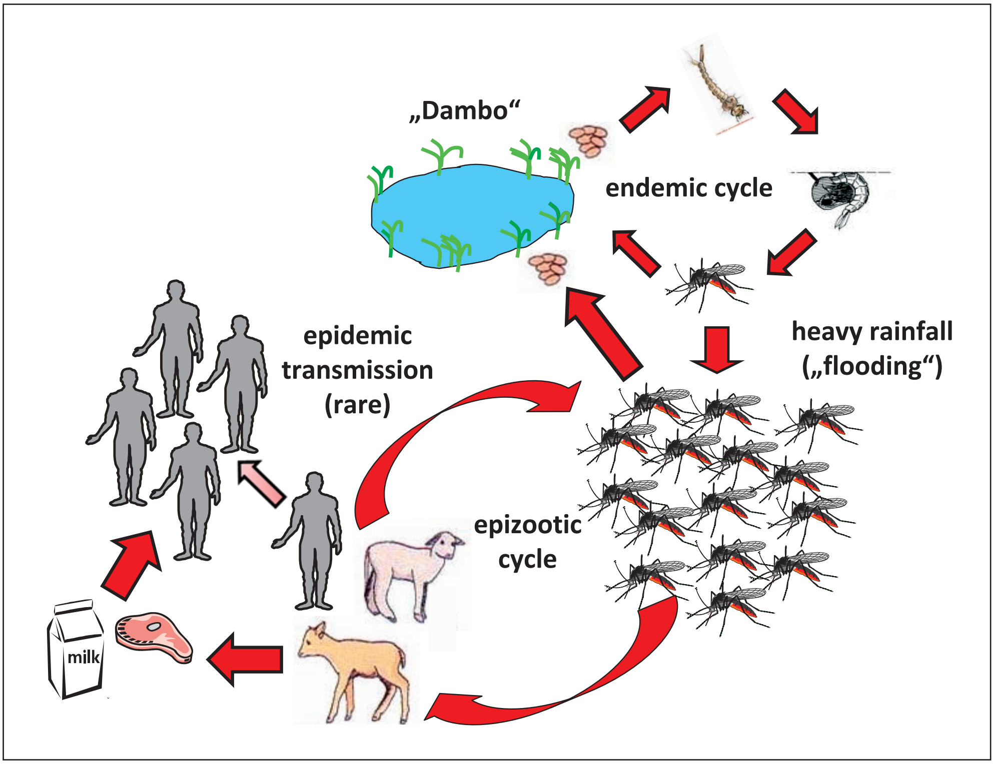

Fig. 1 Ecology and epidemiology of Rift Valley fever virus. RVFV is maintained in an endemic transmission cycle involving various floodwater mosquito species and transovarial (female mosquito to egg) and transstadial (eggs to larvae to pupae to adult mosquitoes) transmission. Upon flooding, huge numbers of mosquitoes hatch and infect livestock animals as well as herders in the vicinity of the "Dambo". The majority of human cases, however, are thought to result from handling tissues, secretions and excretions after abortions, and from milking, slaughtering and butchering sick animals. Human-to-human transmission seems to be a very rare event.

thus linked to farming, slaughtering, and butchering activities when the first wave of infections washes through the endemic area. In summary, for an epidemic to occur, pre-existence or introduction of RVFV in the area, the presence of large numbers of susceptible ruminants, and favorable environmental conditions for an explosion of vector mosquito populations must coincide.

4. Rift Valley Fever Transmission and Climate Change

Mechanisms of emergence are directly weather-related, and satellite remote sensing imagery for RVFV detection has been in use since the 1980s (Linthicum et al. 1987). With the rapid gain of computing power, climate and landscape data were used to successfully develop predictive models for future RVFV outbreaks in the late 1990s (Linthicum et al. 1999). Analyses of recent outbreaks confirmed the strong correlation between flooding and RVFV incidence. This seems to follow the El Niño/Southern Oscillation phenomenon which is manifested by episodic anomalous warming and cooling of sea surface temperatures associated with strong variations in precipitation (Anyamba et al. 2009). The benefit is that climate forecast data may contribute to effective RVFV surveillance. The models developed to construct risk maps, and thus to allow timely prevention strategies, turned out to be very precise when applied to the last outbreak in Kenya, Tanzania, and Somalia in 2006–2007. In other words, the combination of climate variables, i.e. seasonal rainfall anomaly, expressed either as cumulative daily rainfall or cumulative daily long-term mean rainfall, in conjunction with the normalized difference vegetation index (NDVI) provided enough information to map and monitor potential risk areas for RVF outbreaks (Anyamba et al. 2009). However, when using the same methodology to predict the risk of RVF outbreaks in Madagascar or countries in West Africa, the corresponding correlations were missing. RVF is known to be endemic in both Madagascar and West Africa, and has been for decades, but its ecology is not as well studied as in East Africa (Diallo et al. 2005, Corso et al. 2008). Although the reasons are not understood why the RVF risk mapping does not work the same way as it does in East Africa, differences in the main transmitting mosquito species as well as the pattern of local rainfall anomalies may contribute to the observed differences. When analyzing the vector species in West Africa, it seems that at least four mosquito species maintain RVFV in nature: *Aedes dalzieli*, *Aedes ochraceus*, *Culex poicilipes*, and *Aedes vexans* (Ba et al. 2005). While the first two species are not abundant enough to play a role in RVF outbreaks, *Culex poicilipes* is too short lived to efficiently transmit the virus. Hence, *Aedes vexans* seems to be solely responsible for driving RVFV infections to a level that may result in an outbreak situation. In contrast to East Africa, RVFV outbreaks were not observed in years with only one peak of *Aedes vexans* abundance, e.g. after severe flooding. Years with RVFV activity seem to be characterized by a bimodal population dynamic curve for *Aedes vexans*. In consequence for the RVF risk analyses, the local and interrupted rainfall patterns, instead of unique main flooding, seem to be the key to predict RVF outbreaks in Senegal and Mauretania (Ba et al. 2005, Diallo et al. 2005, Corso et al. 2008).

