Emerging diseases in a changing European environment

Annual meeting 2008

Brno, Czech Republic, 14-18 January

Executive summary

In recent years, several vector-borne, parasitic or zoonotic diseases have (re)-emerged and spread within Europe with major health, ecological, socio-economical and political consequences. Most of these epidemics are linked to global and local changes caused by either climate change, human-induced landscape changes or the direct impact of human activities. The EDEN Integrated Project offers a unique opportunity to prepare for uncertainties about the future of the European environment by exploring the potential impact of environmental and other changes on human health.
Emerging Diseases in a Changing European Environment

Part 1 – Project overview

Preamble: throughout this document, “old” material (dating back to the beginning of the project) is written in black while new results and comments are written in blue.

 Eden’s aims are to identify, evaluate and catalogue European ecosystems and environmental conditions linked to global change, which can influence the spatial and temporal distribution and dynamics of human pathogenic agents. Through a coordinated approach, the project develops and coordinates, at the European level, a set of generic methods, tools and skills such as predictive disease-emergence and spread models, and identifies requirements for early warning, surveillance and monitoring tools and scenarios, which can be used by decision makers for risk assessment, decision support for intervention and public health policies at either the EU, the national or regional level. A part of the innovative aspects of EDEN are to combine spatial information (earth observation, geographic information systems, etc) and epidemiological data.

Recognition that the environment may affect the risk of both infectious and vector-borne diseases is not new, but over the past decade a better understanding has been reached of the mechanisms that underlie the complex interactions between infectious agents, the hosts and the biological and physical environment. Vector-borne zoonoses tend to be the most ecologically complex infectious diseases in which environmental changes may have the greatest number and diversity of effects, some promoting transmission and others diminishing it. Habitat and species losses may reduce the normal buffering within ecosystems leading to disease outbreaks. Finally, the juxtaposition of new vectors, hosts and parasites within disturbed ecosystems provides a potential for the evolution of novel transmission pathways and thus new ‘emerging diseases’.

EDEN integrates research from 49 leading institutes from 24 countries (see map) with the combined experience and skills to reach the project’s common goals. The eco-geographical diversity of the project area covers all relevant European eco-systems from the Arctic Circle in the North to the Mediterranean Basin and its link with West Africa in the South, and the Atlantic Ocean in the West to the Danube Delta in the East.

EDEN has selected for study a range of diseases that are especially sensitive to environmental changes and are studied within a common scientific framework (involving landscapes, vector and parasite bionomics, public health, and animal reservoirs). Some of these diseases are already present in Europe (tick- and rodent-borne diseases, leishmaniasis, West Nile fever), some were present historically (malaria) and may re-emerge, whilst others are found on the fringes of Europe (Rift Valley Fever) in endemic regions of West and Northern Africa. The diseases are studied in so-called “vertical” sub-projects (SP). Each of these subprojects conducts health-environment epidemiological studies, i.e., studying patterns and processes of diseases as part of their environment, organized in the same set of five “work packages”:

1. WP1 – Landscapes, biotopes and habitats,
2. WP2 – Vector bionomics and competence,
3. WP3 – Public health and human activities,
4. WP4 – Animal reservoirs,
5. WP5 – Data management, analysis and modelling.

The integration of these studies which leads to the development and application of generic tools is achieved through a series of shared horizontal activities (Horizontal Integration Team, HIT) including:

(i) Data management and information systems,
(ii) Remote sensing tools, both High resolution environmental change and Low Resolution spatial modelling,
(iii) Disease transmission modelling,
(iv) Biodiversity monitoring and assessment.

New concepts are then explored in EDEN, the “horizontal” activities on biodiversity, for example providing intellectual and logistical support to the SPs in the general field of evolutionary epidemiology and ecosystems analysis.

From the general timeframe of the project shown below, it is clear that studies on specific disease patterns and processes (health-environment research) conducted during the first half of the project will enable in the second half, the development of integrative models which can then be translated to tools to assist decision support and to feed dissemination will become increasingly important later in the project lifetime.

![Fig. 1. Timeframe of the EDEN project. HIT: horizontal integration team. DMEWS: disease monitoring and early-warning systems.](image)

The general timeframe has been respected by now (December 2007) though important delays were met with EC payments. The challenging issues for the end of EDEN are to successfully address the last two items:

(i) Develop generic disease models including risk maps,
(ii) Propose tools and scenarios for disease monitoring and early warning systems.

These topics were discussed during steering committee meetings held in Antalya, London and Brussels, as well as during workshops and informal meetings with key stakeholders of human and veterinary public health (DG-Sanco, WHO, FAO, OIE, ECDC, EFSA…).

Coordinator contact details
Renaud LANCELOT
Centre de Coopération Internationale en Recherche Agronomique pour le Développement (CIRAD)
Campus International de Baillarguet, TA A-DIR / B F34398 Montpellier

Tel. +33 (0)4 67 59 37 17
Cell. +33 (0)6 77 52 08 69
Secr. +33 (0)4 67 59 37 37
Fax +33 (0)4 67 59 37 95

eden@cirad.fr
www.eden-fp6project.net
1. Objectives and achievements

1.1. General objectives of EDEN

The goal of EDEN is to identify, evaluate and catalogue European ecosystems and environmental conditions which can influence the spatio-temporal distribution and dynamics of pathogen agents involved in emerging human diseases in Europe. A coordinated European approach was adopted to provide predictive emergence and spread models including global and regional preventive, early warning, surveillance, and monitoring tools and scenarios. Such tools will have a major impact on improved EU policy development and decision making.

