An integrative approach of emerging, vector-borne diseases and the global changes: example and perspective

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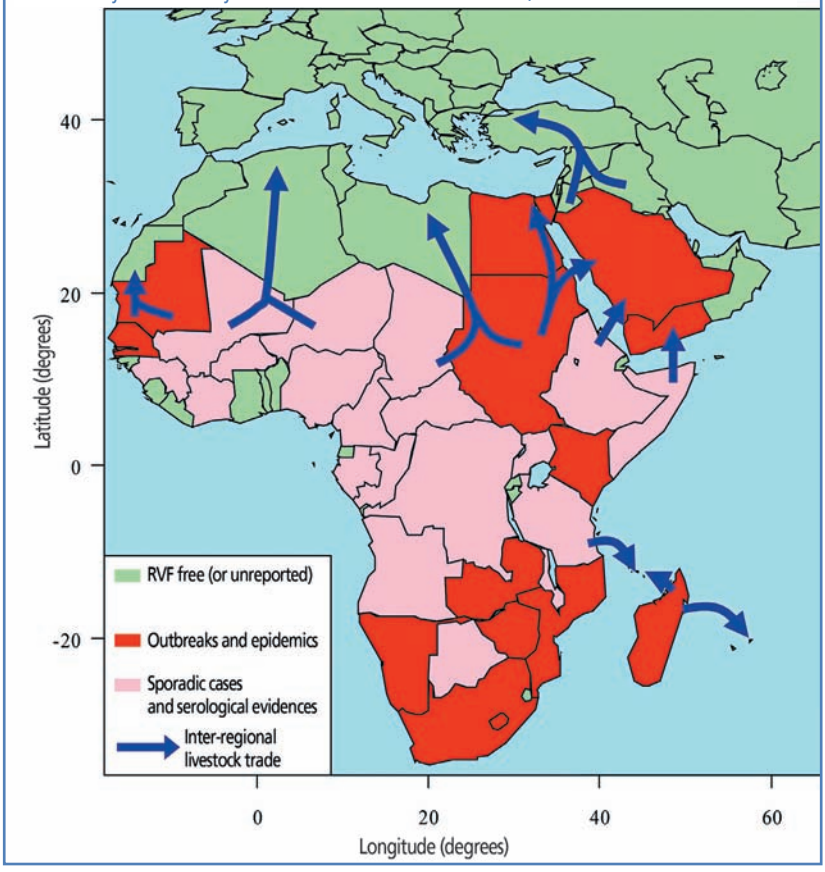
Abstract Vector-borne diseases (e.g., bluetongue or Rift Valley fever) are very sensitive to environmental changes. As such, they are excellent models to study disease emergence in a changing world, with more intense commercial exchanges, climate changes, and social and economic alterations. To address this question, a research framework was developed by the EDEN project on vector-borne, emerging diseases in a changing European environment. Because southern countries are poorly prepared to deal with emerging, infectious diseases, such an integrative, multidisciplinary approach would be helpful to federate available means and skills. Expected outcome would be the definition of priority diseases and ecosystems at highest risks, as well as the scientific bases to improve disease monitoring and early-warning systems.

Emerging vector-borne diseases and global changes

Several vector-borne diseases have recently emerged and spread with major health, ecological, socio-economical and political consequences. For example, a series of Rift Valley fever (RVF) epidemics has been occurring and spreading since 2006 in Kenya and Tanzania (2006-2007), Sudan (2007) and western Indian Ocean (2007-2009: Comoros and Madagascar). RVF is a viral, mosquito-borne disease affecting both humans and domestic ruminants. In ruminants, it causes mass abortions and neo-natal mortality. In humans, severe forms can be observed: in large epidemics, hundreds of human deaths have been reported. A recent virus phylogeny study indicated that the most recent common ancestor of RVF viruses was as recent as the late 1800s, the colonial period in Africa, a time of dramatic changes in agricultural practices and introduction of non-indigenous livestock breeds [1].

[1] Bird B.H., Khristova M.L., Rollin P.E., Ksiazek T.G., Nichol S.T., 2007. Complete genome analysis of 33 ecologically and biologically diverse Rift Valley fever virus strains reveals widespread virus movement and low genetic diversity due to recent common ancestry. *Journal of Virology* 81: 2805-2816.