5. Vectors Transmitting Rift Valley Fever Virus

A second guarantee for a great emerging potential of RVFV is its promiscuity in terms of the arthropod vector. It has been isolated from more than 40 mosquito species belonging to six genera in the field (Bouloy 2001) and vector competence has been demonstrated in numerous additional mosquito species in the laboratory (Jupp et al. 2002, Gargan et al. 1988, Turell and Perkins 1990, Turell et al. 1984, 1990, 2008, Moutailler et al. 2008). Among these were many species native to Europe or North America. In consequence, RVFV is a prime candidate which will be able to fit in any new ecological niche which can be occupied by a mosquito. Thus, global warming together with global trade and traffic may lay the ground for establishing autochthonous occurrence of RVFV in Europe or the Americas in the future (Dufour et al. 2008). Direct effects of an increased temperature on the transmission rates of RVFV have been demonstrated in *Aedes taeniorhynchus* in two ways: first, dissemination of the virus within the mosquito appeared earlier and with higher viral titers, and secondly, higher temperatures shortened the extrinsic incubation period (Turell 1993). This period is the time required by the virus to infect the mosquito midgut cells, then spread into the haemolymph, find its way to the salivary gland, infect it, and will be ready to be transmitted to another host with the saliva during the next blood meal. The shorter the extrinsic incubation period of a virus in a given mosquito, the faster the virus will be spread by this vector. Similar effects have been described for many arboviruses in their main vector mosquito species, e.g. *Aedes aegypti* and dengue virus, *Culex quinquefasciatus* and Japanese encephalitis virus, *Culex pipiens* and West Nile virus. Higher temperatures also reduce the time required for the aquatic life stages in the mosquito life cycle. For the main RVFV vector *Aedes vexans,* an increase of the average temperature in May of 4.6 °C almost cuts this time period by half, from 50 to 27 days (Becker 2008). In combination with a drastically shortened extrinsic incubation period, the influence of warm temperatures to vector potential is enormous.

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Impact of Global Climate Change on Wildlife Hosts and their Pathogens

Heribert Hofer and Marion L. East (Berlin)

With 1 Figure

Abstract

Wildlife hosts and their pathogens and parasites play a key role in emerging infectious diseases (EID). Therefore, detailed knowledge of the impact of pathogens and parasites on wildlife hosts would be desirable, but is sadly lacking. This hampers the assessment of the potential impact of climate change on pathogen-host dynamics. Because climate change and other anthropogenic factors typically coincide, evidence of changes in pathogen-host dynamics induced by climate change is difficult to collate. Yet, there is both direct and indirect evidence that climate change exacerbates the impact of pathogens and parasites on wildlife, through direct temperature effects or by promoting stress and immunosuppression of hosts. Eradication and vaccination are often ineffective for wildlife pathogens and threaten wildlife populations without achieving the desired improvement in (veterinary) public health. Sustainable control of zoonotic wildlife pathogens will require an “ecohealth” approach that links the ecology of wildlife hosts, pathogens and parasites to public health concerns.

Zusammenfassung

Wildtiere, ihre Krankheitserreger und Parasiten spielen eine Schlüsselrolle beim plötzlichen Auftauchen neuer Krankheiten („emerging infectious diseases“, EID): Daher wäre es aus der Perspektive des öffentlichen (Veterinär-)Gesundheitswesens sinnvoll, das Ausmaß des Einflusses von Pathogenen und Parasiten auf die Ökologie ihrer Wildtierwirte zu kennen. Leider ist dies selten der Fall, und das erschwert eine Abschätzung der Auswirkungen globaler Klimaänderungen. Da globale Klimaänderungen oft mit anderen anthropogenen Faktoren zusammenwirken, ist es schwierig, direkte Beweise für einen Einfluss globaler Klimaänderungen zu finden. Dennoch gibt es Belege, dass globale Klimaänderungen über Temperatureffekte, erhöhte Belastungen und Immunsuppression den Einfluss von Pathogenen und Parasiten auf ihre Wirte verstärken und so den Ausbruch von Epidemien und Massensterben erleichtern. Die Ausmerzung von Erregern und ihren Wirten oder deren Impfung ist zur Bekämpfung häufig ineffektiv und kann Wildtierpopulationen bedrohen, ohne dass die Gefährdung des öffentlichen Gesundheitswesens wesentlich reduziert wird. Eine nachhaltige Bekämpfung zoonotischer Erreger erfordert einen Ansatz, bei dem die Ziele des öffentlichen Gesundheitswesens mit dem Ziel der Erhaltung der Gesundheit natürlicher Lebensräume zusammengeführt werden.

1. Introduction

In this contribution we are concerned with four questions: How important are wildlife hosts and their pathogens and parasites for emerging infectious diseases (EID)? Does global climate change modify the impact of (zoonotic) pathogens and parasites on their wildlife host populations? How can the impact of global climate change on wildlife pathogens and parasites and the likelihood of EID be monitored? How can the zoonotic/EID potential of wildlife pathogens and parasites be controlled?

2. How Important are Wildlife Hosts and their Pathogens and Parasites for Emerging Infectious Diseases (EID)?

Two major reviews have considered the importance of wildlife pathogens for people and livestock. A taxon-based review (Taylor et al. 2001) identified 1415 organisms pathogenic to humans of which 868 (= 61 %) were zoonotic. Of these, 175 were associated with EID, of these in turn 132 (= 75 %) were zoonotic. Zoonotic pathogens were therefore twice as likely to be associated with EID as non-zoonotic pathogens, and protozoa and viruses were particular likely to be associated with an EID. An event-based review (Jones et al. 2008) demonstrated that zoonoses were responsible for 60.4 % of 335 EID events during the period 1940–2004. Amongst zoonoses, 71.8 % originated in wildlife (i.e. 43.4 % of EIDs originated in wildlife). Drivers for EID include environmental changes, shrinking habitats, concentration of wildlife, and the movement of people, animals, pathogens, or vectors. Thus, both studies conclude that wildlife pathogens are important for EID in people and livestock and we ignore them at our peril.

3. Studying the Impact of Pathogens and Parasites on their Wildlife Hosts

There are very specific problems associated with gaining knowledge about wildlife pathogens and parasites that has hampered rapid advances in our understanding of their possible impact and how this is likely to change under global climate change.

First, knowledge of the influence of pathogens on the population dynamics of their host is available for only a few pathogens and their mammalian hosts. The impact of pathogens is often not assessed because field ecologists often overlook pathogens and thus do not design studies that consider them.

Second, in studies of host mortalities several factors may interact: the source of mortality of an ungulate killed by a spotted hyena (*Crocuta crocuta*) or a lion (*Panthera leo*) may be recorded as predation, unless samples are obtained to assess whether pathogens such as anthrax (*Bacillus anthracis*) may have severely weakened the prey and may have ultimately been responsible for the ungulate's death.