![Project objectives diagram]

Fig. 2. EDEN Objectives and overall timeframe

The general objectives of EDEN are related both to scientific innovations and knowledge improvement on the epidemiological processes involved in the emergence and spread of diseases in a changing environment, and to the methodological development of tools for risk assessment, early warning and policy making. In chronological order this translates as follows:

1. Health-environment research. To describe the epidemiological cycles of selected candidate diseases (see Table 1 below) in a variety of representative environmental settings through an integrated and multidisciplinary approach.

   a. To characterize the infectious agents most likely to emerge in Europe, and the competence and capacity of vectors, hosts and reservoirs likely to integrate, perpetuate or spread new functioning disease cycles.

   b. To identify factors triggering or modulating emergence and spread in Europe and the endemic disease areas: i.e., change indicators and risk factors.

   c. To develop and implement methods for Pan-European predictive emergence and spread models.

   d. To examine current and expected changes in the European environment likely to favor the emergence or re-emergence of vector-borne diseases.

2. EDEN strategy for integration. To develop and apply a strategy proposing an innovative integrated trans-disciplinary approach for the unified analysis and exploitation of the various EDEN health-environment research outputs. This strategy aims at the development of generic tools based on the description and follow up of the set of change indicators and risk factors identified after the study of disease patterns and processes. A major expected output is to define new methods combining statistical approaches and biological models in the definition of these indicators. An effort is put on the involvement of environmental sciences.

3. Tools and policies. To develop and make available to the EDEN and international
Emerging Diseases in a Changing European Environment

The community needs a set of generic tools for risk assessment and decision making (maps, risk indicators, scenarios) enabling improved public-health decision making at the EU and country level, and more specifically:

a. To catalogue ecosystems and environmental conditions considered, or predicted, to be at risk (hot spots).

b. To develop preventive, early warning, surveillance and mitigation tools and to examine future “what if” scenarios at different spatial and temporal scales (from local to global).

c. To contribute to decision support and policy making through collaborative initiatives with relevant groups.

4. Dissemination. To promote, through a coordinated approach, the dissemination of information through awareness-raising and communication in line with social demand from the general public, user groups and the scientific community: website, leaflet, newsletter, workshops and international meetings, articles and papers, collaborative initiatives, etc.

To achieve these objectives, a series of ‘indicator diseases’ were selected:

(i) with a strong link with the environment,

(ii) currently at risk of (re-)emerging or spreading due to environmental and other changes,

(iii) representative as a group of a wide geographical range of changing ecosystems,

(iv) representative of the epidemiological processes involved in disease emergence.

Table 1: Selected pathogen groups

<table>
<thead>
<tr>
<th><strong>Tick-borne pathogens</strong></th>
<th>cause widespread diseases in Europe that have shown significant recent increases in incidence, at least partly due to changes in human behaviour in relation to the environment.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rodent-borne viruses (hanta, arena, cowpox)</strong></td>
<td>cause widespread but under-reported diseases within Europe, with strong links with habitat and landscape structures.</td>
</tr>
<tr>
<td><strong>Leishmaniasis</strong></td>
<td>is transmitted by sandflies (biting midges). It is endemic on the southern fringes of Europe and beyond (southern Mediterranean basin, Middle-East...), with the potential to expand with its vector as environments change.</td>
</tr>
<tr>
<td><strong>West Nile virus</strong></td>
<td>is transmitted by different mosquito species. It causes periodic and occasionally severe local outbreaks, especially on the eastern fringes of Europe which currently are showing strong associations with landscape patterns but also (the American experience) potential for explosive spread.</td>
</tr>
<tr>
<td><strong>Malaria</strong></td>
<td>is transmitted by mosquitoes. It is an ancient scourge of Europe, currently now on her southern and eastern fringes, with the potential for re-emergence following environmental changes.</td>
</tr>
<tr>
<td><strong>African source diseases.</strong></td>
<td>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.</td>
</tr>
</tbody>
</table>

Integration of pathogen studies through the development and application of generic tools and is achieved through a series of horizontal activities managed by HITs. These include:

(i) data management and information systems,

(ii) Remote sensing tools, both high resolution environmental change and low resolution spatial modelling,

(iii) Disease transmission modelling,

(iv) Biodiversity monitoring and assessment.
The selected diseases are used as applications and horizontal activities bring forward the development of new methods for an integrated health-environment approach and innovative indicator-driven policy tools. A strategy document was elaborated during year 1 by the steering committee (SP and HIT leaders) with back-up from the advisory group (international experts and specialists).

For the selected diseases, EDEN aims at:

(i) contribute to the understanding of past and present epidemics,
(ii) develop spatial and temporal models of amplification and spreading risk,
(iii) contribute to the establishment of improved public-health policies at the sub-national, national and regional level.