❶ Rift Valley fever country status in Africa and the Middle East, and livestock trade movements



Many mosquito species may transmit RVF, including *Aedes* spp. with possible transovarian transmission and a bio-ecology well adapted to long dry periods, and *Culex* spp., found in rice fields, irrigation canals, etc. RVF epidemics are triggered by mosquito proliferations occurring during the rainy season or when flooding large areas, e.g., for crop irrigation (Sudan and Egypt, Mauritania, Madagascar). Thus, there is a fear that large hydro-agricultural development projects will increase the risk of RVF epidemics.

On the eastern African coast, RVF epidemics are related to heavy rainfalls associated with *El Niño* events. Predictive models have been developed using surface sea temperature and normalized difference vegetation index. They are used in early warning systems [2], but not in regions where the influence of *El Niño* events is smaller (e.g., Egypt, Sudan or Mauritania). Therefore, there is a need for better prediction models to focus prevention and surveillance where RVF is endemic, and to increase vigilance where RVF may be introduced: Middle East, Mediterranean and Black Sea regions.

Movements of infected animals are an efficient route for long-distance RVF dissemination (fig. ❶). This is the reason for trade bans of live animals, with severe economic consequences for

[2] Anyamba A., Chretien J., Small J., Tucker C.J., Linthicum K.J., 2006. Developing global climate anomalies suggest potential disease risks for 2006-2007. *International Journal of Health Geographics* 5: 60.

the Horn of Africa after the RVF epidemic in Yemen and Saudi Arabia in 2000, or more recently, for Sudan after the 2007 epidemic. In a recent economic modelling study on the benefits and costs of compliance of sanitary regulations in livestock markets [3] have concluded that Somali region's growth domestic product had been reduced by 25% as a consequence of the ban. In addition, poor and better off producers experienced total losses in value added of around 50% of their respective levels in a normal year.

Climate changes will deeply impact the structure of African livestock systems: a likely scenario is that livestock population will increase, leading to more intense livestock movements. The distribution of arthropods and rodents will also be affected. A recent study showed that habitat suitability of 73 African tick species will improve from 1 to 9 million km^2 at the scale of the planet, according to the tick species and climate-change scenario between 1990 and 2100 [4]. These changes may result in more frequent vector-borne diseases epidemics. Because of the inter-regional livestock trade movements, northern Africa, Middle East and Europe will be at higher risk of these diseases.

Trade globalization and development of international travels also favours the dissemination of vectors and pathogens. The trade of used tires was thus at the origin of the invasion of *Aedes albopictus*, from Asia to many places of the world. This mosquito may transmit many viruses: its dissemination is a major threat for public health. The Chikungunya epidemic involving Africa, Indian Ocean, Asia and even Europe, is an example of such coming problems.

Social and economic changes may also have consequences in the incidence of vector-borne diseases. This was demonstrated for tick-borne encephalitis in Europe [5]. In a very different context, the long-term trend for increasing human food price will cause an extension of irrigated crops. Consecutively, breeding habitat will increase for many mosquito species, thus altering the transmission pattern of many vector-borne diseases: malaria, Japanese encephalitis, West Nile fever, RVF, etc [6].

To mitigate these risks, disease and vector surveillance must be strengthened at the local, regional and international level to implement efficient disease monitoring and early warning systems (DMEWS). This is of particular importance in the Middle East and Africa which are highly exposed to the risk of emerging, vector-borne (and other) diseases of humans and animals, with scarce human, scientific and technical resources to deal with [7].

To give a relevant, scientific basis to this DMEWS, we need to better understand vector biology and ecology, assess the competence and capacity of vectors to transmit pathogens, evaluate the possible impact of climate and other changes on their distribution and on disease transmission,

[3] Pratt A., Bonnet P., Jabbar M., Ehui S. & de Haan C., 2005. Benefits and costs of compliance of sanitary regulations in livestock markets: the case of Rift Valley fever in the Somali region of Ethiopia. *International Livestock Research Institute* (LIRI), Nairobi; Kenya: 71 p.

[4] Cumming G., 2000. Using habitat models to map diversity: pan-African species richness of ticks (Acari: Ixodida). *Journal of Biogeography* 27: 425-440.

