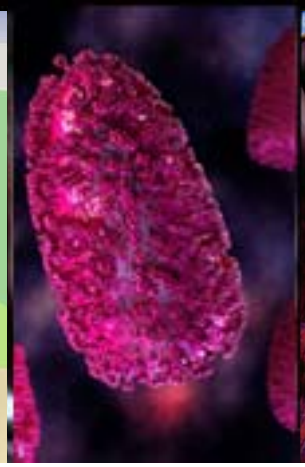
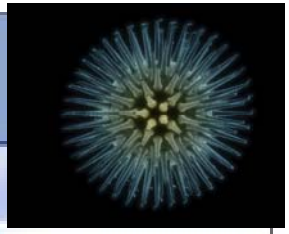
# CHIROPTERA: Cornerstones of rabies research and other diseases


CE Rupprecht VMD, MS, PhD
Professor (Adjunct), Wistar Institute;
CEO, LYSSA LLC;
Member, WHO Expert Advisory Board;
RITA INC, International Steering Committee;
CARIBVET Member;
Scientific Advisory Board, Bat Conservation International;
ETC.

# Global Emerging Diseases*

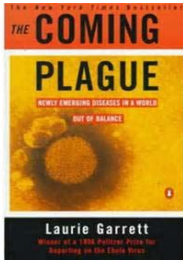


★ ZOONOTIC
★ VECTOR-BORNE

Vancomycin-resistant *S. aureus*
Cryptosporidiosis
Multidrug-resistant tuberculosis
Drug-resistant malaria
Cyclosporiasis
*E. coli* O157:H7
Hepatitis C
vCJD
Diphtheria
SARS
*E. coli* O157:H7
H5N1 influenza
Human monkeypox
Lyme disease
West Nile virus
Typhoid fever
Anthrax bioterrorism
Vancomycin-resistant *S. aureus*
Rift Valley fever
Lassa fever
Nipah virus
Hendra virus
Whitewater arroyo virus
Hantavirus pulmonary syndrome
Enterovirus 71
Human monkeypox
Dengue
Yellow fever
Cholera
Marburg haemorrhagic fever
Ebola haemorrhagic fever
Plague

EMERGING
RE-EMERGING

* Modified from Morens et al. 2004 *Nature* 430:242

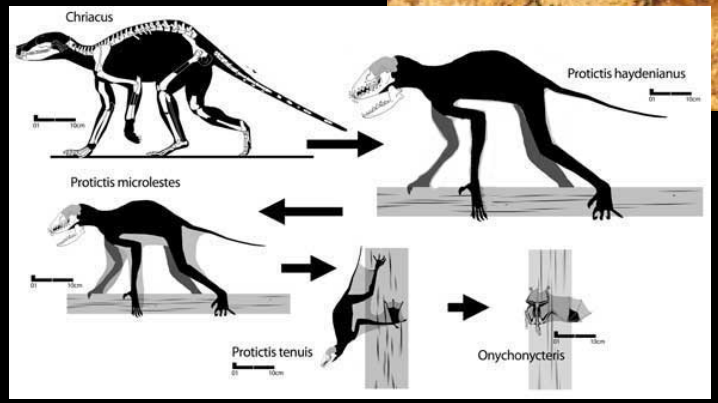


# Objectives

- Compare basic biological attributes of bats
- Cite selected reports on bat pathogen discovery
- Infer applications from bat lyssavirus introspection as to perceived relevance for other pathogens
- Discuss perspectives on recent agent emergence, host changes, potential management & future concerns


Order Chiroptera
Global Distribution
➢ 1,100 species
➢ Echolocation
➢ Volant
Are Bats Special (or just 'die Fledermaus')?
© J. Scott Altenbach

# CHIROPTERA ARE AN ANCIENT GROUP



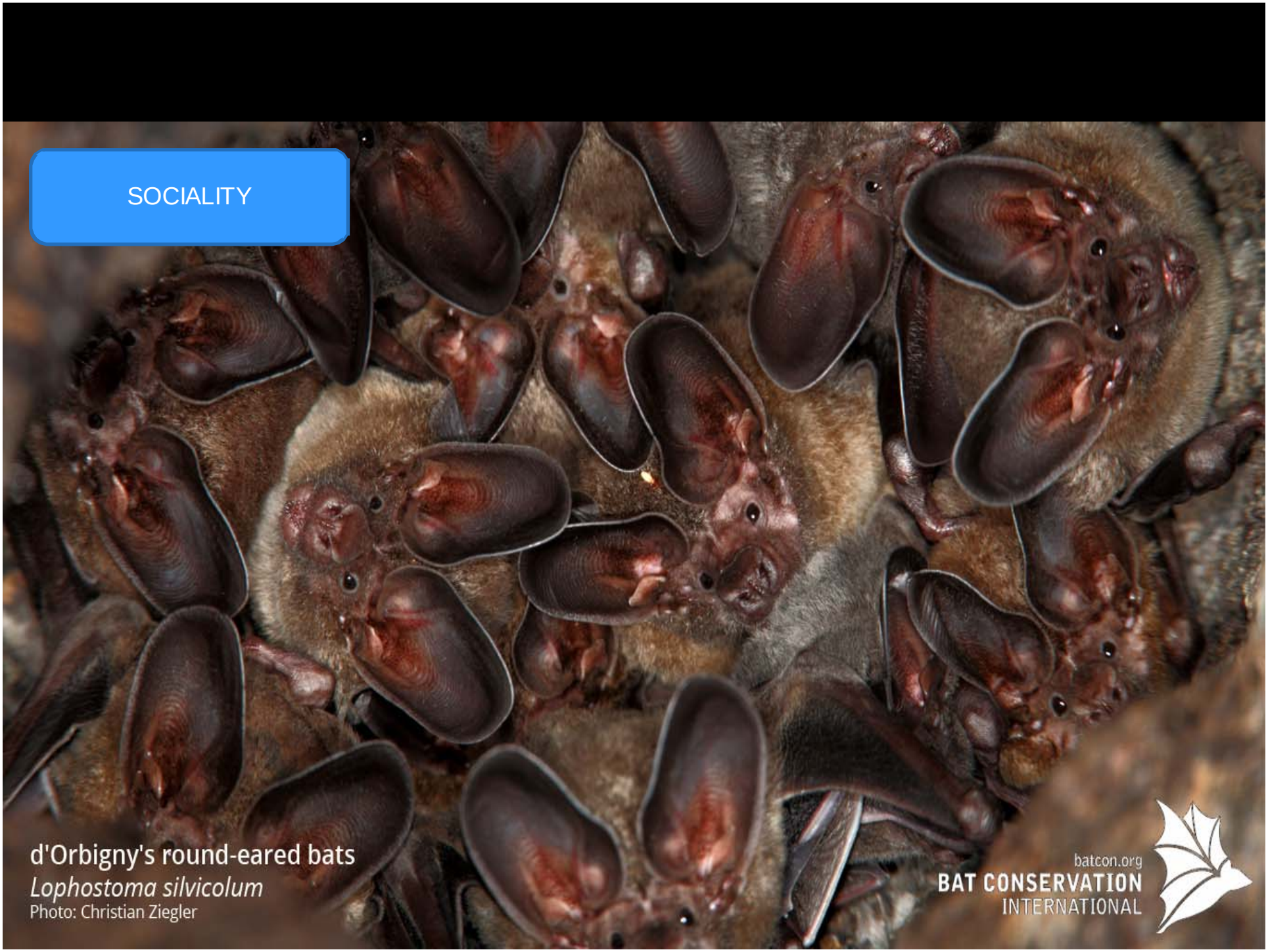
If one really loves nature,
one can find beauty everywhere.

