Chapter One: General introduction

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I built this thesis on the basis of two recent facts about disease ecology in animals and humans: the majority of emerging diseases involve more than one host and the majority of these hosts are wildlife hosts; the disease spill-over occurs often at the wildlife/domestic interface. My main research question was: how do we study disease ecology in multi-host systems at the wildlife/domestic interface? Which tools integrating epidemiology (which is, to a certain extent, a subset of ecology) and ecology can we develop to adapt health surveillance and control to multi-host systems? Are there common properties in the ecology of disease transmission that we can estimate and use for disease control and surveillance? I develop the argumentation justifying this approach in this chapter and present an outline of this thesis.

The struggle against infectious diseases has a universal cost for living organisms. Parasites species represent between 10 and 50% of known living organisms depending on the definition one applies (Poulin and Morand 2000). Despite this reality, the ecological impact of parasitism on organisms and ecosystems has received little attention in the literature with dedicated studies on the matter blooming only recently (Hudson 2002). The ecology of parasites is of particular interest in the study of ecological interactions (since the parasite depends on one or more hosts for the completion of their life cycle) and because their role in ecosystems is poorly understood (Hudson et al. 2006). If the question of their importance is not in question in ecology, their impact on “important” species from an anthropological perspective makes some of them unwanted or in need for control. They have important implications for human health, domestic animal health, a key component of human food production systems and also wildlife health for direct conservation purposes or for ecosystem health or services. Humans, positioned de facto as nature managers, need to deal with the infectious diseases of those species they consider to be important. Understanding how some pathogens kill and others influence their hosts, how they are transmitted and how we can interfere with these processes for managing or controlling the disease is therefore
fundamental. This thesis aims at increasing theoretically our knowledge about the ecology of parasites in their hosts and improving practically our surveillance and control options.

The genetic and social evolution of the human species has produced a succession of stages defining our relationship with pathogens, sometime inducing huge impacts on the population dynamics of our own species and often initiated by crucial advances in technology or societies (Barrett et al. 1998). The plague epidemic in Europe in the XIVth century has been linked to the emergence of urban centres connected to each other by more efficient terrestrial or maritime routes (Gage and Kossy 2004). The recent globalisation in terms of movements of goods, animals, people and indirectly pathogens, encroachment in natural ecosystems, human and domestic animal population growth and the cultural mixing mainly influenced by a few centres of cultural diffusion, may have created the context for a new host-pathogen stage (Woolhouse and Gaunt 2007). How do we adapt our surveillance and control of diseases to these new contexts? Can we simply use the standard one host-one pathogen approach?

Historically, the one host-one pathogen concept has been successful in controlling and sometimes eradicating diseases of domestic and human species. In the field of animal diseases, the control of bovine tuberculosis (bTB) in Europe, and the likely global eradication of rinderpest in the entire world are commonly cited examples of successes of this standard approach (Rweyemamu and Cheneau 1995). Albeit not single host infectious diseases, the epidemiology of these two pathogens afforded the disease to be controlled by single host management. The classical approach in epidemiology consists in targeting one pathogen in one host and trying to control host-pathogen interaction by acting on the host (e.g. vaccination, treatment, culling). If past experiences such as the control of trypanosomiasis in Southern Africa was based on the perception that wildlife would play a role in disease epidemiology, only recent research has indicated that most human and domestic animal
pathogens share their epidemiological cycle with wildlife hosts (Artois et al. 2001, Cleaveland et al. 2001, Woolhouse and Gaunt 2007, Jones et al. 2008). This observation is the result of two factors: 1) the human species and its domesticated species represent only a small fraction of the biodiversity of mammals and birds. Most epidemiological cycles have more than one host (Cleaveland et al. 2001) and statistically wildlife species must represent an important fraction of the available hosts; 2) more recently, an array of human induced worldwide changes has increased movements and contacts between humans, domestic and wild species (Daszak et al. 2000, Cleaveland et al. 2007). Movements of animals, their products (for trade purposes) and people (e.g. emigration-immigration, tourism) are used by pathogens to move with their hosts. The contacts induced by these movements, often impossible in a natural context, are used by pathogens to spill-over from one susceptible host to another. Furthermore, the encroachment of human populations into natural areas for different reasons (various socio-economical, political or demographic contexts) creates also contact between humans, domestic and wild species that would not occur naturally. As a consequence, the one host-one pathogen approach is no longer effective in many situations resulting in the need to work on complex multi-host and multi-pathogen system approaches.

