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Meeting report

Emerging diseases in Chiroptera: why bats?

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A conference entitled '2nd International Berlin Bat Meeting: Bat Biology and Infectious Diseases' was held between the 19 and 21 of February 2010 in Berlin, Germany. Researchers from two major disciplines, bat biologists and disease specialists, met for the first time in an interdisciplinary event to share their knowledge about bat-associated diseases. The focus of the meeting was to understand why in particular bats are the hosts of so many of the most virulent diseases globally. During several sessions, key note speakers and participants discussed infectious diseases associated with bats, including viral diseases caused by Henipa-, Filo-, Corona- and Lyssaviruses, the spread of white-nose syndrome in North American bats, bat immunology/immunogenetics, bat parasites, and finally, conservation and human health issues.

Keywords: immunology; infectious disease; virus ecology; white-nose syndrome; conservation; zoonosis

1. INTRODUCTION

Approximately 1200 Chiropteran species inhabit our planet and every fifth mammalian species worldwide is a bat. For many decades, scientists and the public have recognized the important ecosystem services that bats provide as seed dispersers, plant pollinators and consumers of vast quantities of insects, many of which harm agricultural crops. As evidence of their critical role in numerous ecosystems increased, so did the necessity to implement conservation strategies against declining populations. But while many research efforts focused on environmental questions, disease issues played a subordinate role and investigations involving bats and infectious agents were largely limited to rabies. This situation changed during the last two decades when physicians were faced with a number of highly virulent disease outbreaks, resulting in the search for unknown reservoir hosts and attention being drawn to bats as potential reservoirs for the disease agents (Chua *et al.* 2002; Lau *et al.* 2005; Leroy *et al.* 2005; Li *et al.* 2005; Halpin *et al.* 2007; Towner *et al.* 2007). Nevertheless, bat biology research remained rather untouched by these critical findings. Apart from some early collaborative projects, disease investigators and bat researchers had no significant overlap between their respective fields. In recent years, it has become evident that each group can benefit from the expertise and knowledge of the other, especially to gain a more comprehensive understanding of why bats are associated with numerous infectious diseases. Based on these circumstances, a conference on bat biology and infectious diseases was held in Berlin, Germany, organized by the Leibniz Institute for Zoo and Wildlife Research (Germany). The particular aim of this conference was to build a bridge between researchers from two mostly diverging disciplines: the study of bat biology and that of infectious diseases.

2. EMERGING PROBLEMS: FOR HUMANS AND FOR BATS

(a) *Infectious viral diseases*

In his plenary talk, Hume Field (Queensland Primary Industries and Fisheries, Australia) opened the session 'Bats and emerging infectious diseases' with an introduction of the important infectious diseases involving chiropterans and humans in Australia and southeast Asia. Besides describing the disease characteristics, he aimed to elucidate why bats seem to be different with respect to diseases when compared with other animals. A strong emphasis was placed on explaining the seemingly sudden emergence of infectious agents connected to bats. Pathogens coevolved with bats and circulated for thousands or even millions of years within bat populations. But not until recently, when human populations encroached upon ecosystems, did these agents infect new host species. Alison Peel (University of Cambridge, UK), winner of the student presentation award, introduced her investigations on the genetic metapopulation structure of the straw-coloured flying fox, *Eidolon helvum*, a migratory species from sub-Saharan Africa. By using a combination of mitochondrial and microsatellite markers, she investigated the spatial dynamics of concurrent viral pathogens in this highly mobile species. Using radiotelemetry, a large-scale study of the ecology of henipaviruses in southeast Asia showed that flying foxes can easily travel more than 1000 km and cross water boundaries into neighbouring countries (Epstein *et al.* 2009), which highlights the fact that these bats are ideal candidates for the spread of harmful agents. Notably, a number of additional viral and bacterial infectious agents have been detected in various bat species throughout the world, but only some are known to be pathogenic to bats. So far, one of the few experimental studies on the pathogenesis of viral infections in bats by Tony Schountz and co-workers investigated the impact of *Tacaribe arenavirus* on Jamaican fruit bats (*Artibeus jamaicensis*). Besides, bats displaying clinical signs of neurological disease, detection of viral RNA in various tissues was associated with histopathological inflammatory changes within the different organs. Such animal models will be crucial for understanding the circulation and transmission of viral diseases among bat populations as well as to other mammalian hosts.