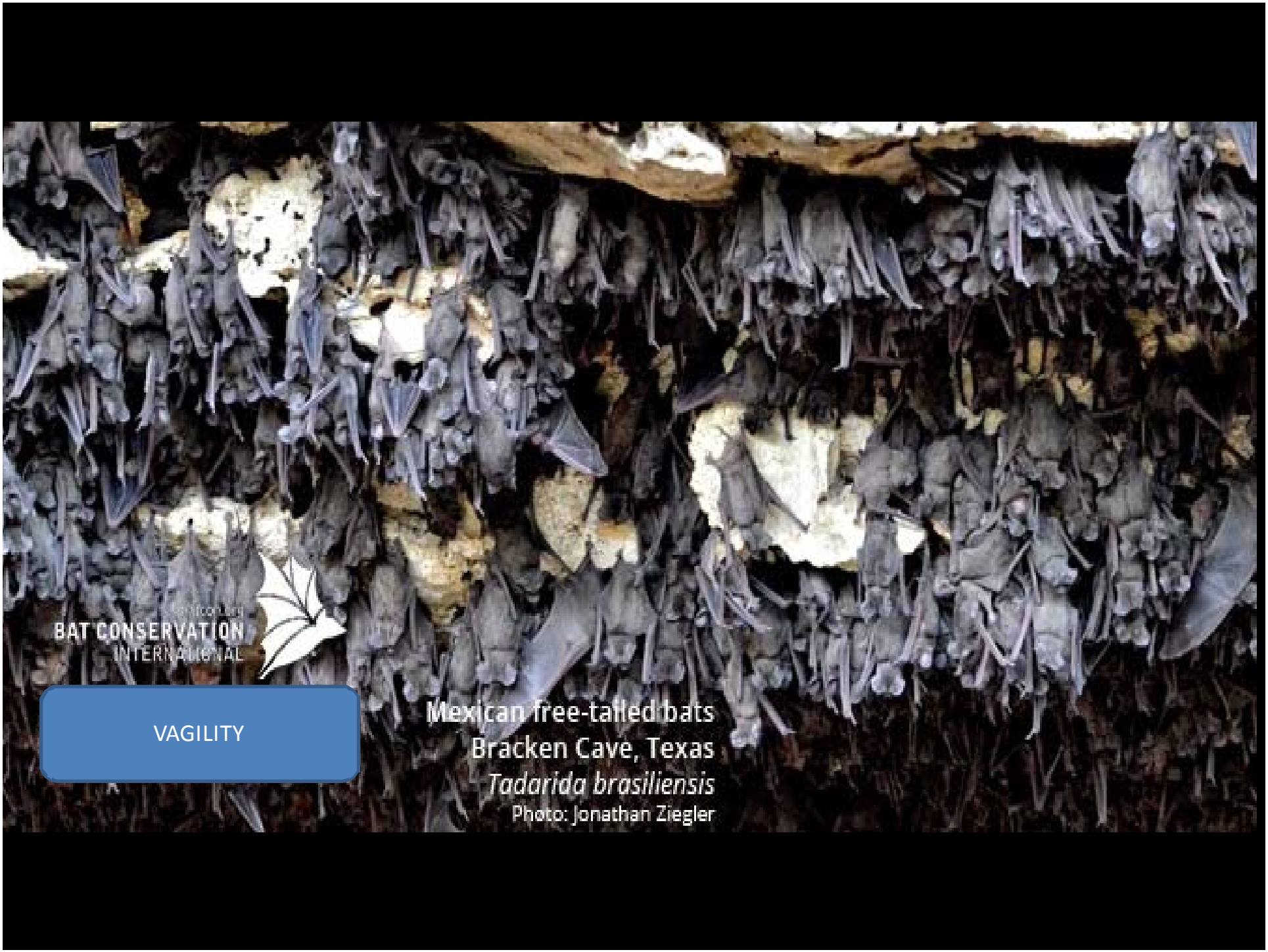
Vincent van Gogh

batcon.org
BAT CONSERVATION
INTERNATIONAL

BIODIVERSITY

Wahlberg's epauletted fruit bat
*Epomophorus wahlbergi*
Photo: Merlin D. Tuttle


SOCIALITY
d'Orbigny's round-eared bats
*Lophostoma silvicolum*
Photo: Christian Ziegler
batcon.org
BAT CONSERVATION
INTERNATIONAL