Clearly, a new approach to the study of host-pathogen interactions is required. The interaction of a pathogen with one of its hosts will be modified if other susceptible hosts are present in the ecosystem. Similarly, the presence of other pathogens in the same host and in other hosts in the ecosystem will influence the outcome of the interaction between a pathogen and one host. Standard epidemiology has not taken into account this dimension of host-pathogen relation and must therefore be re-enforced by various fields of ecology, such as community ecology and evolutionary biology. Epidemiology investigates the interaction between pathogen and their hosts and therefore is a subset of ecology which looks at the interaction of organisms with their biotic and abiotic environment (Begon et al. 2006). In the
last couple of decades, integration between these fields has begun (see Kitron 1998, Galvani 2003, Guernier et al. 2004, Guégan et al. 2005, Lafferty 2009 for a few examples). Disease ecology has been proposed as a new scientific field to represent this integration (Sheldon 1997, Collinge and Ray 2006). However the full multidisciplinary integration has not been achieved mostly because of the segregation of academic careers.

This thesis aims at filling part of this gap, namely at developing the integration between the fields of epidemiology and ecology in order to address disease ecology in its new dimensions. Each scientific field has developed tools for particular purposes (e.g. molecular tools for characterising specific pathogen species, parasite community comparison for community ecology) and I have tried to use some of these tools in a combined research framework. The premise of this thesis is to shift the focus of health studies from a pathogen- or host-centred to a process-centred focus. The host-pathogen interaction is an ecological process and I defined the term of “epidemiological interaction” as any ecological interaction which results in the transmission of one or more pathogens. Looking at “epidemiological interactions” between host populations, I am interested in the ecological processes involved and try to explore the common properties of these processes. The practical goal of this thesis is to provide a new research and surveillance framework to address the risk of disease transmission (including emergence) at the human/wildlife/domestic interface.

**Thesis Outline**

The structure of this thesis is composed of theoretical chapters (**Chapter Two and Seven**) which aim to explain why greater integration between epidemiology and ecology is required, and explores how to theoretically and practically implement this integration. Between these theoretical chapters, four chapters develop the research framework, step by
step, using both epidemiology and ecology to explore the dynamics of avian influenza viruses at the wild/domestic bird interface in a Southern African wetland. The main chapters (1 to 8) correspond to the core of this thesis. Chapters in appendix represent complementary work achieved during the course of this thesis, for which I have been strongly involved and my contribution as a co-author reflects this. The last chapter in appendix is a requested book chapter written before main Chapter Seven and the version is different enough from this core chapter to appear in appendix.

**Chapter Two** (Caron et al. 2009) presents a research framework using host and pathogen data to identify host species and populations at risk of introducing, spreading and/or maintaining a specific pathogen. This chapter was developed after extensive field work on avian influenza and wild birds in Africa (**Appendix One & Two**), which continued during part of this thesis (**Appendix Four**). The epidemiology of Highly Pathogenic Avian Influenza (HPAI) H5N1 is still unclear despite the efforts of the research community. Studies bringing new insights add more variability in the host-pathogen system and uncertainty in the prediction of local risks. Global analyses of wild birds’ flyways in parallel with virus outbreaks have brought limited conclusions once the raw information was extracted from relevant maps. In this chapter, we suggest an integration of epidemiology, evolutionary biology and community ecology in a research framework for a local level study (at the scale of the ecosystem). This multidisciplinary approach aims at understanding the pathogen transmission processes at the interface between different bird groups whether wild or domesticated. I believe that this ecological data brought together with the epidemiological and molecular data is a key element to explore the mechanism of the AIV ecology in their hosts.