Third, prevalence of infections is often measured in adults where the infection may be benign – but not in young animals, often the most vulnerable life stage of mammals, where infections may be fatal. This is simply because obtaining access to free-ranging young of wildlife species can be challenging. An example is infection with *Hepatozoon*, a tick-borne apicomplexan hemogregarine intracellular protozoan parasite of African carnivores. Carnivores are infected when they ingest ticks infested with *Hepatozoon* during self-grooming or allo-grooming. Adult carnivores demonstrate high but sub-clinical prevalence of infections. For instance 100 % of adult lions and cheetah screened in Serengeti National Park, Tanzania, were infected but showed no clinical signs (Averbeck et al. 1990), and 93 % of African wild dogs (*Lycaon pictus*) screened in Kruger National Park, South Africa, were infected but showed no clinical signs (Van Heerden et al. 1995). In spotted hyenas in Serengeti National Park, more than 90 % of adults and 100 % of young were infected; none of the adults showed clinical signs whereas 18 % of young died (East et al. 2008).

Fourth, accurate identification of pathogens may be difficult, and pathogens may be missed unless there is long-term monitoring of host populations. For instance, in 11 years of monitoring spotted hyenas in the Ngorongoro Crater, one outbreak of *Streptococcus equi ruminatorum* occurred, a subspecies of *S. equi* unknown at the time of the outbreak and identified using molecular genetic techniques (Höner et al. 2006).

More studies, and preferably long-term studies, on the impact of pathogens and parasites on their free-ranging wildlife hosts are urgently needed.

4. Incorporating Global Climate Change into Wildlife Host-Pathogen Studies

Wildlife pathogens and parasites are a natural component of the ecology of their hosts (e.g. Lafferty 2009). From an ecological perspective, pathogens join predation as a top-down process (Fig. 1). The biggest problem in terms of study design is that global climate change is likely to interact with other anthropological changes such as habitat fragmentation, habitat destruction or crowding (Fig. 1). Baseline values are frequently not available as they would require the documentation of pathogens and their wildlife hosts from the last 30 or more years. Most information is correlative; experiments are difficult to design and execute. We also simply need more information on the mechanisms that affect pathogen development, vector biology, host physiology and the habitats they inhabit in order to assess what effect changes in global and local climate in terms of temperature, humidity, seasonal patterns, or the accumulation of extreme values will have. In particular, rare, catastrophic effects such as unusually high temperatures may be important to a host or a pathogen but difficult to predict and impossible to prevent.

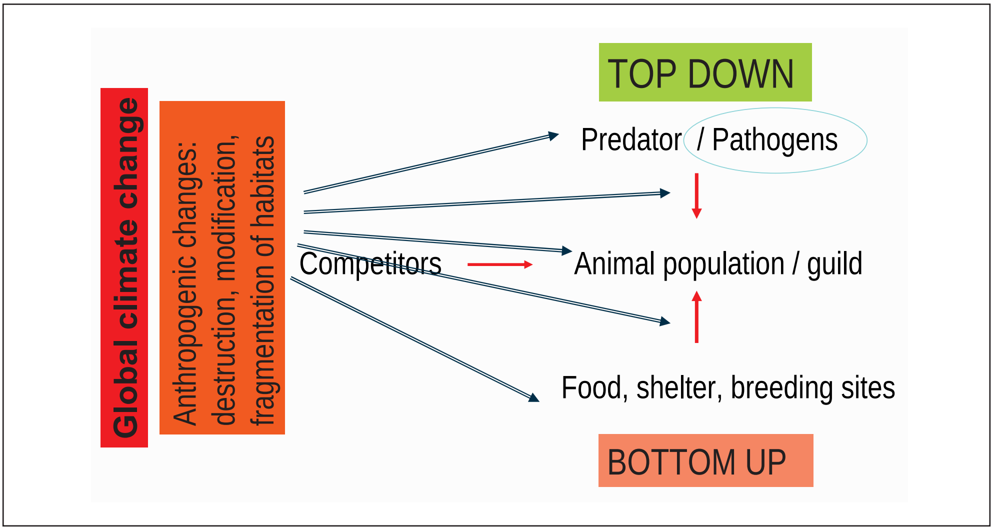

Fig. 1 Predator and Pathogens from an ecological perspective

It is therefore useful to consider very carefully whether an observed effect is the consequence of anthropogenic changes that are part of global change but not part of global climate change. An example is provided by the recent confirmation that nipah and hendra viruses occur not just in south east Asia but also in west Africa (Hayman et al. 2008) where their hosts are forest fruit bats. Here, forest destruction and the erection of pig farms and the planting of fruit trees close to pig farms has helped outbreaks of encephalitis in local people. Outbreaks of hemorrhagic fever caused by ebola virus in central Africa are another example. Here contact of local people to the natural host of the virus, fruit bats (Leroy et al. 2005), has increased substantially in the past decades. This is most likely because of increased human encroachment on the forest, improved access to the forest owing to logging companies, forest fragmentation, and an increase in bushmeat hunting, including the hunting and consumption of fruit bats.

5. Direct Effects of Global Climate Change

Some of the best examples of direct effects of global climate change come from arctic ecosystems, where the consequences of climate change on pathogen or parasite development have been well documented. In principle, warmer conditions increase the rate of development of parasites during their larval stages either as a free-living larva or as a larva inside poikilothermic hosts. For instance, there are outbreaks of the nematode *Elaphostrongylus rangiferi* (Protostrongylidae) in reindeer (*Rangifer tarandus*) when summer temperatures are 1.5 °C above the long-term average (Handeland and Sletbakk 1994). Musk oxen (*Ovibos moschatus*) in the Canadian arctic are host to the nematode *Umingmakstrongylus pallikuukensis* (Protostrongylidae). The parasite completes its development in the host's lungs where it causes respiratory compromise and may reduce the ability of the host individual to escape their major predators, brown bears (*Ursus arctos*). Recent surveys indicate 100 % parasite prevalence in musk oxen (Kutz et al. 2001, 2004). The larvae develop faster in warmer conditions and avoid high winter mortality in intermediate snail hosts. Predictive models of altering host-parasite interactions with global climate change show that under modest conditions, the third larval stage can significantly accelerate development from a two-year cycle to a one-year cycle – if a minimum of 167 "degree days" are available. This increases parasite prevalence and may have facilitated recent population declines because parasitized musk oxen individuals suffer higher predation by brown bears (Kutz et al. 2005). Finally, a warm (+3.2 °C above average, 3.3 standard deviations above 30 year mean) and humid summer led to an outbreak of pneumonic pasteurellosis (*Pasteurella* or *Mannheimia*) in a translocated population of musk oxen in Norway at its southern range boundary in 2006. The observed mortality exceeded average mortality by more than three times (Ytrehus et al. 2008).