BAT CONSERVATION
INTERNATIONAL
Mexican free-tailed bats
Bracken Cave, Texas
Tadarida brasiliensis
Photo: Jonathan Ziegler

VAGILITY


"Life in the Slow Lane..."
Adult survival high
Longevity (~5-30+ years)
Reproductive success high
litter sizes small (~1-2/yr)
slow to independence
late sexual maturity
Population growth slow
cannot respond quickly to rapid changes in population size
Torpor & Hibernation
© J. Scott Altenbach

# Pest Suppressors & Pollinators Extraordinaire

Economic value of the pest control service provided by Brazilian free-tailed bats in south-central Texas

Ann. N.Y. Acad. Sci. ISSN 0077-8923

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Issue: *The Year In Ecology and Conservation Biology*

**Ecosystem services provided by bats**

Thomas H. Kunz,[1] Elizabeth Braun de Torrez,[1] Dana Bauer,[2] Tatyana Lobova,[3] and Theodore H. Fleming[4]

[1]Center for Ecology and Conservation Biology, Department of Biology, Boston University, Boston, Massachusetts. [2]Department of Geography, Boston University, Boston, Massachusetts. [3]Department of Biology, Old Dominion University, Norfolk, Virginia. [4]Department of Ecology and Evolutionary Biology, University of Arizona, Tucson, Arizona

Address for correspondence: Thomas H. Kunz, Boston University, Boston, MA 02215. kunz@b

Ecosystem services are the benefits obta valuation is conducted by measuring the of ecosystem services. Bats have long b dispersal, and pollination; however, only Here, we review the available literature o bats. We describe dietary preferences, for frugivorous, and nectarivorous bats worldi ensemble, we discuss the consequences o Throughout this review, we highlight the Finally, we provide a comprehensive ove studies estimating the economic value of e we outline a framework that could be used provided by bats, such as food and guan economic value. Nonmarket valuation m services, including inputs to agricultural p economic value of ecosystem services prov protect or restore bat populations and ass

Keywords: arthropod suppression; biolog pollination; seed dispersal; sustainable agri

**Introduction**

Ecosystems consist of living organisi interactions with the abiotic enviro physical and chemical). Terrestrial ec clude forests, grasslands, deserts, w caves. Aquatic ecosystems include riv lakes, ponds, estuaries, and oceans. F of years, both terrestrial and aquatic ec been subject to human alterations, in version of natural ecosystems to agricul tems that were needed to sustain incre population growth. Natural ecosystem

doi: 10.1111/j.1749-6632.2011.06004.x
Ann. N.Y. Acad. Sci. 1223 (2011) 1–38 © 2011 New

POLICYFORUM

CONSERVATION

**Economic Importance of Bats in Agriculture**

Jonas E. Boyles,[1]* Paul M. Cryan,[2] Gary F. McCracken,[3] Thomas H. Kunz[4]

White-nose syndrome (WNS) and the increased development of wind power facilities are threatening populations of insectivorous bats in North America. Bats are voracious predators of nocturnal insects, including many crop and forest pests. We present here evidence suggesting that loss of bats in North America could lead to agricultural losses estimated at more than $53 billion/year. Urgent efforts are needed to educate the public and policy-makers about the ecological and economic importance of insectivorous bats and to provide practical conservation solutions.

**Infectious Disease and Wind Turbines**

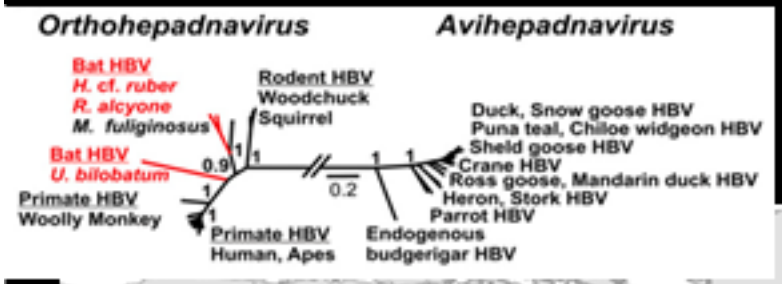
Insectivorous bats suppress populations of nocturnal insects (1, 2), but bats in North America are under severe pressure from two major new threats. WNS is an emerging infectious disease affecting populations of hibernating cave-dwelling bats throughout eastern North America (3). WNS is likely caused by a newly discovered fungus (*Geomyces* sp. nov. *destructans*). This fungus infects the skin of bats while they hibernate and is thought to trigger fatal abnormalities in behavior and/or physiology (e.g., premature depletion of energy reserves) (3, 4). Since February 2006, when WNS was first observed in bats in upstate New York, *G. destructans* has spread west of the Appalachian Mountains and into Canada. To date, over one million bats have probably died, and winter colony declines in the most affected region exceed 70% (5). Populations of at least six species [illegible] have declined so precipitously that regional extirpation and extinction are imminent (5).

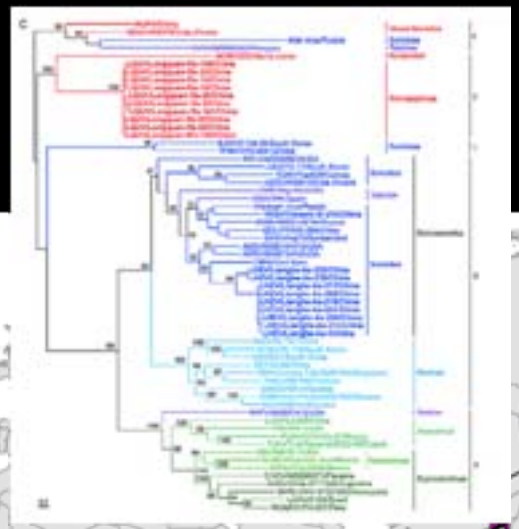
**The worth of insectivorous bats.** Estimated annual value of insectivorous bats to the agricultural industry in the county level. Values (in $/ha per county) assume bats have an estimated corn value of ~$74/acre of cropland ($30/ha) or more.