**Chapter Three** (Caron et al. 2010) is a direct response to the ideas developed in **Chapter Two** on two aspects: 1) after the first snapshot done on avian influenza viruses (AIV) in Africa, we needed to explore the dynamics of AIV in some African ecosystems and
required therefore time series data in order to understand the ecology of these viruses in Africa; 2) it combines a community ecology approach on host species and a risk factor-based methodology borrowed from epidemiology to ascribe a quantitative risk to epidemiological interactions between different bird species (belonging in our case to different avian compartments as defined in the chapter). The ecology of hosts is crucial in understanding mechanisms of pathogens transmission and spread in complex multi-hosts systems. This paradigm is used to infer epidemiological interactions in the context of avian influenza virus (AIV) maintenance and spread at the interface between wild and domestic birds in an African ecosystem. I use the overlap of bird communities in space and time combined with ecological dynamic and non-dynamic risk factors to evaluate a risk of AIV introduction, maintenance and transmission between bird populations. From this, I produce hypotheses on the dynamics of circulation of AIV strains in waterfowl populations and on the potential “bridge” species at the wildlife/domestic interface. This protocol is a) reproducible and useful to explore AIV risk and identifies wild bird species potentially acting as reservoirs or spreaders of pathogens at a local scale; b) can be used as a management tool to improve surveillance at a local level. It is the first protocol to our knowledge providing a quantitative framework to identify bridge species potentially spreading AIV from wild to domestic birds and vice versa. I sampled the potential “bridge species” between wild and domestic bird populations identified in this chapter to test the model (on-going work).

Chapter Four (Caron et al. 2011) summarises the ecology of AIV in the wild bird community as we have observed it during two years in a Zimbabwean ecosystem. This chapter shows for the first time the persistence of AIV in a Southern African ecosystem (and in Africa as well) in waterfowl. It is an important achievement for the understanding of AIV ecology in Africa. This communication about the ecology of AIV in Africa with the suggestion that AIV are endemic in Africa is part of broader research collaborations at the
regional and continental level. **Appendix Four and Five** present these large-scale approaches (currently on-going) that I have been involved with during the course of this thesis. Waterfowl were counted and sampled in a Zimbabwean wetland over 24 months. Low Pathogenic AIV (LPAI) strains were detected during 20 consecutive months, providing the first evidence of regional yearly persistence of LPAI. I discuss the role of Afro-tropical ducks in viral maintenance and transmission and attempt to explain the observed patterns. The role of the environment is also suggested through the seasonality of rainfall and lake levels. The environment-host-pathogen link is at the core of the “One World, One Health” concept. The modification of any of these three components will have an impact on the others. One needs to take into account the full spectrum of this triptych in a particular ecosystem in order to understand which effects an action on one component will have on the others.

**Chapter Five** uses the data produced in the previous chapters to build a probabilistic model based on possible scenarios of spread of HPAI through wild birds from one bird compartment to another one in the study ecosystem. The question addressed is: what is the probability of spread through wild birds of a HPAI from one avian compartment to the next and can targeted control reduce significantly this risk? By using: 1) prevalence data obtained in domestic and wild bird species: 2) Community richness and abundance on host species as well as simple population dynamics model for each bird compartment; 3) Estimation of epidemiological interaction based on shared community of birds (as in **Chapter Three**), we construct a risk analysis framework to build this model. The model suggests 1) that risk varies by season; 2) limiting contact between the infected compartment and a few potential bridge species could control the majority the spread of the HPAI through wild birds; and 3) that the risk of diffusion in the entire ecosystem varies considerably with the avian compartment into which the HPAI is introduced (wild birds and ostrich farms). These findings give a direct contribution to AIV control and wild/domestic bird management in the ecosystem. If any
sanitary threat appears in one compartment, this model will point at the interactions at risk of spreading the threat from the infected compartment to another, giving the opportunity for management and control options.