A major expected output is the extension of the EDEN approach to other similar vector-borne diseases, e.g., Chikungunya, dengue...

Through the integration and dissemination of this information, EDEN will trigger the development of more generally applicable scenarios enabling:

(i) delimitation of disease risk areas, i.e., ecosystems at risk,
(ii) monitoring of temporal risk windows linked to eco-climatic events,
(iii) quantification of exposure to risk factors,
(iv) identification of population groups at risk (behavioural, professional).

EDEN outputs will contribute to the development of decision support tools enabling the implementation of adapted monitoring and control strategies at the local level. They will also allow a more efficient allocation of efforts and resources at a larger scale and the improved analysis of the impact of land-use planning and reallocation strategies resulting from changes in the agriculture policies and urban demography.

Finally, through its dissemination network, EDEN contributes to the improvement of public awareness of emerging disease risks and their management.

Fig. 3. EDEN work-package structure
2. State of the art

The state of the art in most EDEN disciplines is one in which we have some idea of patterns and are now working on processes. Thus, land-use and land-cover monitoring has moved from the identification of the patterns of land-use change\textsuperscript{1,2} to a study of the underlying processes involved\textsuperscript{3}. Predictions of the effects of global warming on vector-borne diseases are based on a matching of current patterns to climatic variables now and into the future\textsuperscript{4}. We need to work on processes but these are still poorly understood for most vector-borne diseases\textsuperscript{5-6}. Careful analyses of historical and more recent changes in both malaria and tick-borne diseases show that a variety of factors – agricultural, sociological, economical and climatic – contributed to changes in disease patterns over time, with no single one of overriding importance\textsuperscript{7-10}. These examples illustrate that a cohesive, integrated approach is more likely to give us the right answer than ideas emerging from separate scientific disciplines about the reasons for changes in human disease patterns. Such an approach must be within a quantitative modelling framework, and EDEN includes world-recognized teams working on all aspects of modelling host-parasite systems; ecosystems\textsuperscript{11}, vertebrate hosts\textsuperscript{12}, vectors\textsuperscript{13}, pathogens and pathogen dynamics through space and time\textsuperscript{14}. We envisage a future in which the generic tools developed by EDEN will form the basis of a rapid scientific response methodology (involving both experts and methods) for new and emerging diseases within Europe – essentially an intelligent monitoring and surveillance arm for the European Centre for Disease Control and Prevention (Stockholm). Currently, no disease monitoring and early warning system (DMEWS) exist, except in vague outlines and for relatively few diseases. EDEN’s bold ambition is to contribute to a DMEWS system on a solid scientific foundation running from the understanding of the reasons for the emergence of new diseases in vulnerable ecosystems, through an understanding of complex disease dynamics, to the practical application of such knowledge to disease control.

3. Lambin E, Rounsevell M, Geist H. Are agricultural land-use models able to predict changes in land-use intensity? Agriculture Ecosystems & Environment 82, 321-331 (2000).
1. Vertical sub-projects

Whilst in the first year the main focus was on team building, establishment of common protocols, selection field sites, start of field activities, collection of historical data sets, the development of lab tools and the development of a common data archiving system, during the second year the first full season data sets were collected and field activities were extended to cover all the areas under study. This field work routine was further carried out during year three. In addition to the intra sub-project activities the horizontal collaborations towards achieving the second level of EDEN integration, i.e. the generation of disease specific models, were further extended and carried out.

1.1. Tick-borne diseases

Further progress has been made over the past year in filling the remaining gaps in the hard time-series data relevant to the changing epidemiology of tick-borne diseases (TBD), and more standardized data sets have now been prepared and posted on the EDEN web site. In addition to these on-going exercises, there were three principal activities scheduled for period 3:

(i) field work on ticks and rodents,
(ii) laboratory analyses of infection prevalence in ticks and rodents,
(iii) data analysis towards a unified model of TBD epidemiology in Europe.

All have been achieved with one major exception; the delay in releasing funds from the EU coffers to each partner has prevented many from the less well-endowed institutes in Eastern Europe from purchasing reagents for the molecular diagnosis of infection in ticks. Furthermore, some junior staff employed on EU-funded salaries can no longer be supported. This has had an extremely serious adverse effect on progress and may even jeopardize the success of the whole project.

Despite these problems, monthly sampling of ticks (mainly *Ixodes ricinus*, but also *I. persulcatus* where it occurs) throughout the tick activity season, from a total of 78 sites in 13 countries from Switzerland in the west to Romania and the Baltic States in the east, has yielded much better data this year.

The patterns of seasonal population dynamics vary considerably from site to site, which can be related to local climatic conditions. Most field sites fall within areas where TBE infection in humans occurs to a greater or lesser extent, but Romania offers some valuable sites apparently beyond the SE edge of the European TBE distribution, and here the tick seasonal dynamics do indeed appear to be incompatible with TBEV transmission, according to our current understanding.

All ticks are stored and ready for molecular diagnosis of infection with TBE virus, *Anaplasma phagocytophilum*, *Babesia* spp and five different genospecies of *Borrelia burgdorferi* s.l. Those for which preliminary results are available confirm the common observation that *B. burgdorferi* s.l. is approximately 10-20 times more prevalent than TBEV, while the prevalences of *Anaplasma* and *Babesia*, which are less commonly surveyed, appear to fall in between. Data on variable prevalences in relation to the tick’s seasonal dynamics are eagerly awaited.