*To whom correspondence should be addressed. E-mail: jboyles@uwaterloo.ca

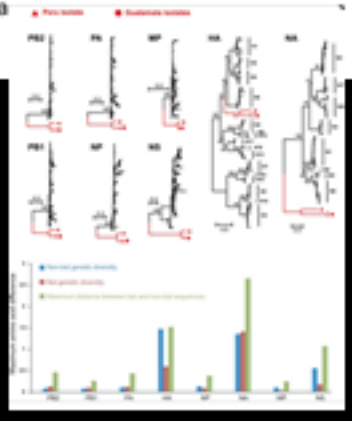
www.sciencemag.org SCIENCE VOL 332 1 APRIL 2011

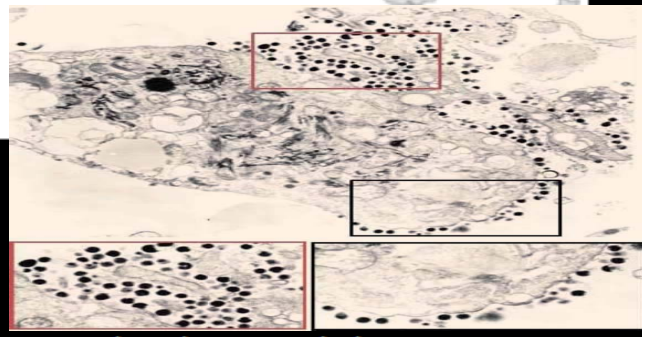
# A VERITABLE PLETHORA OF PATHOGENS SEEM TO BE ASSOCIATED WITH BATS…





RS. Shabman et al. Isolation and Characterization of a Novel Gammaherpesvirus from a Microbat Cell Line. mSphere, published online February 17, 2016

BAT PHYSIOLOGY– "Flight As Fever"?

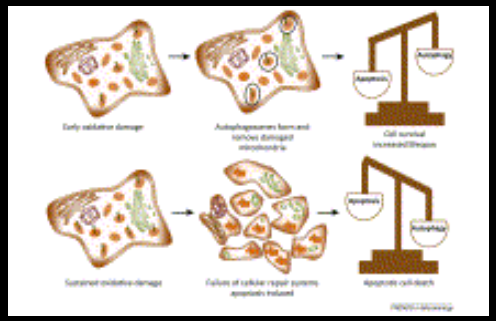
••Bats experience morbidity to many extracellular infections.

••Bats may control intracellular pathogens via cellular pathways to apoptosis/autophagy.

••These mitigation pathways could support longevity and tumor avoidance.

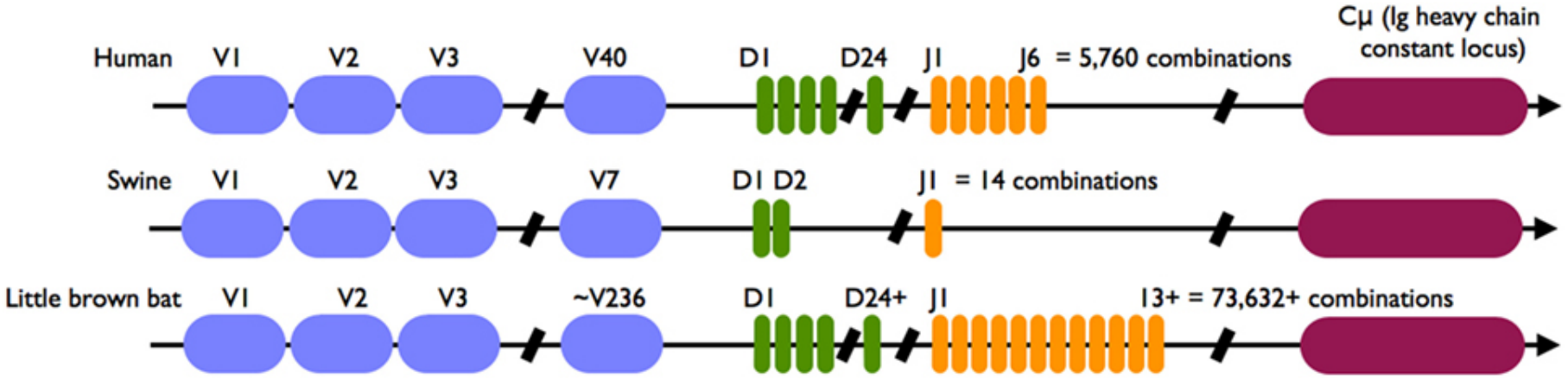
••Extracellular pathogen-associated morbidity may result from immunopathology.

•Mitochondrial mechanisms of bat physiology may have evolved to mitigate oxidative stress incurred during metabolically costly and 'hot' activities such as flight.