**Chapter Six** is a comparative analysis of waterfowl communities and avian influenza ecology at a regional level using the epidemiological functional group (EFG) concept presented in **Chapter Seven**. The dataset was produced by the GAINS-SA project, consisting of the three main sites of the project, including the Zimbabwean site that I managed (**Appendix Five**). I have the possibility in this chapter to put the capture bird sample for AIV detection in perspective with the bird community present in the ecosystem. This level of study adds complexity in the analysis. However, the information extracted from the bird census data is crucial to understand the viral dynamics and detect the bias in the sampling technique. The comparison of the proportion of bird orders in the sample and in the counted community reveals which species the protocol has failed to sample and should be targeted in the future.

The use of the EFG concept is helpful to reduce the complexity of bird community (with dozens of species present) by allocating bird species into groups of expected similar function in the viruses’ ecology. The outputs of this chapter are threefold: 1) I can compare the dynamics of different bird community in three different ecosystems and suggest hypotheses on viral circulation based on bird ecology; 2) Applying the EFG approach, I am able to analyse the AIV results per groups of birds and validate or not my hypotheses on the function of these bird groups; 3) I conclude by challenging for Southern Africa the idea that AIV epidemiology is mainly dependant on Anseriforms and/or Charadriiforms. The remaining bird community seems to play a role in AIV epidemiology.

**Chapter Seven** is the second theoretical chapter. The first approach presented in detail in **Chapter Two**, using host data to infer epidemiological interactions is developed in **Chapter Three, Four, Five and Six**. In this chapter, I explore and define the basis for the
pathogen approach. Emerging infectious diseases result from the spill-over of pathogens to new species within multi-host systems. The current disease surveillance systems cannot anticipate emergences because they fail to identify future culprits (pathogens and reservoir or spreader hosts) in these complex systems. The actions of public health officers and veterinarians are restricted to later stages of epidemics once the severity of outbreaks can be much higher. However, recent advances in community ecology, molecular ecology and network analysis open new perspectives for the integration of epidemiology and ecology and for the understanding of disease transmission in multi-host systems. Shifting the focus from host-pathogen relationships to transmission processes, we develop a framework building networks of epidemiological interactions between host populations (of the same species or from different species) at the ecosystem level. These networks use two types of data: 1) Host movement and contact data (e.g. direct observation, telemetry as a proxy of disease transmission); 2) Parasite community data from different host populations, assuming that past transmission pathways inferred from this data are the most likely transmission pathways for emerging pathogens. The field of parasite community ecology has provided analytical tools to compare parasite communities by controlling for confounding factors (e.g. phylogenetic distance). We define also the concept of epidemiological functional groups to which host populations can be allocated according to their potential role in epidemiology of parasites, drawing a parallel with the approach adopted by community ecologists to assign species to functional groups. Hosts are grouped together when sharing a similar role in the transmission of a parasite or a group of parasites (e.g. reservoir, spreader, dead-end host). We explore the relevance of this approach to identify the most likely future transmission pathways between host populations in a given ecosystem. Once identified, these transmission pathways can be targeted by disease surveillance and control to prevent the next pathogen emergence. The epidemiological interaction network framework that we present could achieve two objectives:
increasing theoretical knowledge on the ecology of disease transmission and on multi-host multi-pathogen interactions and providing a tool for EID early detection. In Appendix Seven, I have a slightly different angle of approach to define the same ideas and put more emphasis on some key aspects or potential weakness of the methodology (this Appendix is an invited book chapter).

In Chapter Eight, I summarise the main findings of my thesis and how they contribute to disease ecology and, more precisely, to transmission ecology. Transmission ecology focuses on the process of transmission instead of focusing on one host or one pathogen. I try to discuss how (or to what extent) the transmission mechanisms in a particular ecosystem are largely independent of particular parasite species. The common properties of transmission processes enable the development of new hypotheses that can be tested to better understand host-pathogen interactions in a complex system, particularly at the wildlife/livestock interface.
Literature cited