6. Evidence of Indirect Impacts of Global Climate Change

Several case studies point to effects of global climate change on the dynamics of pathogen-wildlife host associations. Perhaps one of the most spectacular cases concerns repeated outbreaks of disease epidemics in seals.

Traditionally, common seals (*Phoca vitulina*) in European waters were free of phocine distemper virus (PDV). Harp seals (*Phoca groenlandica*) are known to be infected with PDV and are thought to be viral carriers but suffer little in terms of clinical symptoms. Harp seals were first observed in Danish waters in 1987/1988, extending their range unusually far to the south and are thought to have come into contact with common seals. The reason for this southward movement of harp seals is unclear – it may have been a consequence of climate-related movements of prey, or human over-exploitation of arctic fish stock. From April 1988 onwards, hundreds of seals died of PDV infection in Danish waters, overall mortality rates in the Wadden Sea and Danish populations comprised 50–60 %, in UK colonies 10–20 %. All the main colonies were infected within 7 months; approximately 18,000 seals died (DIETZ et al. 1989). In May 2002, another outbreak occurred, with high PDV mortality throughout all European common seal populations, and approximately 22,000 common seals are estimated to have died in the epidemic. A contributing cause was the fact that apparently no more than 7 % of the population exposed in 1988 was still alive in 2002 (MÜLLER et al. 2004).

The ultimate cause of the PDV epidemics remains unclear. Several hypotheses have been put forward that invoke global climate change and there is evidence consistent with their predictions: (*i*) There is a positive correlation between temperature and several seal mass die-offs in the 20th century. (*ii*) Particularly high mean monthly temperatures cause seals to leave the sea water and aggregate on land in high densities outside the breeding season, thereby facilitating the widespread transmission of pathogens, with a basic reproductive rate of the pathogen R_0 (KEELING and ROHANI 2008) of around 2.0 to 2.5. (*iii*) In early 1988, a temperature-related exceptional bloom of the alga *Chrysochromulina polylepsis*, which is known to secrete toxic substances, may have contributed to substantial stress and immunosuppression in common seals. (*iv*) Documented stress-related skull bone lesions indicated an immunosuppressed state, possibly caused by high levels of environmental pollution in North Sea water, particularly PCBs (LAVIGNE and SCHMITZ 1990, SIMMONDS 1991, HOFER and EAST 1998, KLEPAC et al. 2009). Thus, both direct and indirect, and therefore potentially multiplicative effects of global climate change may have contributed to these epidemics.

7. How Can the Impact of Global Climate Change on Wildlife Pathogens and the Likelihood of EID be Monitored?

We suggest that a monitoring of the impact of global climate change on wildlife pathogens and the likelihood of the emergence of zoonotic EIDs will require the setting up of long-term studies of pathogens and their wildlife hosts both within an ecological and public health framework. It will further require the development of sophisticated predictive models of wildlife host and pathogen guilds for real habitats/landscapes that can incorporate global or regional climate change. When considering the introduction of exotic pathogens to new host populations, including humans, scientifically curated zoos may have a potential role as sentinels for new EIDs – in that their animal collections may be infected by new pathogens, and zoo veterinarians can identify and document pathogens through tissue sample collections often stored for decades. Examples are tigers (*Panthera tigris*) and leopards (*Panthera pardus*) at Suphanburi Zoo in Thailand that died from eating H5N1-infected poultry (KEAWCHAROEN et al. 2004), and the discovery of the West Nile Virus by Tracy MCNAMARA at Bronx Zoo, in New York (MCNAMARA 2007).

8. How Can the Zoonotic EID Potential of Wildlife Pathogens be Controlled?

In the past and still today, public health authorities attempted to control wildlife pathogens by either eradication or vaccination.

Eradication campaigns by public health authorities were often ill advised and ineffective: They focused on the pathogen or parasite without considering their ecological and evolutionary relationship to its wildlife hosts within natural habitats. This approach ignores the simple observation (see LAFFERTY 2009) that generalist pathogens and parasites may have multiple wildlife hosts, imbedded in ecological webs within natural habitats, and the one specific pathogen and its host of public health concern cannot be viewed as if in isolation. Two examples will suffice: The British Colonial Authority attempted to control rabies in Palestine in the 1940s by targeting the golden jackal (*Canis aureus*) population as the assumed key host with strychnine bait. This bait was readily taken by the much rarer striped hyenas (*Hyaena hyaena*) that became extinct in Palestine as a consequence (HOFER 1998). Rabies remains endemic in Palestine until today. A second example concerns the outbreak of the coronavirus thought to cause severe acute respiratory syndrome (SARS) in southern China in 2003. After the discovery of the SARS coronavirus in an Asian palm civet (*Paradoxurus hermaphroditus*), the Chinese authorities targeted the civets as the likely reservoir and killed thousands of them. As it turned out, the civet was most likely an accidental host infected by people carrying the virus after the SARS epidemic had broken out (JANIES et al. 2008).

Vaccination can be successful, as demonstrated by the successful vaccination campaign of red foxes (*Vulpes vulpes*) in central Europe and Canada, but also tricky. Specific vaccines are usually not available for wildlife, and the efficacy and reliability are rarely checked before vaccines developed for domestic animals are applied, with possible fatal consequences for the targeted wildlife hosts. A key problem in vaccination evaluation studies is the focus on the humoral immune response and the neglect of the cellular immune response. Several disastrously failed vaccination campaigns against rabies and canine distemper virus in African wild dogs in Africa in the 1990s caution against the uncritical application of vaccination without careful validation studies (BURROWS et al. 1994, EAST and BURROWS 2001, VAN DE BILDT et al. 2002).