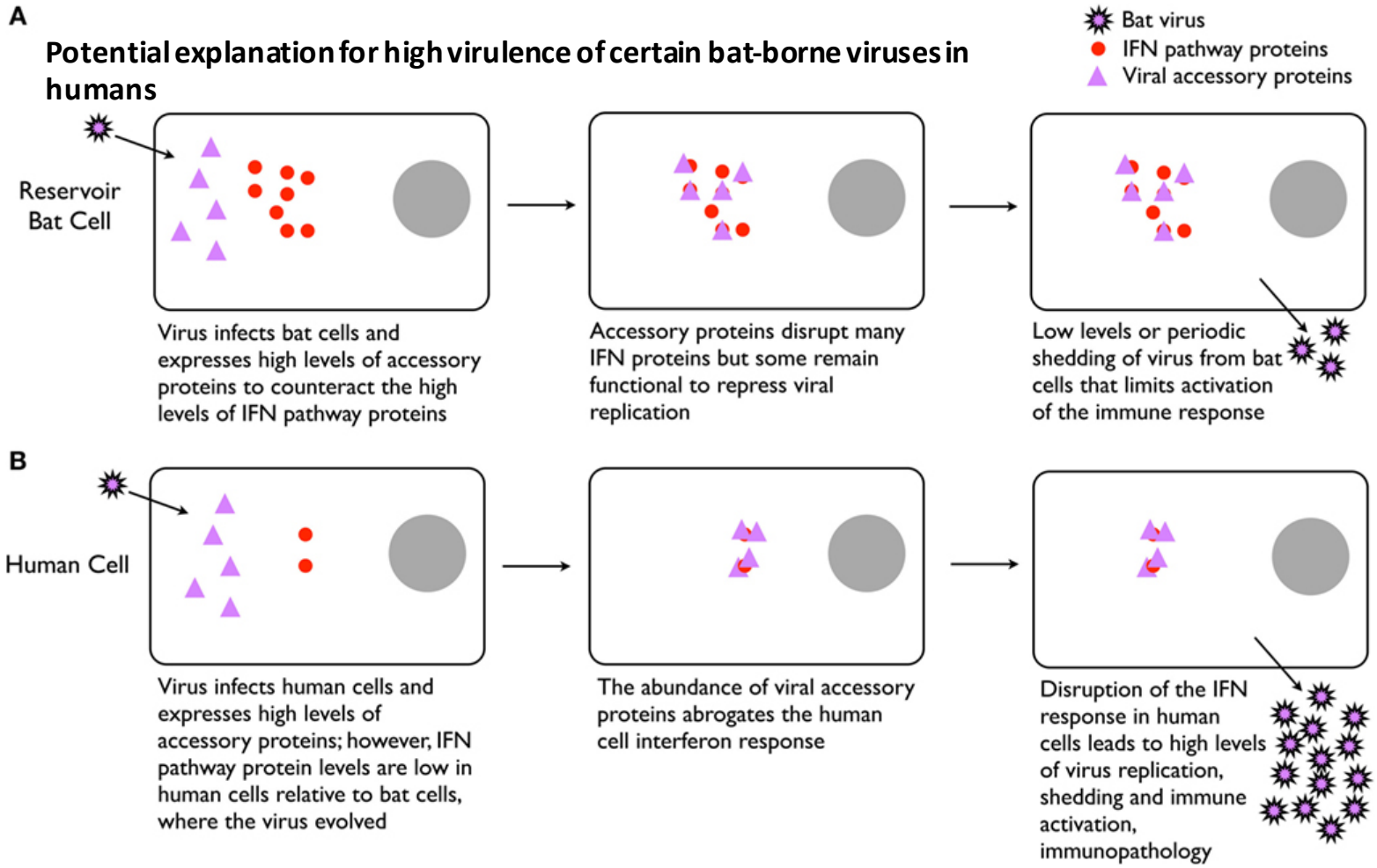


Brook & Dobson 2015:23, p172–180, Trends Microbiol
O'Shea et al 2014:20, p.741-745, EID

**Immunoglobulin combinatorial diversity potential of humans, swine and little brown bats**




Schontz et al. Control of Viral Infections in Bats and the Emergence of Viruses Highly Pathogenic to Humans. Front Immunol. 2017 Sep 11;8:1098.