Field observations on tick infestations and pathogen infections in rodents at sites in Italy and Slovakia have continued for a second year, with the objective of relating these factors to the variable abundance of deer. Analysis by the Italian team (CEA) has confirmed the significance of both deer abundance and local climate in determining the abundance of ticks and the presence of TBE virus.

Based on further acquisition and collation of archival data for 1970-2005, it is clear that the major changes that occurred in the agricultural and industrial sectors at the time of political transition in Central and Eastern Europe (CEE), together with consequent changes in the abiotic and biotic environment and socio-
economic conditions, could have increased the abundance of infected ticks and the contact of humans with those ticks. For example: abandoned agricultural fields became suitable for rodent transmission hosts; use of pesticides and atmospheric industrial pollutants plummeted; wildlife hosts for ticks increased; tick populations appear to have responded; unemployment and inequality increased in all countries. Unemployment and low income have been shown in Latvia to be statistically associated with high-risk behaviour involving harvest of wild foods from tick-infested forests, and also with not being vaccinated against TBE (see EDEN-Periodic-report-13-24M). Causal linkage between national socio-economic conditions and epidemiology is strongly indicated by striking correlations across eight CEE countries between the degree of upsurge of TBE and both poverty and household expenditure on food. These factors, by acting in synergy but differentially between and within each country, can explain the marked spatio-temporal heterogeneities in TBE epidemiology better than can climate change alone, which is too uniform across wide areas (Fig. 4). Different degrees of socio-economic upheaval caused by political transition can apparently explain the marked variation in TBE upsurge.

Fig. 4. Annual TBE incidence per 100,000 population (y-axis) in each county of Estonia, Latvia and Lithuania, 1970-2004 (x-axis). *I. ricinus* is present throughout and *I. persulcatus* occurs in the darker shaded areas of Estonia and Latvia. The numbers refer to the 20 counties for which meteorological data have been analyzed: Estonia, 1 Saaremaa, 2 Läänemaa, 3 Pärnumaa, 4 Harjumaa, 5 Ida-Virumaa, 6 Jõgevamaa, 7 Tartumaa, 8 Võrumaa; Latvia, 9 Gulbene, 10 Rezekne, 11 Kraslava 12 Jelgava, 13 Talsi, 14 Liepaja; Lithuania, 15 Klaipeda, 16 Siauliai, 17 Birzai, 18 Utena, 19 Kaunas, 20 Vilnius.

Emerging Diseases in a Changing European Environment

Publications with an EDEN number


1.2. Rodent-borne diseases

The work on animal reservoirs and viruses has progressed well. We are starting to have a clear picture of phylogeography of both hosts and hantaviruses.

Research on the possible role of MHC1-genetics predisposing rodents to Hantavirus infection has produced first results. A detailed study on the S and M segments of Puumala virus (PUUV) in a highly endemic region in Finland went on and showed surprisingly large genetic variation, and also reassortments at a local scale. The knowledge on the abundance of LCMV 2-type group of new arenaviruses has strengthened and we suppose that there are several LCMV-type strains in Europe. Ecological studies on cowpox have progressed well. First evidence on Borna virus in rodents was found.

Intensive longitudinal monitoring on host dynamics and rodent-borne disease transmission dynamics continues on 3 selected regions, and these studies happily coincided with the great HFRS3 outbreak in Belgium and adjacent countries down to North of Italy; in Finland there was a strong increase phase after the severe rodent crash in 2006.

---

1. Major Histocompatibility Complex
2. Lymphocytic Choriomeningitis Virus
3. Hemorrhagic fever with renal syndrome
We could show for the second time in a row that in a homogeneous taiga landscapes, *Puumala* Hantavirus spreads immediately with the rodent increase, in contrast to the fragmented landscapes in temperate Europe.

We have a lot of new information of the role of host population structure on rodent-borne disease prevalences in various population subgroups. Annual / biannual monitoring surveys are running in several countries. Work on the kinetics of *Hantavirus* infection process in rodent hosts showed the major output early in the chronic infection. We have first evidence of impaired winter survival in the bank vole due to PUUV. Modelling on masting is in progress.

The available European human data on HFRS has been compiled. The Belgian human HFRS data are being analysed together with High Resolution and Low Resolution HITs. Swedish and Slovenian human data have been submitted, and the huge Finnish data set (almost 20,000 cases) has been organized in cooperation with Finnish National Public Health Institute, and sent to LR HIT (Fig. 5). Large human serological samples from Italy, Switzerland and Hungary have been screened.

A case-control study from Finland showed that smoking is an important risk factor for PUUV infection.

Micro-array diagnostics have been developed for human and rodent screening, and it should be ready next year. First high resolution and low resolution models have been done for Belgium HFRS data.

Ecological niche modelling has been started. The aim of the study is to relate environmental features to occurrence of human PUUV infection on a large geographical scale within West/Eastern Europe using new modelling techniques.

At the annual meeting of year 2 in Antalya, all partners and participants in the ROBO group had an extensive review on their work, and several PhD students participated in the PhD meeting.