We will most likely need a "Third Way" which incorporates the basic fact that zoonotic wildlife pathogens are part of the natural ecology of their hosts. This requires a good understanding of the ecology of hosts, using careful habitat and people management strategies to reduce the overlap of their zones of activities to a minimum and reduce the factors likely to promote the spread of either pathogen or host populations. A preventive rather than curative approach is more likely to be financially viable, more likely to be sustainable in the long term, and more likely to be applicable in many tropical countries from where a good part of zoonotic pathogens emerge. In short, this requires a more holistic approach by public health authorities than at present, embracing a concept of "ecohealth" (AGUIRRE et al. 2002) and a more profound understanding and appreciation of ecological relationships between pathogens and wildlife hosts.

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The EDEN Research Project: A Successful Integrated Research Management Approach

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With 3 Figures and 1 Table

Abstract

EDEN (Emerging Diseases in a Changing European Environment) is a large European Integrated Research project which aims at identifying ecosystems at risk for the introduction of infectious vector-borne diseases in Europe. The project links 49 institutions from 24 countries. The project was operational over a five year period from November 2004 to October 2009, and has now been extended, on a no-budget basis, until May 2010. In this paper we focus on research management issues, and their impact, which need to be addressed for the successful management of such a complex Integrated Research Project (IP) as EDEN. Particular attention is given to the adopted integrated EDEN research approach, the EDEN PhD Network and the EDEN DMT website. Where applicable, examples of currently achieved long term sustainability are given.

Zusammenfassung

EDEN (*Emerging Diseases in a Changing European Environment*) ist ein europäisches integriertes Forschungsprojekt, das auf die Identifizierung von Risikoökosystemen für vektorbasierte Infektionskrankheiten in Europa ausgerichtet ist. Das Projekt verbindet 49 Einrichtungen aus 24 Ländern. Das Projekt arbeitete zunächst für eine Fünfjahresperiode von November 2004 bis Oktober 2009 und wurde dann, ohne besonderes Budget, bis Mai 2010 verlängert. Der Beitrag behandelt die Forschungsmanagementaufgaben und deren Bedeutung für die erfolgreiche Durchführung eines so komplexen integrierten Forschungsprojektes (IP) wie EDEN. Besondere Beachtung wird dabei dem gewählten EDEN-Forschungszugang, dem EDEN-Doktoranden-Netzwerk und der EDEN-DMT-Webseite geschenkt. Wenn passend, werden Beispiele für derzeit erreichte längerfristige Nachhaltigkeit angeführt.

1. Introduction

In recent years a series of vector-borne diseases (VBD) have been (re)-emerging and spreading across the world and are having a profound impact on human and veterinary health, ecology, socio-economy and disease management. A recent review conducted by Jones et al. (2008) has shown that between 1940 and 2004 the majority of new emerging infectious diseases (EID) occurred in areas with the greatest movement of people and the highest human population, notably the east coast of the United States of America and in Western Europe. During the last decade of the previous century, nearly a third (29 %) of recorded EID events were caused by VBDs and this proportion is increasing.

This increase in EID outbreaks in general, and VBDs in particular, can be linked to global and/or local changes resulting from climate change, human-induced landscape changes and/or the changing activities of human populations. The FP6 funded EDEN project “Emerging Diseases in a Changing European Environment" aimed at addressing these issues, i.e.: Identify, evaluate and catalogue European ecosystems and environmental conditions linked to global change, which can influence the spatial and temporal distribution and dynamics of pathogenic agents. To achieve this, a coordinated European approach was developed to provide predictive emergence and spread models, including global and regional prevention, early warning, surveillance, and monitoring tools and scenarios.

In this paper we focus on research management issues (and their impact) which need to be addressed for the successful management of such a complex Integrated Research Project (IP) as EDEN.

2. Selected Diseases

By definition VBDs 'sensu lato' are transmitted either by arthropod vectors such as mosquitoes, ticks and phlebotomes, or through rodent hosts, the survival of which is closely linked to the eco-climatic environment. VBDs are thus highly sensitive to environmental and eco-climatic conditions and shifts, and were therefore selected as the prime choice to address the objectives of EDEN (see Tab. 1).

Tab. 1 Selected pathogen groups

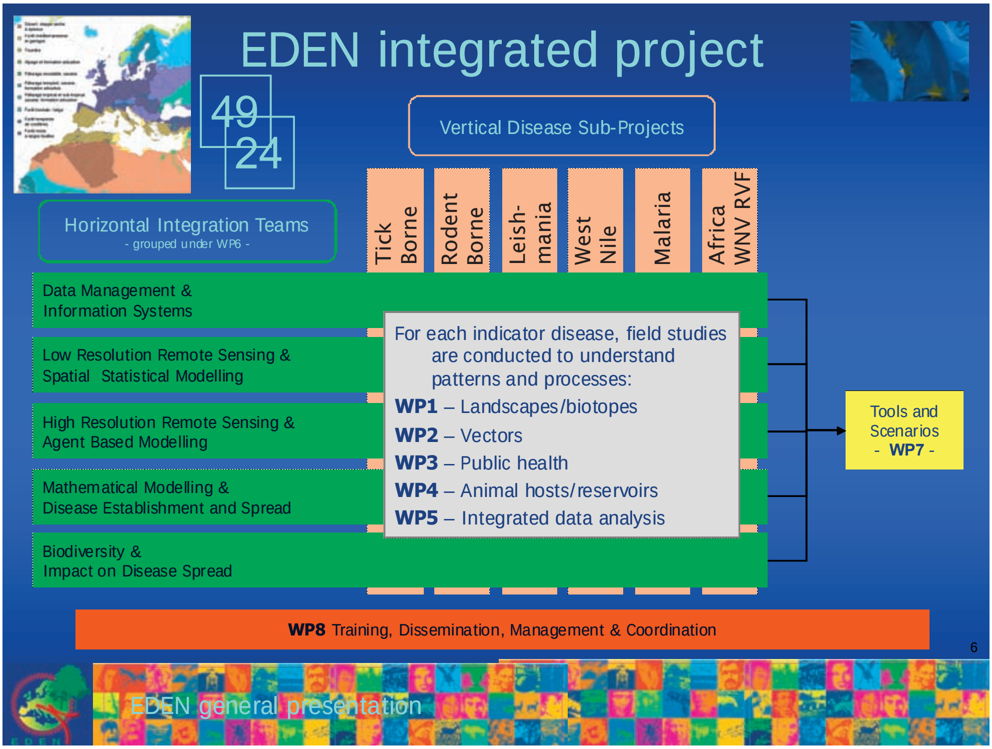
Tick-borne pathogens (TBE, Lyme) – TBD	causing diseases already present in Europe that have recently shown significant recent increases in incidence, at least partly due to changes in human behavior in relation to the environment.
Rodent-borne viruses (hanta, arena, cowpox) ROBO	widespread but under-reported diseases within Europe, with strong links with habitat and landscape structures.
Phlebotome-borne Leishmaniasis – LEI	persistent on the southern fringes of Europe and beyond (southern Mediterranean basin), with the potential to expand as environments change.
Mosquito-borne West Nile Virus – WNV	periodic and occasionally severe local outbreaks, especially on the eastern fringes of Europe, currently showing strong associations with landscape patterns but also (the USA experience) potential for explosive spread.
Malaria – MAL	an ancient scourge of Europe, currently now on her southern and eastern fringes, with the potential for re-emergence following environmental changes.
African source mosquito-borne viruses – AFR	new strains of West Nile Virus and new diseases such as Rift Valley Fever may be introduced to Europe from tropical regions linked by bird and other (e.g. traded livestock) migratory routes to Europe.