[5] Sumilo D., Bormane A., Asokliene L., Vasilenko V., Golovljova I., Avsic-Zupanc T., Hubalek Z., Randolph S.E. 2008. Socio-economic factors in the differential upsurge of tick-borne encephalitis in central and Eastern Europe. *Reviews in Medical Virology* 18: 81-95.

to assess efficiency of control plan and develop simulation models to test different climate-change and disease-control scenarios. In addition, building local capacities, and offering them appropriate scientific and biotechnical platforms, as well as establishing regional and international networks of human and technical resources, are major issues. The problem is both global and complex; it involves many biological, mathematical and social disciplines. Therefore, a multidisciplinary, integrated approach looks relevant to develop a relevant and efficient DMEWS.

The EDEN integration model

Emerging diseases in a changing European environment (EDEN) is an integrated project launched by the European commission, 6th framework programme for research and technological development. It was designed in the frame of the scientific debate on global warming and other changes, and their consequences on human and animal health. Little is known about the causes and mechanisms involved in the changes in epidemiological patterns, and the relative contributions to them of human-induced landscape changes, changing behaviours, breakdown of traditional control methods and global and local changes in climate.

The goals of EDEN were to identify, evaluate and catalogue European ecosystems, environmental and socio-economic conditions linked to global change which can influence the spatial and temporal distribution and dynamics of pathogenic agents. The outcomes are predictive, spread models including global and regional preventive, early warning, surveillance, and monitoring tools and scenarios. Such tools are targeted to improve EU policy development and decision making, both for national or international agencies.

Many disciplines and skills were needed to fulfil these goals: biology and ecology, geography, sociology, epidemiology and public health, statistical and mathematical modelling, etc. Moreover, it was necessary to cover a wide geographic area to compare and catalogue the ecosystems and describe the ecological and epidemiological processes. In addition, field studies, data analysis and modelling had to be implemented for each vector-borne disease and ecosystem with a common methodology to produce comparable results. A research consortium was constituted gathering 49 public and private institutes from 24 countries. The ecological and geographical diversity of the project area covers all relevant European ecosystems (fig. ❷).

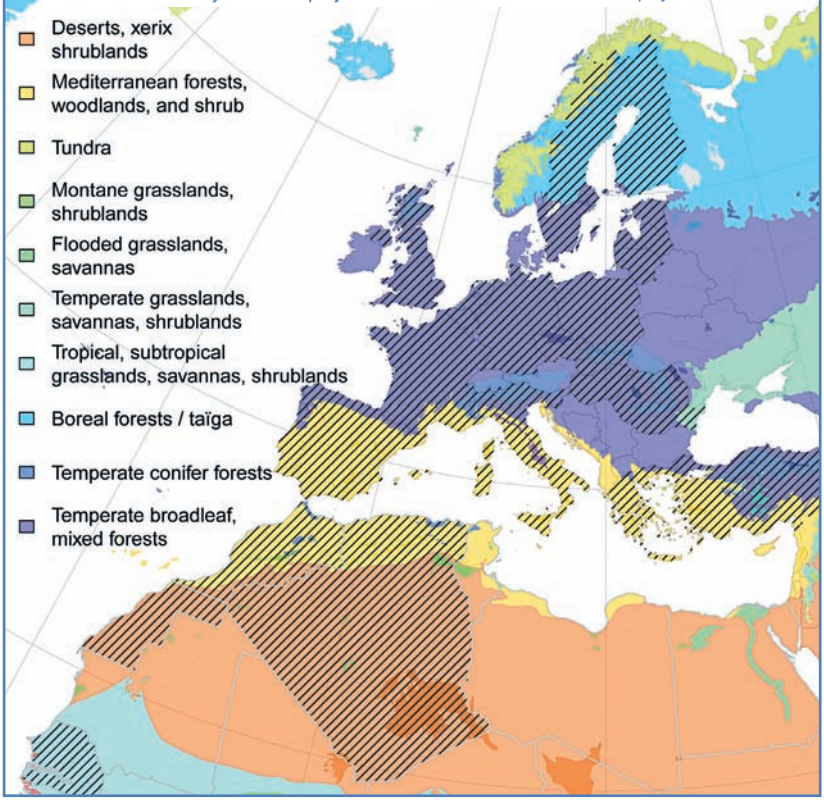
A set of "model" vector-borne diseases was selected, representing the diversity of ecological and epidemiological situations encountered in Europe:

- Tick-borne and rodent-borne diseases have recently shown significant increases in incidence, partly due to changes in vector habitat, landscape structures and human behaviour with respect to environment.