### Risk for NE in Fennoscandia based on a statistic model

- Altitude explained most of the infection risk location (99/100)
- Second most important factor was the mean daily temperature (96/100)
- Infection risk is higher at low altitudes and low temperatures
- Less snow but cold contributes to the infection risk

### VALIDATING OF MODEL

Human incidence in Finland

- 20%
- 20%
- 50%
- 0%

Map: Brummer-Korvenkontio et al. 1999

Fig. 5. Risk map for *nephropathica epidemica* in Sweden and Finland. Highest risks are drawn in red, lowest risks are drawn in green. Risk level was estimated from statistical models involving environmental variables (temperature, elevation, snow days...) fitted on Swedish data. Predictions were made for Finland based on this model.

### Publications with an EDEN number

survival of its rodent host. *Ecology* 88: 1911-1916. EDEN 0022


1.3. Leishmaniasis

Good progress was made with field surveys of environments (WP1), the sandfly vectors of *Leishmania infantum* (WP2), and canine leishmaniasis (WP4) by the LEI partners: CNM 9 (central Spain), UB 38 (northeastern and southern Spain), UM1 39 and NHM 34 (France), ISS 12 (northern and central Italy), SZIE 37 (southern Hungary), UoC 40 (Attica, Greece) and EUMS 35 (western Turkey). Concerning data analysis (WP5), sub-project workshops were held in Barcelona (month 30) and Piacenza (month 31) for planning surveys and for training in the manipulation of data layers (using ArcView and statistical packages, led by LSHTM 36). Collaborations with the HITS were continued (to produce a climate-based risk map for sandfly vectors, with the LR Spatial mapping HIT, see Fig. 6), or initiated (to investigate the effects of habitat fragmentation on sandfly distribution, with the HR Environmental Change HIT), or planned (aiming to produce $R_0$ biological models, with the Mathematical modelling HIT). A significant development was the production of a Europe-wide risk map for the prevalence of canine leishmaniasis (led by LSHTM 36).

Fig. 6. Observed and predicted occurrence of *P. perniciosus* in France. High-risk areas are drawn in green, and low risk are drawn in red (Rogers and Ready, 2006)

1.4. West-Nile fever

An encouraging year; well-structured data is now available across the span of the project, from the Guadiilquivir delta in south-west Spain to the Danube delta in eastern Romania.

Collaboration between the French (CIRAD) Horizontal Integration Team, the French (CIRAD and EID) ornithology/entomology teams, and the Romanian (Delta Danube Institute) field teams has yielded promising progress in descriptive ecology and the
integration of habitat-host-vector associations in a GIS model. The Italian teams have also worked with the CIRAD HIT team on their land cover map (Fig. 7).

There has been good progress in the vector studies. The principal ornithophilic species and potential bridge vectors (to humans) have been identified by bird-baited trapping, except in Spain. Seasonal profiles of species are well established, although extremes of weather in the past 3 years (drought in some areas, flooding in others) have modified the likely pattern of “normal” years, particularly Spain and Romania. The Bucharest team (NIRDMI), in collaboration with the Danube Delta (DDNI) ornithologists, have accumulated interesting data for Bucharest, the Romanian Plain, and the Danube Delta. They have also detected virus in several pools of mosquitoes using a RAMP kit (an immuno-chromatic test); 2 isolates have been made from positive pools and await sequencing. [The Romanian and French PhD entomologists made exchange visits to compare techniques]. The Czech team also have 4 virus isolates, 2 of Tahnya virus (Bunyavirus, California group) and 2 that remain to be identified. All 38 pools of Mallophaga ectoparasites collected in the Danube Delta, including two collected from seropositive birds, were virus-negative. The NIRDMI/DDNI teams are monitoring the survival rate of overwintering Culex pipiens at several sites. An exciting finding has been the detection of virus in 2 pools of such mosquitoes.

The Italian laboratory (IZSAM) is now processing all bird serological samples from Italy, France and the Danube Delta by neutralization, as are the Spanish and Czech teams. The unfortunate backlog of samples from the French team is now nearly cleared; a mass of interesting data is anticipated from their intensive studies. The Czech (IVB) team has tested three species of wild mammals: 7/53 (13%) of wild boars and 1/35 (3%) of fallow deer were seropositive (cross-reactivity with tick-borne encephalitis was ruled out); none of 43 Red Deer were positive.

Only 3 human cases of WNV (all in Romania) have been confirmed for the whole of Europe.
This is not unexpected: many zoonotic diseases are characterized by short periods of recrudescence, with accompanying human infections, interspersed with long periods when transmission is undetected or minimal. Understanding the dynamics of such recrudescence is the main goal of EDEN-WN.

**Publication with an EDEN number**


1.5. Malaria

According to the central question on risk assessment, most of 3rd year efforts focused on Anopheline mosquitoes. Mosquito environmental parameters have been recorded. Most of the partners have developed a GIS including environmental data.

Longitudinal surveys on mosquito biology and dynamics are almost finished in selected model field sites, and have been initiated (or continued) in several “secondary” sites. Precise data have been obtained on *Anopheles atroparvus, An. labranchiae* and *An. hyrcanus* (Fig. 8). As planned in 2006, more attention was given to the tree-hole mosquito *An. plumbeus*.