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Rabies remains a significant viral zoonosis and 10 of the 11 Lyssavirus species causing this fatal encephalitic disease are associated with bats. Four viruses occur in Africa alone, some of which seem to have vanished, including Lyssaviruses like Lagos bat virus (LBV) and Duvenhage virus (DUVV) in South Africa. However, Wanda Markotter (University of Pretoria, South Africa) and co-workers demonstrated that LBV and DUVV are still present, with LBV primarily circulating among frugivorous bats and DUVV circulating among insectivorous bats. Other studies showed a close connection between seroprevalence, seasonality and behaviour, with highest levels of neutralizing antibodies found in large colonies as well as during annual migration. Gary McCracken (University of Tennessee, TN, USA) pointed out that bats in maternity roosts face increased contact rates while searching for their pups, and antibody levels against rabies were indeed highest in such roosts.

Whereas many bats seem to perform well despite carrying infectious agents, mass mortalities can occur in bat populations, the most important and recent case being the sudden emergence of white-nose syndrome (WNS) in North American bats.

(b) *White-nose syndrome*

WNS is an emerging fungal disease of hibernating bats in North America, causing the most precipitous decline in bat populations ever reported. As the plenary speaker David Blehert (USGS; USA) pointed out, mortality rates have averaged 95 per cent in some hibernacula in the northeastern United States since this condition was first observed in 2006. Known characteristics of WNS include: (i) a cutaneous infection caused by a previously undescribed psychrophilic and keratinophylic fungus (*Geomyces destructans*) appearing as white, filamentous or powdery growth on the nose, ears and wing membranes (Blehert *et al.* 2009); (ii) emaciation (Blehert *et al.* 2009); (iii) atypical behaviour causing bats to emerge prematurely from hibernacula in mid-winter (A. Hicks 2010, personal communication); and (iv) ulcerated, necrotic and scarred wing membranes in bats that recently emerged from hibernation (Reichard & Kunz 2009). Preliminary evidence suggests that WNS may also be associated with atypical arousal patterns, elevated metabolic rates, reduced bacterial flora in digestive tracts and disruptions in immune responses (reviewed in Turner & Reeder 2009). Currently, there is no effective mitigation practice known to control the spread of WNS. David Blehert also presented recent findings from infection trials and announced a recently developed rapid polymerase chain reaction diagnosis, which will provide researchers with a non-lethal method for determining if *G. destructans* is present in bat populations (Lorch *et al.* in press).

Marianne Moore and co-workers demonstrated that WNS-affected *Myotis lucifugus* are immunocompromised when compared with unaffected bats, but only in some measures of immune response. A talk presented by Thomas Kunz (Boston University, USA) emphasized the potential negative effects of WNS on ecosystem services provided by insectivorous bats using an example of the model system (*Tadarida brasiliensis*) from the USA, while Gudrun Wibbelt discussed current knowledge regarding the presence of *G. destructans* in European bats, and presented results from surveillance conducted in several countries during the winter of 2008–2009. A poster authored by Sébastien Puechmaille (University College Dublin, Ireland) reported that, in 2009, *G. destructans* was cultured from *Myotis myotis* near Périgueux, France. The isolate had similar morphology and 100 per cent sequence identity with *G. destructans* isolated from North American bats (Puechmaille *et al.* 2010). Thus far, it has not been reported that the fungus causes mass mortalities in Eurasia as well, and this fact sparked lively discussions about potential explanations of this difference. These include: (i) the European fungus may be avirulent; (ii) North American and Eurasian bats differ in their immunogenetics; (iii) fungal infections in US bats may be a symptom of some condition that results in immunosuppression, or constraints associated with hibernation physiology specific to the affected species.

3. BAT IMMUNOLOGY AND IMMUNOGENETICS

Despite being of central relevance for understanding bat-related diseases, surprisingly little is known about bat immunology and how bat immune responses engage pathogenic and non-pathogenic micro-organisms and parasites. This is principally because of a historical lack of appreciation of pathogens that cause diseases in bats and the role of bats as reservoirs of zoonotic disease agents. Since bat species have been increasingly identified as reservoirs for many diseases affecting humans, and because of the emergence of WNS, a concerted effort has been made by researchers to address these deficiencies, some of which were reported at the meeting.