[6] Keiser J., Maltese M.F., Erlanger T.E., Bos R., Tanner M., Singer B.H., Utzinger J. 2005. Effect of irrigated rice agriculture on Japanese encephalitis, including challenges and opportunities for integrated vector management. Acta Tropica 95: 40-57.

[7] Jones K.E., Patel N.G., Levy M.A., Storeygard A., Balk D., Gittleman J.L., Daszak P. 2008. Global trends in emerging infectious diseases. *Nature*, doi:10.1038/nature06536, 451: 990-993.

❷ Biomes covered by the EDEN project. Shaded countries are involved in the project



• Leishmaniasis is a sandfly-borne, parasitic disease. It is persistent, and extending, on the southern fringes of Europe and beyond (southern Mediterranean basin), with the potential to expand as environments change.

• West Nile fever is a mosquito- and bird-borne, viral disease endemic in sub-Saharan Africa. Periodic and occasionally severe local outbreaks, especially on the eastern fringes of Europe, are showing strong associations with landscape patterns but also potential for explosive spread (the USA experience).

• Malaria, an ancient scourge of Europe, currently on her southern and eastern fringes, with the potential for re-emergence following environmental changes.

• Endemic diseases in Africa, e.g., West Nile fever (WNF) or RVF, may be introduced to the Middle East and Europe by bird migrations (WNF) or livestock trade (RVF), and subsequently establish and spread according to changes in environment, with or without the introduction and spread of exotic vectors.

Methodological developments were made to model these data with environmental variables remotely sensed at various resolution scales, to account for environmental parameters in math-

ematical models of disease transmission, or to characterize and account for biodiversity in these models [8]. Advances were made in the understanding of the biological, ecological and epidemiological processes [9], and to step from statistical to biological models and from specific to generic models of disease emergence and dissemination [5].

From October 2005 to June 2009, > 150 papers reporting these findings were published or submitted to journals. A strategy document and concept notes were written to summarize and promote ideas, methods and tools that have been developed within the frame of the EDEN project: risk maps, strategies and scenarios to monitor and manage vector-borne emerging diseases, etc. Follow-up projects have been designed with methodological inputs from EDEN, e.g., ArboZooNet, a coordination action for improving surveillance and control of zoonotic, vector-borne diseases. A large expert consultation has also been undertaken to assess magnitude and importance of vector-borne diseases in Europe on behalf of the European Centre for Disease Prevention and Control. Other projects were launched by the European Commission to delve into issues raised by EDEN, and build on new knowledge produced by the project.

Perspectives

In developing countries, poor communication facilities make collaborative research more difficult. To overcome this, regional centres should be reinforced to help in methodological dissemination, and co-ordinate research activities at the national level. However, EDEN's experience showed the importance of national structures to undertake field work and to ensure collaboration with national public health agencies. On the other hand, national research partners (NARS, universities) must be able to bear their share of work. Another limitation is the weakness of diagnostic and laboratory facilities. Regional excellence centres may be used as reference laboratories, or helped to reach this role. In addition, capacity building is both a goal and an outcome, and should be supported as such.

In general, for a relevant coverage of the main areas at high risk of vector-borne diseases in developing countries, observatories should be implemented in five broad categories of ecosystems:

- Areas exposed to high annual and seasonal variability of climatic conditions, and unstable vector-population dynamics, and strong fluctuations of human and livestock populations;
- Wetlands and irrigated-crop regions, with a continuous vector activity, and high incidence of vector-borne disease;
- Pioneer front in forested areas, and region-wide changes in agricultural practices, favouring contacts of livestock and humans with new pathogens and/or wildlife reservoirs;

[8] Hartemink N.A., Randolph S.E., Davis S.A., Heesterbeek J.A.P. 2008. The basic reproduction number for complex disease systems: defining R_0 for tick-borne infections. *The American Naturalist* 171: 743-754

[9] Linard C., Lamarque P., Heyman P., Ducoffre G., Luyasu V., Tersago K., Vanwambeke S.O., Lambin E.F. 2007. Determinants of the geographic distribution of Puumala virus and Lyme borreliosis infections in Belgium. *International Journal of Health Geographics*, 6: 15. Ponçon N., Balenghien T., Toty C., Ferré J.B., Thomas C., Dervieux A., L'ambert G., Schaffner F., Bardin O., Fontenille D. 2007. Effects of local anthropogenic changes on potential malaria vector *Anopheles hyrcanus* and West Nile virus vector *Culex modestus*, Camargue, France. Emerging Infectious Diseases 13: 1810-1815.