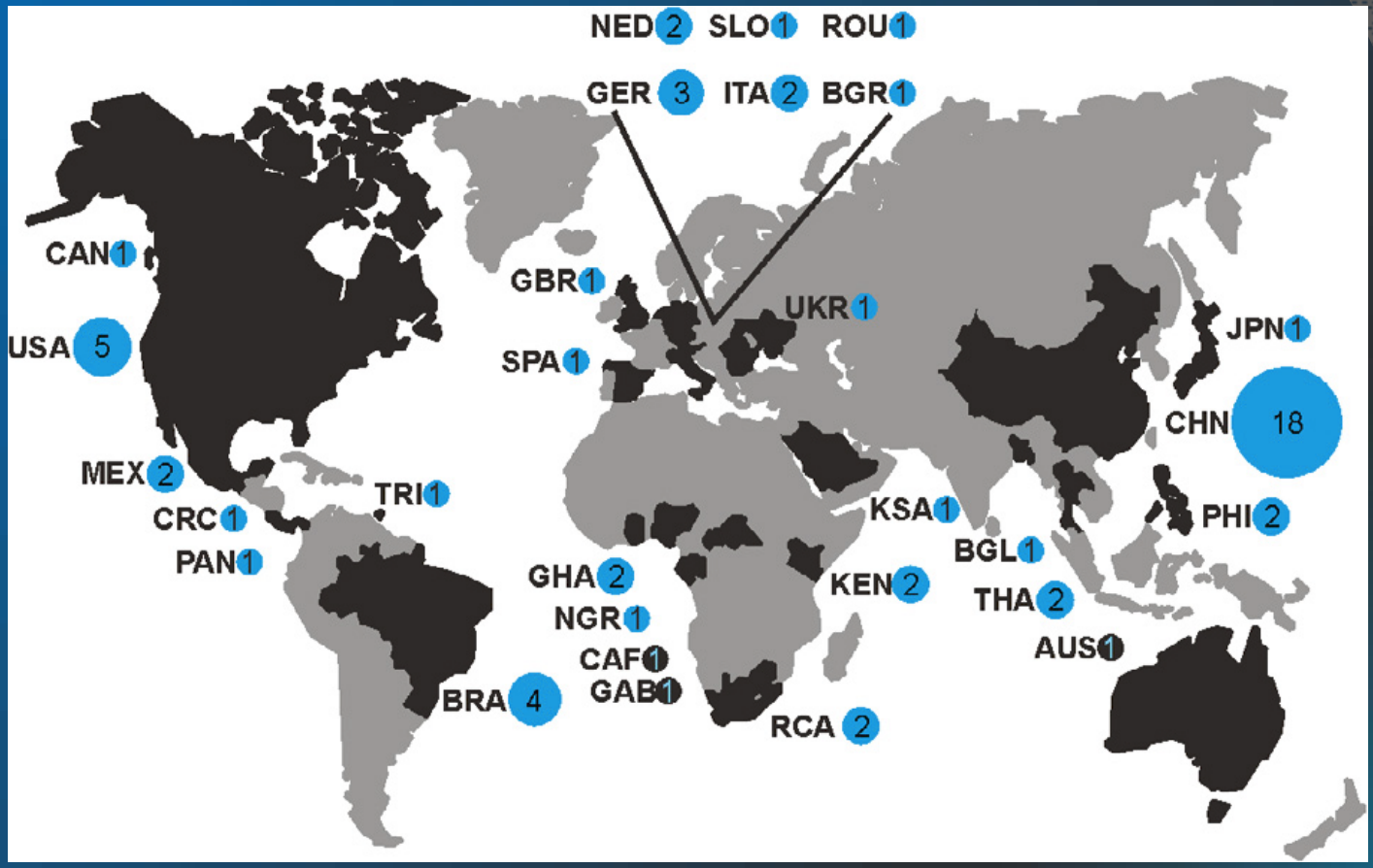

Schontz et al. Control of Viral Infections in Bats and the Emergence of Viruses Highly Pathogenic to Humans. Front Immunol. 2017 Sep 11;8:1098.





# SEARCH FOR ZOONOTIC PATHOGENS ASSOCIATED WITH BATS AT THE HUMAN, DOMESTIC ANIMAL & WILDLIFE INTERFACES: SELECTED CASE STUDIES

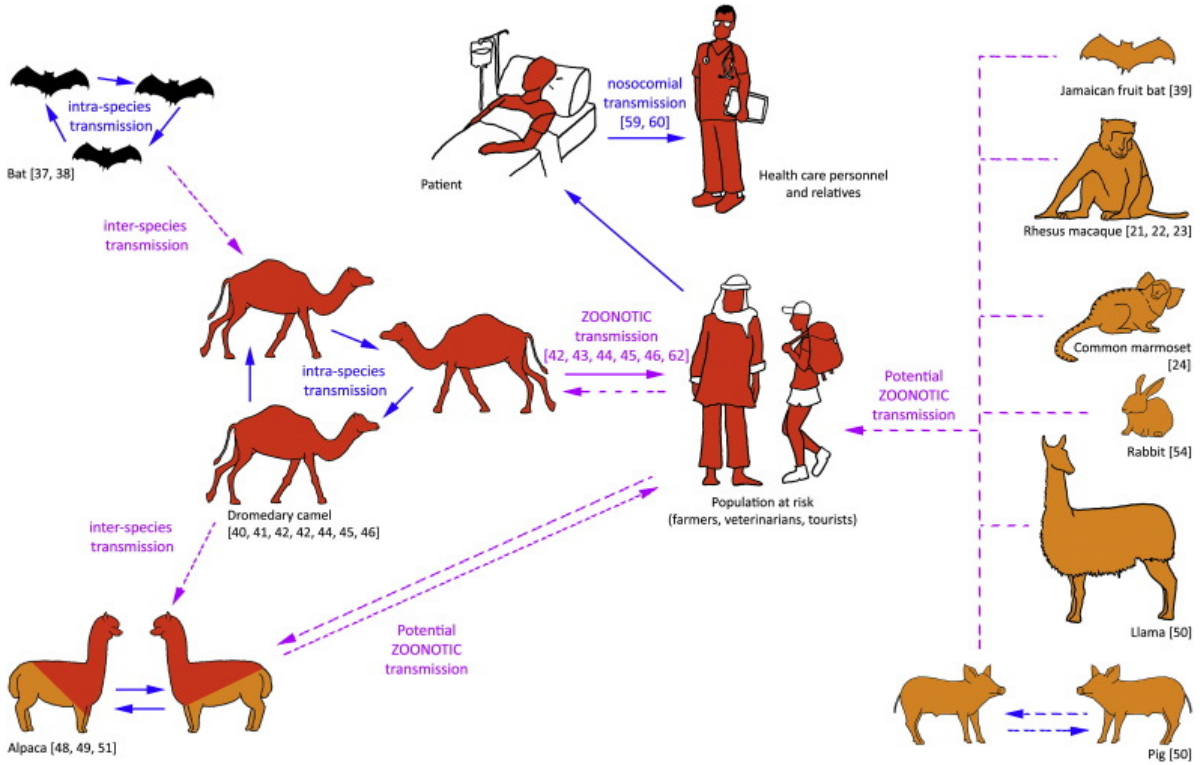
# Coronaviruses in bats




Bats are recognized as hosts of coronaviruses (CoV) on different continents. The biodiversity of CoVs suggests that bats may be the primary hosts where alpha- and betacoronaviruses evolved, including at least 3 of the 6 known human CoVs (*Drexler et al., 2014*).

- Evidence points to the SARS CoV as originating from Chinese bats (presumably of the *Rhinolophus* genus) where anthropogenic factors promoted interspecies transmission to other mammals and thereafter to humans.
- Further studies performed in China and Hong Kong led to identification of several novel CoV groups in various bat species (*Woo et al., 2006*).
- Specific drivers and mechanisms of CoV host shifts and switches, as well as associated evolutionary changes, are unknown.

# MERS




Vergara-Alert, et al. One Health. 2017 Jun;3:34-40.