Genetic studies presented at the meeting identified orthologous bat immune genes, including major histocompatibility class II genes and multiple alleles in *Eptesicus fuscus* and *Noctilio albiventris*. Data suggested that certain alleles may be associated with parasite burden. Innate, antiviral and interferon genes from *Pteropus alecto*, *P. vampyrus* and *M. lucifugus* have also been identified. Most Toll-like receptors orthologues involved in microbial pattern recognition have been detected in *Pteropus* genome scans by Baker (CSIRO Livestock Industries, Australia) and co-workers. Speakers agreed that specific assays for immunoglobulin subtypes are needed, particularly in the light of the study by James Aegerter (FERA, UK) and co-workers who demonstrated the potential use of an IgA detection assay that may be helpful in characterizing mucosal antibody responses. Functional assays also demonstrated bactericidal and fungicidal activity of complement from *M. lucifugus* (Moore and co-workers, Boston University, USA) and *E. fuscus* (Warburton and Vonhof, Western Michigan University, USA), as well as T-cell assays assessing delayed-type hypersensitivity, and plasma hormonal modulation in *Carollia perspicillata* (Greiner and co-workers, IZW, Germany). Efforts from Hjalmar Bouma and co-workers (University of Groningen, The Netherlands)

found reduction of neutrophils, monocytes and lymphocytes in torpid hamsters (*Mesocricetus auratus*), a finding that may have relevance to immunocompetence in torpid bats, particularly for those affected by WNS.

4. RECONCILING BIODIVERSTY CONSERVATION AND PUBLIC HEALTH

In his plenary talk, Paul Racey (University of Exeter, UK) emphasized the global distribution and pivotal ecological importance of bats, while stressing that one-fifth of this group of mammals is threatened with extinction and almost nothing is known about disease agents that are pathogenic to bats. The problem of bushmeat-hunting and associated risks of diseases transmission from bats to humans highlights the need for educational programmes, particularly in southeast Asia and Africa, where bats are frequently consumed. These outreach programmes could become as important in preventing future disease outbreaks as in-depth studies of molecular mechanisms underlying the virulence of agents. Without downplaying the importance of investigating bats as reservoirs of infectious diseases and establishing control measures, Racey emphasized that every effort must be taken to avoid a reductionist approach to newly described infectious diseases and that all factors associated with the emergence of infectious diseases must be considered so that bats do not simply become targets for persecution and eradication.

5. THE FUTURE

Bats have been shown to serve as reservoirs for a multitude of infectious agents. To unravel the ecology of these diseases, it will be necessary to further elucidate their impact onto the individual bat, particularly since it remains unclear how and over which periods of time infectious agents are maintained within bat hosts. The answer to these questions will be central for understanding transmission mechanisms between bats and other mammals, including humans. Moreover, this knowledge will be key to modelling the emergence and spread of diseases. Modern technologies like genomic approaches will additionally provide new insights about bats and pathogens, particularly regarding their evolutionary histories.

Several informal sessions were held to specifically discuss Eurasian and North American approaches to investigating WNS, providing a fruitful opportunity for researchers to discuss the potential for collaborations both in Europe and North America to contribute knowledge regarding the aetiology, epidemiology and development of WNS on both continents.

Oral and poster presentations highlighted the many challenges that must be overcome to understand the immunological relationships between bats and their disease agents, and how zoonotic agents that are hosted by bats evade sterilizing immune responses to establish persistent infections. It is likely that studies in these two areas will complement each other and lead to a better understanding of the ecology of these infectious agents. Research in basic bat immunobiology will foster the development of applied immunological methods relevant to conducting experimental infections and studying natural populations of bats.

In a final discussion, the audience agreed that public perception of bats is often skewed by the fear of contracting deadly diseases such as Ebola haemorrhagic fever or rabies. It is in the responsibility of the scientific community to communicate scientific facts and provide a better understanding of the possible dangers, while simultaneously fostering a beneficial coexistence of bats and humans. As one delegate pointed out: 'bats are of fundamental importance for the global ecosystem, even if they carry potentially harmful diseases'.

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