• Peri-urban and urban areas of megalopolis, including shantytowns as well as refugee camps in conflicts areas, with high densities of animal and human populations, poor hygiene conditions and health infrastructures;

• Ecosystems with high human population density, poor biodiversity and high risk of introduction of invasive pathogens and vectors.

Three main objectives may be targeted:

• Poverty alleviation: develop prevention and control programmes against vectors and vector-borne diseases of major economic importance at the household level, such as heartwater, East-Coast fever, African swine fever, or animal trypanosomosis.

• Surveillance and control of vector-borne, transboundary diseases restricting access to the world market: RVF, bluetongue, African horse sickness...

• Human public health: provide disease monitoring and early-warning systems for diseases representing a threat for human public health: RVF, Crimean-Congo haemorrhagic fever, Lassa fever (rodent-borne disease), human trypanosomosis...

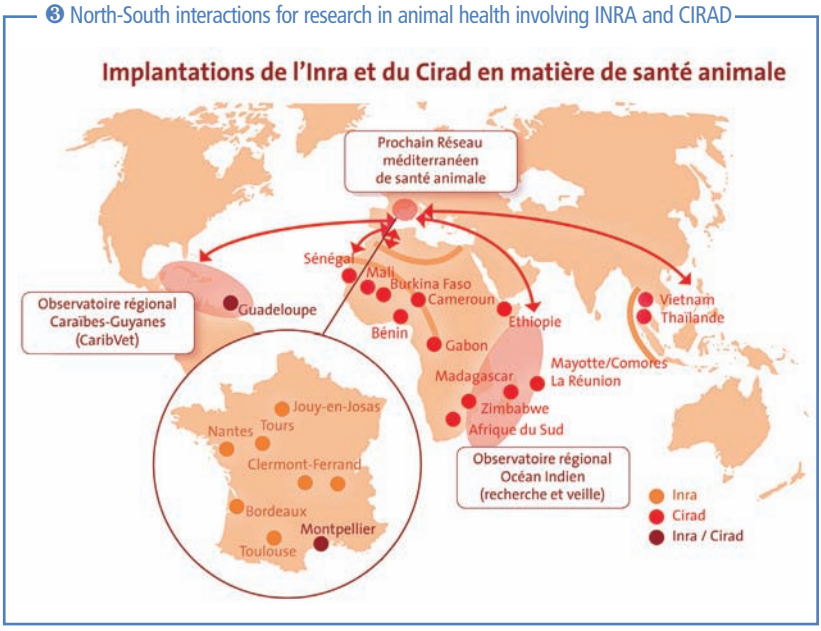
Field work is essential for the understanding and modelling of vector-borne diseases. The development, at a national level, of a fully operational disease surveillance system is out of reach for a research project. Alternative solutions have been investigated by CIRAD and INRA (fig. ❸).

The implementation of multi-disciplinary observatories in selected ecosystems was retained for a research project on the epidemiology and ecology of avian influenza and Newcastle disease, funded by the French cooperation: Mauritania, Mali, Ethiopia, Madagascar, Zimbabwe, and Vietnam.

In south-western Indian Ocean, after the Chikungunya epidemics which occurred in 2005 and 2006 in La Réunion Island, research and public-health bodies, and local authorities, established a scientific and health consortium to support a centre devoted to research and surveillance of the emerging diseases. This centre is based on a multidisciplinary approach and its scope covers human and animal diseases in Madagascar, and other Indian Ocean islands and archipelagos.

A more advanced implementation of a regional strategy, and synergy between research and development, is the Caribbean Animal Health Network (CaribVET). This network of institutions and professionals aims at improving animal health and the quality and safety of animal products throughout the Caribbean. Its members include veterinary services, veterinary laboratories, government agencies, research institutes, farmers' associations, NGOs and universities mainly from the Caribbean but also North, Central or South America.

❸ North-South interactions for research in animal health involving INRA and CIRAD



At last, recent political initiatives such as the Euro-Mediterranean network for animal health, supported by OIE, FAO and UA-BIRA, may be of great interest to promote the rise of a similar dynamics in the Mediterranean region.