3. Adopted Research Management Approach

To cover both the wide range of expertise needed to address these different diseases and the variety of state-of-the-art methods and tools to achieve this, the EDEN Integrated Project (IP) linked more than 80 scientific teams from 49 partner institutions in 24 countries in Europe and abroad.

From the early stages it was clear that in addition to the complexity of the scientific challenge, the management of such a large and diverse group may be even more complex.

Therefore, it was decided to provide a clearly defined project structure with three layers of integration (see Fig. 1).



EDEN integrated project

49

24

Vertical Disease Sub-Projects

Tick Borne

Rodent Borne

Leish-mania

West Nile

Malaria

Africa WNV RVF

Horizontal Integration Teams
- grouped under WP6 -

Data Management & Information Systems

Low Resolution Remote Sensing & Spatial Statistical Modelling

High Resolution Remote Sensing & Agent Based Modelling

Mathematical Modelling & Disease Establishment and Spread

Biodiversity & Impact on Disease Spread

For each indicator disease, field studies are conducted to understand patterns and processes:

WP1 – Landscapes/biotopes

WP2 – Vectors

WP3 – Public health

WP4 – Animal hosts/reservoirs

WP5 – Integrated data analysis

Tools and Scenarios
- **WP7** -

WP8 Training, Dissemination, Management & Coordination

6

EDEN general presentation

Fig. 1 EDEN integrated research management structure

- Six pathogen group oriented sub-projects (SP): TBD, ROBO, LEI, WNV, MAL, AFR (see also Tab. 1). Each of which addresses specific research questions to commonly achieve the EDEN objectives.
- Five horizontal integration teams (HIT): Data management and information systems (DMT), Low resolution remote sensing and spatial statistical models (LRRS), High resolution remote sensing and agent based modeling (HRRS), Mathematical modeling of disease introduction, establishment and spread (MATMOD), Biodiversity and its impact on disease spread (BIODIV).
- A common research framework to study patterns and processes within each pathogen group: Landscape and biotope field studies, vector-related field and laboratory studies, Public Health (PH)-related issues mainly based on historical time series, animal host and reservoir field and laboratory studies, and finally a common data integration and analysis approach.

In this framework each pathogen group operates as an independent research group under the leadership of an internationally recognized SP leader, has access to the same horizontal integration tools as the other pathogen groups and adopts the same field research approach.

This aspect appeared essential to simplify the chain of command: each project partner reports to her/his SP leader and the SP and HIT leaders report to the Project Coordinator who is the sole contact with Brussels. The EDEN Steering Committee (SC) meets three times per year, and its members include the eleven SP and HIT leaders together with the Project Coordinator and the Secretary of the SC. The former is executive manager and the latter operational manager.

In addition to the scientific excellence of the teams involved, this simple and compartmented management structure enables the rapid identification and isolation of problems and is arguably one of the major reasons for the success of EDEN.

4. EDEN Achievements

4.1 Integrated Research

Through its integrated approach a pan-European (and beyond) EDEN[1] community was established which used comparable field approaches in more than 120 field sites scattered throughout Europe (see Fig. 2). The combined research effort totals more than 200 EDEN research years and currently more than 185 scientific research papers are in the peer-review pipeline, of which more than 135 have already been accepted. The EDEN annual meeting has become increasingly focused on the presentation of novel scientific results and will culminate in an EDEN International Conference to be held in Montpellier from May 10 to 12. During the EDEN AGMs, one day was devoted to the scientific presentation of EDEN results open to the public, contributions of other research teams working on EDEN related topics have been encouraged for the final conference. Currently the EDEN Scientific Committee is reviewing a total of 154 submitted abstracts of which 44 have been submitted by non-EDEN teams. In addition 164 posters have also been submitted.

The existence of this successful EDEN community inspired the European Centre for Disease Prevention and Control (ECDC, Stockholm, Sweden) to fund the establishment of a European Network for Arthropod Vector Surveillance for Human Public Health (Vbornet[2]) which started its activities in September 2009. This network was primed by an ECDC funded study on the assessment of magnitude and importance of vector-borne diseases in Europe (V-borne).

4.2 PhD Network

During EDEN's lifetime more than 60 PhD students have contributed directly to EDEN-related activities. All are members of the EDEN PhD network which has two main activities: the maintenance of the EDEN PhD network website, and the organization of the annual EDEN PhD network meeting.

This network is representative of a large proportion of future VBD researchers in Europe and is therefore one of the key assets of EDEN. Its website[3] is specifically designed to

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[1] http://www.eden-fp6project.net.

[2] http://ecdc.europa.eu/en/activities/diseaseprogrammes/Pages/VBORNET.aspx.

[3] http://ergodd.zoo.ox.ac.uk/edenphd/tiki-index.php.