Molecular and population genetics studies have been initiated on *An. atroparvus, An. labranchiae* and *An. hyrcanus* through the EDEN MAL collaborative network. This study enabled scientists and students to be trained in different countries: Italy, France, Algeria, Morocco, Turkey and Romania.

Vector competence has been assessed by experimental transmission of an African *Plasmodium falciparum* strain, in Nijmegen. Almost all partners have sent mosquito populations to Nijmegen to be tested. All species but *An. hyrcanus* were able to replicate *P. falciparum*. However, infection rates were generally low compared to highly susceptible control strain, and depend of species and rearing conditions.

Studies related to disease, human migration and imported / autochthonous malaria have been improved in year 3 and are almost finished in some countries, while just initiated in some others. Epidemiological $R_0$ models are under development (finished in France, initiated in Turkey), as well as agent-based models (almost finished in France, initiated in Portugal).

The malaria networks are now fully operational. Several scientists and students have visited other partners. Many posters and communications related to EDEN MAL have been presented during national and international meetings. Many scientific articles related to EDEN MAL have been published or submitted during year 3. A film produced by Arte German-French TV channel showed research work on malaria conducted in Turkey (Ozer group) and France (Fontenille group). The first EDEN MAL PhD thesis will be defended in January 2008 (Nicolas Ponçon).
Emerging Diseases in a Changing European Environment

![Density map of An. hyrcanus in Camargue](image)

Fig. 8. Density map of An. hyrcanus in Camargue using a predictive model based on field records and satellite data (Tran et al., submitted).

Publications with an EDEN number


1.6. Africa platform

For the current reporting period, scientist in the African EDEN platform have addressed several issues contained in five work packages as scheduled in the project. Drafts of ecological unit maps have been improved for the Senegal River delta as they have been completed with new layers of mosquitoes and birds (Fig. 9). Data from the Mauritanian side of the Senegal River are expected for the next reporting period. The RVF outbreaks have been documented and results put together in either a scientific report at ISRA virology laboratory or organised as a publication project at IPD.
Emerging Diseases in a Changing European Environment

West Nile serological prevalences have also been measured in horses and poultry in Senegal and in Morocco. High correlation between age and serological prevalence was observed in horses in the two countries.

Studies on potential RVF and WNF vectors bionomics have generated lots of data organised in monospecific samples for virus research; however first results in this area are all negative so far. Rearing of first candidates as *Aedes vexans* and *Culex poicilipes* has been successfully achieved. However for practical and administrative reasons, rearing of *Cx poicilipes* and test on its vectorial competence have been postponed until satisfactory security conditions are reached. First analyses on wild-bird sera have also generated some interesting results in Barkedji and Djoudj where 1.3% and 1.2% were found positive for WN virus in wild resident birds.

Phylogenetic analysis of WN virus strains confirmed that two lineages (I and II) circulate in Senegal and that lineage I isolates display important genetic variability. A close relationship is found between Senegalese, Mediterranean, and European isolates, suggesting exchanges of lineage I viruses between the latter regions and Senegal. Furthermore a new lineage of WNV was identified and its full length genome was sequenced.

Animal movements have extensively been studied in Senegal. Mauritanian data are expected in 2008.

Finally, the EDEN-AFR GIS is being fed with additional data handed over and last, integration of a modelling expert in our team is expected.

Fig. 9. Avifauna specific richness (top: pale-arctic migrant species; bottom: resident species), Senegal River Delta (draft)
2. Horizontal integration teams

The aim of the horizontal integration teams (HIT) is to provide shared state-of-the-art data and methods in order to enhance scientific and technical integration in EDEN and provide all partners with additional inputs to reach the objectives of EDEN. In this third reporting period the main tasks of the horizontal integration teams was to establish and make available through the EDEN website common data bases of spatial data sets; provide processed low resolution remote sensing data to prepare for disease modelling, provide high resolution remote sensing data matching field study sites; contribute to the EDEN strategy document; and to further implement horizontal integrative research collaborations with SP.

Major progress has been made on all fronts. The main achievements of this reporting period are per HIT:

2.1. Data management

Technical achievements focussed on streamlining the main EDEN DMT website, adding to its content and in providing a new EDEN PhD website in response to requests from the EDEN PhD student body (Fig. 10). The site is now sufficiently complex that maintenance, and keeping the content up to date, requires significant time and resources.

The archive content continues to expand – both in terms of public-domain data added for general consumption and in the volume of SP data added to which processing and interpretive contributions continue to be made (TBD). Further GIS training modules have also been added, and datasets of specific value to individual SP have been provided. The DMT has also responded to requests for advice for data dissemination, data processing and archive construction from WNV, TBD, AFR, and MAL SP.

Membership of the EDEN DMT website is increasing by up to 5 each week now stands at about 300, majority of which is still external to EDEN. Hit rates are now nearing 1,500 per month – almost double the 2006 level, and a rise of 30% has been observed in the last 6 months. Users are from well over 100 countries with the majority from the United States (Fig. 11).
The EDEN PhD website also attracts a large number of visits for its type – well over 1,000 per month which suggests that the tiki-Wiki format is a successful addition to the EDEN Data Management portfolio of dissemination tools and utilities.