# Filoviruses in bats

To date, bats are the only major group, besides apes and humans, from which filoviruses were isolated, or viral RNA was detected (Uganda, Democratic Republic of the Congo, Gabon, Kenya, Spain).


***(Imported cases in Europe and North America are not shown)***

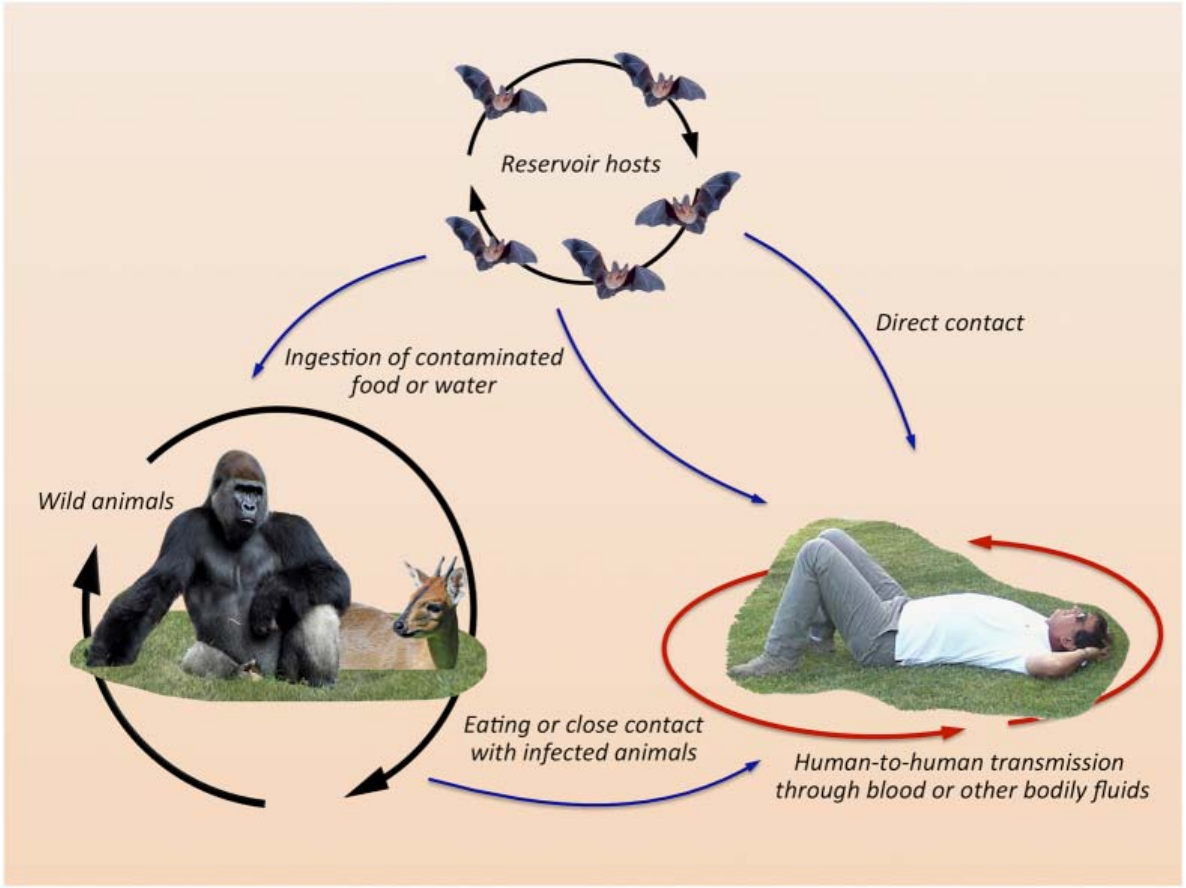
- EBOV RNA was detected in tree roosting fruit bats in Gabon: 19% *Hypsignathus monstrous*; 4% *Epomops franqueti*; 3% *Myonycteris torquata.* Seroprevalence 24%, 7% and 7%, respectively (*Leroy et al., 2005*).

- An EBOV outbreak in DRC during 2007 was implicated as a result of direct exposure to migratory fruit bats (*Leroy et al., 2009*), however, the migratory fruit bat species such as *Eidolon helvum* were never diagnosed positive for EBOV.
- In Ghana, EBOV antibodies were detected in sera

Of 10/27 *Epomops franqueti*, 14/37 *Epomophorus gambianus*, 7/16 *Hypsignathus monstrosus*, and 1/4 *Nanonycteris veldkampii* fruit bats (*Hayman et al., 2012*).

- In Uganda, 5.1 % of *Rousettus aegyptiacus* fruit bats were positive for MARV RNA.
- From bats with a high RNA load, MARV has been isolated (liver).
- Seroprevalence of *R. aegyptiacus* to MARV was 2.4-9%.
- In addition, MARV RNA detected in 1/609 (0.2%) insectivorous bats *Hipposideros* sp (*Towner et al., 2007; 2009*).

- In another study, MARV RNA found in 3.0-3.6% of two species of insectivorous bats (*Rhinolophus eloquens and Miniopterus inflatus)* and in *R.aegyptiacus*, seroprevalence up to 20% (*Swanepoel et al., 2007*).




Allocati, et al. Cell Death Discov. 2016;2:16048.