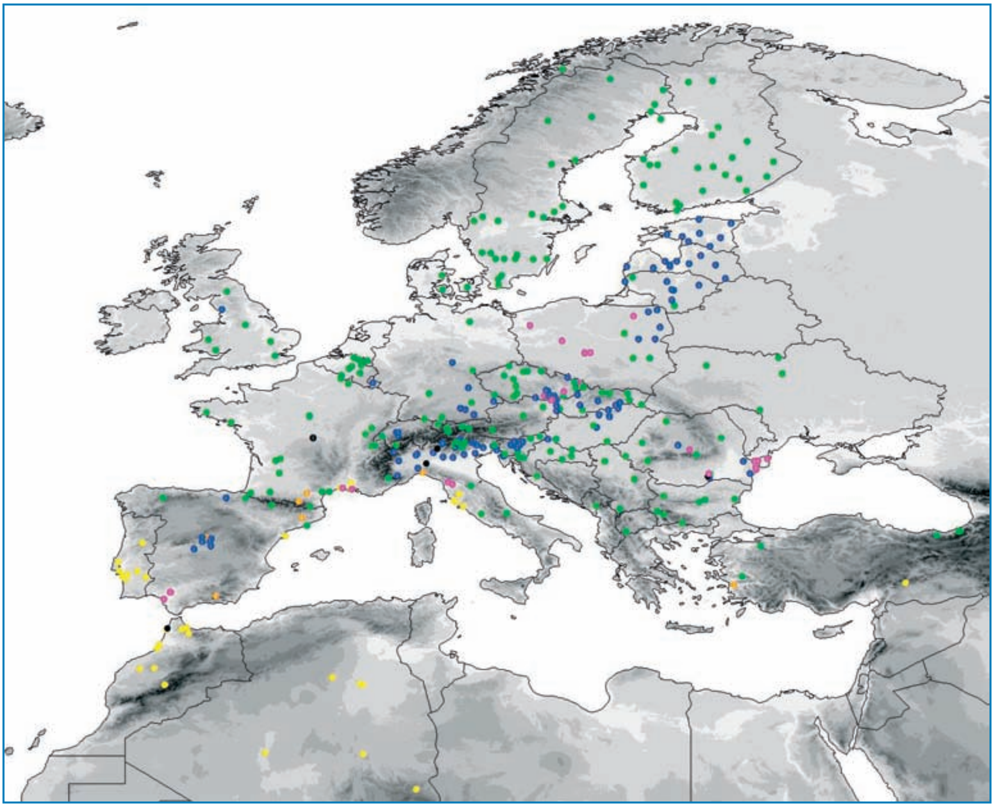

Fig. 2 EDEN documented field sites in Europe and North Africa: blue (TBD), green (ROBO), orange (LEI), purple (WNV), yellow (MAL) and black (BIODIV)

enhance communication and disseminate information. Each of the PhD students had the opportunity to include their personal page, and currently 46 are online, advertising their skills to their peers, and more importantly to the entire VBD community. Interestingly one of the most successful pages is the job-opportunity page (up to 3,000 hits per day!).

The aim of the annual PhD network meeting was two-fold: to provide experience with public presentation, and to create an informal forum to discuss PhD research results between peers and with the senior EDEN community. During this two day meeting which preceded the EDEN AGM, each PhD student had the opportunity to give a presentation. To further stimulate quality, the three best presentations were peer-selected and presented at the AGM which voted for the much coveted annual PhD prize: a sponsorship to attend a top-rated international conference.

4.3 EDEN DMT website

One of the main tasks of the EDEN Data Management Team (DMT) was to develop a web-based spatial data archive system[4] which includes all the spatial data layers, in a standardized

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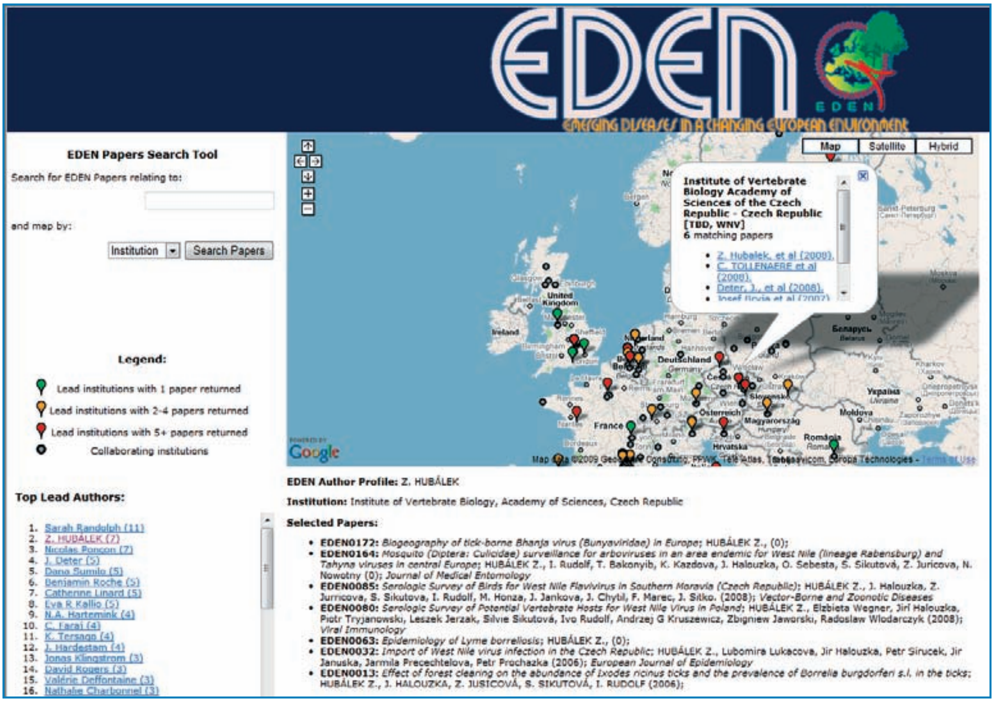
[4] http://edendatasite.com.

format, needed to conduct the necessary EDEN spatial analyses. The data archive currently includes over 2800 data layers divided in 21 categories and approaching a total volume of 100 Gb. Of these, a large proportion is open for public access or is available after a simple password request. Some data, mainly related to epidemiological and other field data collected as part of EDEN activities, have a more restricted access.

In addition, the website also includes training items, a well documented page with relevant links, and an EDEN publication tool. The link page is another flagship which enhances the visibility of the EDEN DMT site, many potential users reach the site through this page.

The EDEN publication tool (see Fig. 3) archives keywords and field sites from all accepted EDEN peer reviewed publications (currently 133 have been indexed). It solves a particularly sensitive data sharing issue. Whilst most researchers readily share ancillary and other descriptive GIS data, they are often more reluctant to post epidemiological data for public access through a website such as EDEN DMT. The tool enables advertises who conducted which VBD related research in which part of Europe and encourages collaborations between research teams. After querying the tool, researchers can readily identify and directly contact the owners of research data to discuss such collaborations.