The only major negative note for this year has been the increasing impact of the lack of payment. All expenses and staff salaries since August 2006 have effectively been funded by the DMT's own resources. This situation has now become unsustainable, especially since the EDEN DMT partner is an SME, and continued activities are dependent on receipt of funds.

2.2. Remote sensing

Two groups contribute to the Remote Sensing (RS) Work Package Outputs: the High Resolution Remote Sensing Horizontal Integration Team (HRRS HIT) with inputs from UCL and CIRAD, and the Low Resolution Remote Sensing Team Horizontal Integration Team (LRRS HIT) with inputs from ZOOX.

2.2.1. HRRS Team

As part of the ‘environmental change’ (HRRS) HIT, we continued to work closely with all sub-projects. With each sub-project, we conducted one or several empirical data analyses on a specific disease, in a specific region or country, and on a dataset collected by sub-project partners. All these projects involved high resolution satellite imagery for land cover classification and change detection, and modelling of these data with vector, host or human data in a spatially-explicit way. We modelled vector/host presence-absence, abundance, and serological prevalence, as well as human cases of infection.

We continued collaboration with UA-ROBO to analyze spatial variations in Hantavirus infection risk in Belgium. At first, relationships between density of bank voles and Hantavirus prevalence in rodents population and a series of landscape level environmental variables were investigated. Secondly, the link between environmental and socio-economic factors and the distribution of Hantavirus human cases in Belgium was explored (Fig. 12).

Collaboration with MAL implements an agent-based model on the evolution of human-mosquito contacts according to global changes to assess the risk of re-emergence of malaria in Camargue (France). It also involves a study of the link between larval distribution and environmental variables.

Collaboration with the University of Liverpool on cowpox and rodent dynamics was continued. We collaborated with TBD to study the relationships between tick-borne encephalitis and land cover and landscape structure in Latvia, first using land-cover data derived from Landsat images and socio-economic data at the parish level.

We conducted a project with the LEI team for leishamniasis in southern France, in the Pyrenees region. Based on land-cover data derived from Landsat images, we computed forest and landscape fragmentation metrics and related these to data on the trapping of sandflies.
We continued collaborations with WNV teams to study the emergence factors of WNV in Southern France and the role of birds/mosquitoes species in the introduction, amplification and spread of the virus. Collaboration with the Danube Delta Institute started to produce habitats map for birds in the Danube Delta; the link between environmental variables and the equine cases in this area was explored. Collaborations with AFR-Senegal teams continued for the study of WNV in the Senegal Delta and RVF in the Ferlo area. We started to study the migration bird pathways from Africa to Europe.

We attended several meetings with vertical project colleagues (in Oxford, London, Antwerp, Tulcea, Montpellier...). Catherine Linard conducted field work in Camargue, Arnaud Roux in the Danube Delta. Eric Lambin attended the scientific committee meetings. We all attended the annual EDEN meeting. We presented our work to international scientific meetings and produced a couple of scientific publications.

**Publications with an EDEN number**


### 2.2.2. LRRS Team

This team operates in 4 modes, ranging from simple (the provision of LR remotely sensed satellite data to EDEN partners) to advanced (the development of new RS approaches and algorithms for problems encountered by EDEN partners).

Our service provision of processed RS data continued this year with the completion of a series of temporal Fourier processed v4 MODIS imagery for 2001 to 2005 inclusive (processing requires entire years' worth of data so cannot be completed until after years' end) in the middle infra-red (MIR), daytime Land Surface Temperature (LST), night-time LST, Normalised Difference Vegetation Index (NDVI) and Enhanced Vegetation Index (EVI) 'channels'. Images were re-projected from the Sinusoidal projection to the latitude/longitude system, for ease of use by EDEN partners (Fig. 13). The LRRS team also worked with EDEN ROBO and EDEN LEI partners to develop risk maps for Hantavirus data from Sweden (collab. with Gert Olsson, see Fig. 5) and for both leishmaniasis and two of its key vectors throughout France (collab. with Paul Ready).

![Fig. 13. Example of processed MODIS imagery (global data), the mean Normalized Difference Vegetation Index 2001-2005 (Sinusoidal projection).](image-url)
We continue to develop algorithms for using disease data recorded at administrative (i.e. polygon) and completed an analysis of the long-term AVHRR time series, investigating ‘significant’ trends in the temporal Fourier components of LST and NDVI imagery. Related work outside of EDEN involved developing risk maps for BT and its vectors in the UK, and for Lassa fever in West Africa.

David Rogers attended the EDEN AGM, all EDEN SC meetings, went on the EDEN mission to Senegal, visited ECDC, ESA and DG-SANCO to discuss EDEN activities/future and made presentations at six international meetings at which the work of EDEN was mentioned or show-cased.

**Publications with an EDEN number**


### 2.3. Risk maps, disease modelling and Biodiversity

Two publications were finalised. One publication, which is a collaboration with WN SP (Fig. 14), is currently in press at *Vector-borne and Zoonotic Diseases*. The second publication was submitted to *American Naturalist* and is the result of collaboration with TBD SP. The paper is currently in press. Both publications deal with the characterisation of the basic reproduction number $R_0$ for WNV and TBD, respectively. In both papers the characterisation of $R_0$ is then used to study a biological problem coming from the SP.