EDEN Papers Search Tool

Search for EDEN Papers relating to:

and map by:

Legend:

- Lead institutions with 1 paper returned
- Lead institutions with 2-4 papers returned
- Lead institutions with 5+ papers returned
- Collaborating institutions

Top Lead Authors:

1. Sarah Randolph (11)
2. Z. HUBALEK (7)
3. Nicolas Poncon (7)
4. J. Deter (5)
5. Dana Sumilo (5)
6. Benjamin Roche (5)
7. Catherine Linard (5)
8. Eva R Kallio (5)
9. N.A. Hartemink (4)
10. C. Farai (4)
11. K. Tersago (4)
12. J. Hardestam (4)
13. Jonas Klingstrom (3)
14. David Rogers (3)
15. Valérie Deffontaine (3)
16. Nathalie Charbonnel (3)

Institute of Vertebrate Biology Academy of Sciences of the Czech Republic - Czech Republic [TBD, WNV]
6 matching papers

- Z. Hubalek, et al (2008).
- C. TOLLENAERE et al (2008).
- Deter, J., et al (2008).

EDEN Author Profile: Z. HUBÁLEK

Institution: Institute of Vertebrate Biology, Academy of Sciences, Czech Republic

Selected Papers:

- **EDEN0172:** *Biogeography of tick-borne Bhanja virus (Bunyaviridae) in Europe*; HUBÁLEK Z., (0);
- **EDEN0164:** *Mosquito (Diptera: Culicidae) surveillance for arboviruses in an area endemic for West Nile (lineage Rabensburg) and Tahyna viruses in central Europe*; HUBÁLEK Z., I. Rudolf, T. Bakonyib, K. Kazdova, J. Halouzka, O. Sebesta, S. Sikutová, Z. Juricova, N. Nowotny (0); *Journal of Medical Entomology*
- **EDEN0085:** *Serologic Survey of Birds for West Nile Flavivirus in Southern Moravia (Czech Republic)*; HUBÁLEK Z., J. Halouzka, Z. Jurricova, S. Sikutova, I. Rudolf, M. Honza, J. Jankova, J. Chytil, F. Marec, J. Sitko. (2008); *Vector-Borne and Zoonotic Diseases*
- **EDEN0080:** *Serologic Survey of Potential Vertebrate Hosts for West Nile Virus in Poland*; HUBÁLEK Z., Elzbieta Wegner, Jirí Halouzka, Piotr Tryjanowski, Leszek Jerzak, Silvie Sikutová, Ivo Rudolf, Andrzej G Kruszewicz, Zbigniew Jaworski, Radoslaw Wlodarczyk (2008); *Viral Immunology*
- **EDEN0063:** *Epidemiology of Lyme borreliosis*; HUBÁLEK Z., (0);
- **EDEN0032:** *Import of West Nile virus infection in the Czech Republic*; HUBÁLEK Z., Lubomira Lukacova, Jir Halouzka, Petr Sirucek, Jir Januska, Jarmila Precechtelova, Petr Prochazka (2006); *European Journal of Epidemiology*
- **EDEN0013:** *Effect of forest clearing on the abundance of Ixodes ricinus ticks and the prevalence of Borrelia burgdorferi s.l. in the ticks*; HUBÁLEK Z., J. HALOUZKA, Z. JUSICOVÁ, S. SIKUTOVÁ, I. RUDOLF (2006);

Fig. 3 EDEN geographical interactive publication tool

The EDEN DMT site also hosts a VBORNET 'mirror' webpage (see above) with additional download capacities for the European Vector Distribution Questionnaire and the VBORNET Newsletters.

The content of the DMT site also attracted the interest of ECDC which is planning to launch the European Environment and Epidemiology (E3) Network. The content of the EDEN DMT will serve as a basis for the E3 Network, and ECDC has offered resources to maintain the EDEN DMT website during a bridging period of one year and to conduct a series of proof of concept studies to help convince decision makers of the added value of such a network.

5. Conclusion

A series of EDEN-related scientific results have been reported elsewhere during this conference. The single most important of these results is that many currently observed changes in disease occurrence are driven by complex multifactor causes and can often not simply be linked to a single cause. Socio-economic factors affecting behavior and contacts between hosts, vectors and pathogens often appear to be more important drivers of change than climatic factors. This complexity should not be overlooked in disease risk studies and public health policy making.

What EDEN also has shown is that such a complex research project can be managed successfully using an rather straightforward integrated management approach enabling all teams involved to conduct research in a comparable way and have access to the same state of the art tools. Whilst many of these tools were already available, the main strength of EDEN was to provide this forum for their integration and further development.

Acknowledgement

The authors, respectively secretary of the EDEN Steering Committee and Project Coordinator are very grateful to the EDEN Steering Committee members and all the EDEN contributors for heir continued efforts to achieve the EDEN objectives. Currently the EDEN contributors address list includes the names of more than 230 scientists. EDEN is funded by EU grant GOCE-2003-EDEN.

References

EDEN Project website: http://www.eden-fp6project.net
EDEN DMT website: http://edendatasite.com
EDEN PhD website: http://ergodd.zoo.ox.ac.uk/edenphd/tiki-index.php
EDEN accepted publications reference list can be downloaded from the EDEN project website at: http://www.eden-fp6project.net/what_s_on/eden_publications. The EDEN publications interactive geographical tool is available at: http://edendatasite.com
Jones, K. E., Pate, N. G., Levy, M. A., Storeygard, A., Balk, D., Gittleman, J. L., and Daszak, P.: Global trends in emerging infectious diseases. Nature *451*, 990–993. URL http://dx.doi.org/10.1038/nature06536 (2008)

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Altern in Deutschland

Die Deutsche Akademie der Naturforscher Leopoldina und die Deutsche Akademie für Technikwissenschaften acatech gründeten im Mai 2005 eine gemeinsame interdisziplinäre Akademiengruppe „Altern in Deutschland“, die auf der Grundlage der besten verfügbaren wissenschaftlichen Evidenz öffentliche Empfehlungen erarbeitete, um die Chancen der im letzten Jahrhundert erheblich gestiegenen Lebenserwartung – die „gewonnenen Jahre“ – vernünftig zu nutzen und mit den Herausforderungen des demographischen Alterns klug umzugehen.

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