In the WNV case this was the relative contribution to the risk of spread of alternative, non-vector-borne, transmission routes. This study was reported on in the previous reporting period. For TBD this was the first study to characterise $R_0$ in a way that is both biologically and mathematically correct. In addition the study goes to great length in explaining in biological terms how the calculations are performed and what biological assumptions are underlying it. This is an example of integration between HIT and a vertical group, where the expertise of both is needed to reach a meaningful conclusion about the effect of climate change on one of EDEN’s target infections.
The collaboration with the Leishmaniasis SP has been delayed due to illness of the key researcher who is the interface between the modelling and the field work. We hope to make up for this in the next period. Fortunately this delay in the collaboration with the Leishmaniasis SP has not led to a delay in the development of the methodology. As described in the results section we have further developed the ideas towards risk mapping using the outbreak of bluetongue virus in the Netherlands, Belgium and Germany in 2006 and 2007 as a guide. We successfully constructed GIS maps for a vector-transmitted infection where we are able to gauge the influence of climate and environmental change. For this we have also been able to combine the $R_0$ modelling with the methods of the HIT on low resolution modelling. This is one of the objectives in the “road map to risk” and is the modelling part of Deliverable 45. A joint publication based on the bluetongue work will be completed in late 2007, early 2008.

**Publication with an EDEN number**

2.4. Management, training and dissemination

The main objective of the central coordination team was to provide all necessary back-up to enable smooth functioning of the project; administrative and financial guidance for partners, distribution of the EC contribution, application of guidelines for management and report, problem solving, as well as pan-EDEN team building, facilitation of communication between project teams, promotion of proper understanding of scientific fields and objectives and organizing the dissemination of EDEN results.

Two changes occurred at the EDEN management level during this reporting period.

- In January 2007, the EDEN coordinator, S de La Rocque, accepted a job in the Animal Health Division of FAO and was replaced by R Lancelot. S de La Rocque stays in EDEN as the chairman of the Advisory Group.

- Following an external audit, it was requested that Avia-GIS would become a full partner of EDEN. G Hendrickx remains secretary of the EDEN steering committee.

These changes had no negative impact on the management capacities within EDEN. The main factor affecting EDEN negatively during
Emerging Diseases in a Changing European Environment

this reporting period was the delayed payment by the EC. Two apparent reasons for these delays:

(i) a quick turn-over of the financial officers in charge of the project at DG Research (4 different officers as from the beginning of the project)

(ii) the slow processing of the results of the first external audit of the EDEN coordination requested by EC: the audit occurred in October 2006 and its results were orally communicated to EDEN coordination in June 2007.

A second financial audit of the EDEN coordination occurred during this reporting period (October 2007). Hopefully this will not delay the EC payments to EDEN partners. Whilst such delays may not affect too much larger EDEN partners, this had and still has a significant negative impact on smaller partners and SME’s.

We were recently informed that an independent impact assessment of the FP6 sub-priority "Global Change and Ecosystems" was launched by EC. This study aims to assess the achievements and impacts of a sample of selected projects mainly from FP6’s sub-priority on Global Change and Ecosystems. EDEN has been selected to be in this sample. This impact assessment mainly consists of a peer review by a group of independent experts. An auto-evaluation survey has to be filled-in and the EDEN coordination will be interviewed. The process is pending (December 2007).

EDEN is now in its third year: management and coordination tasks run smoothly. The permanent coordination tasks are implemented on a daily basis by the EDEN management team. Scientific issues of general interest are discussed by the coordinator (R. Lancelot), the chairman (D Rogers) of the SC and the secretary (G Hendrickx) of the SC. If needed, proposals are further discussed with SC members through e-mails or eventually at SC meetings. The EDEN management officer (O. Pierre) and administrative assistant (S. Pugin) are stand by on a permanent basis to respond relevant questions and contribute to problem solving. Financial monitoring is achieved through the network of financial officers of partner organizations. A bimonthly management and general information meeting is held at CIRAD headquarters in Montpellier, France. Key EDEN milestones are followed up at SC level; per SP or HIT each respective leader is responsible for respective milestones and deliverables.

During this reporting period, neither gender nor ethical issues were raised by EDEN partners.

During this reporting period management the following trouble-shooting trips were organized by the coordination team:

- O Pierre visited Latvia to solve administrative issues raised after the re-organisation of public-health services
- D Rogers and G Hendrickx visited Senegal to propose a framework for data management, data sharing, modelling and publications that would be acceptable for the teams involved in the Africa Platform. Substantial advances were made.
- The CIRAD coordination team visited Pr Hubálek (Academy of Sciences) in Czech Republic to prepare the annual meeting 2008 organised in Brno. On the second occasion, we visited his laboratory in Valtice.

The coordination also organised several dissemination actions:

- Draft version of a dissemination plan which will be presented at the SC in June 2008,
- Shooting of a film about EDEN for the TV channel “Global Change TV” in September.
- Several interviews in the local, French and European media.