# Bat paramyxoviruses

## Henipaviruses

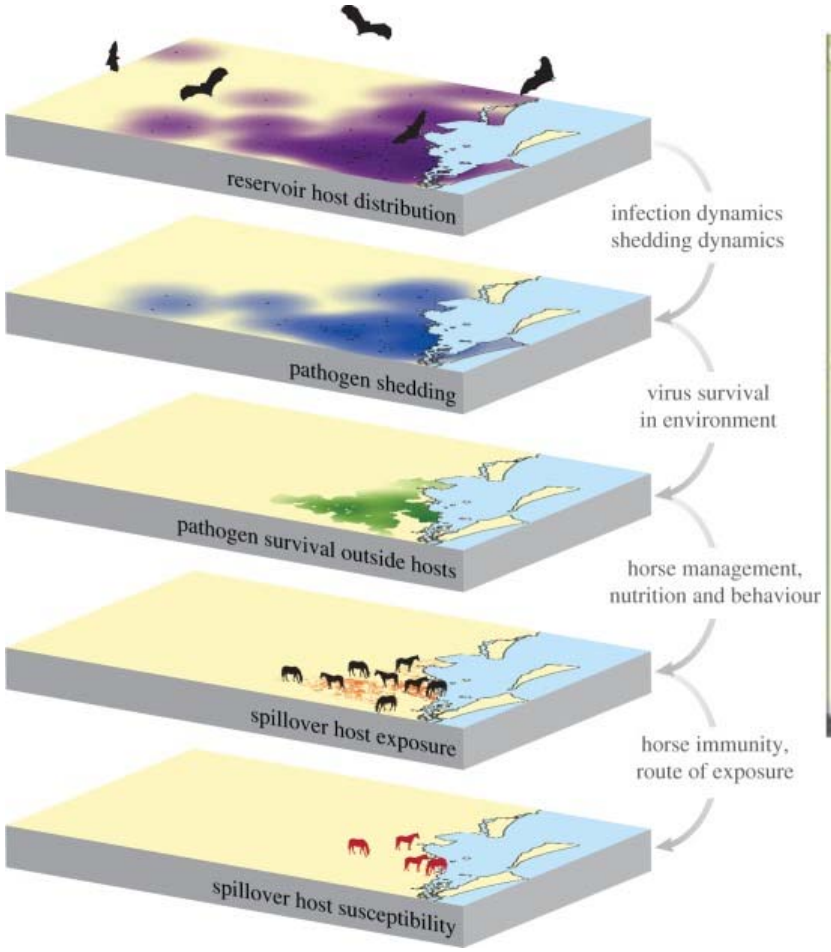
- Hendra virus (HeV) was identified in Australia in 1994. Fruit bats (*Pteropus* spp) are the principal hosts, whereas horses were the amplifying hosts and source of HeV infection (encephalitis with high fatality rate) for humans (*Westbury*, 2000).
- Nipah virus (NiV) was identified in Malaysia in 1999. Fruit bats (*Pteropus* spp) are the principal hosts, and pigs were the amplifying hosts and source of NiV infection for humans, with >300 cases (*Uppal*, 2000).

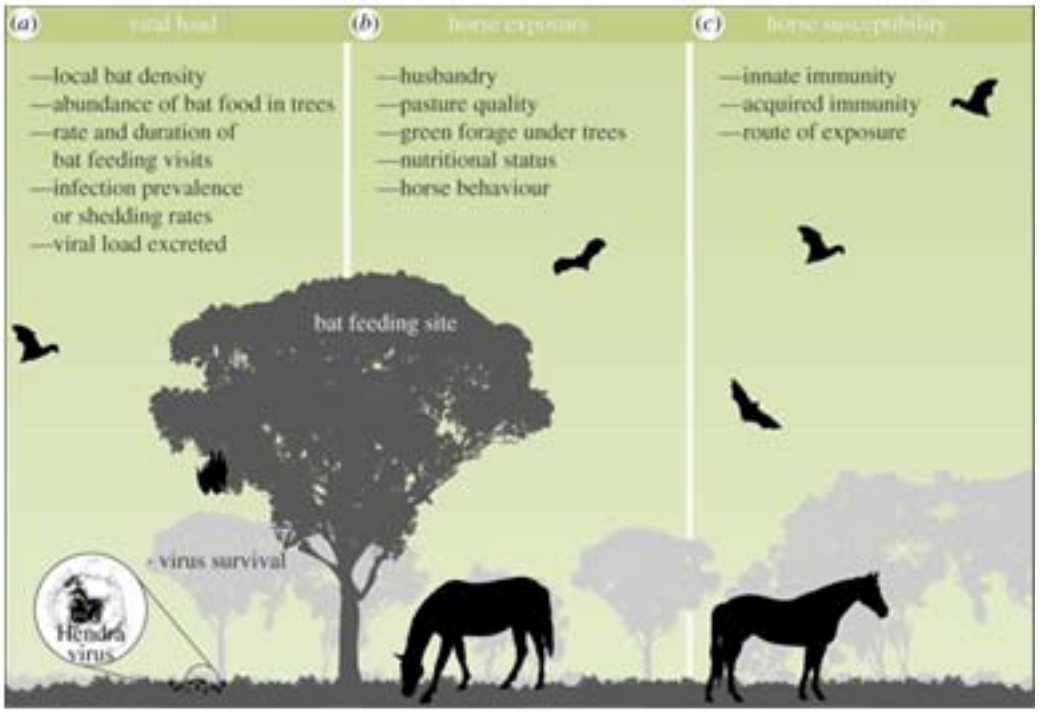
• In Bangladesh during 2001, NiV was transmitted to humans without apparent participation of an amplifying host, presumably directly from pteropid bats via raw date palm sap (*Montgomery et al., 2008*). Further, the virus can be transmitted human to human (*Sazzad et al., 2013*).

• Similar NiV outbreaks were documented in India (*Arankalle et al., 2011*).

• Antibodies to NiV were detected in *Pteropus* spp fruit bats in Bangladesh, Cambodia, India, Indonesia, Malaysia, and Thailand (seroprevalence 11-15%). In some of these cases NiV was isolated (*Johara, 2001; Olson et al 2002; Wacharapluesadee et al 2005; Epstein et al., 2008; Sendow et al 2009*).

Plowright, et al. Proc Biol Sci. 2015 Jan 7;282(1798):20142124.




**Ecological dynamics of emerging bat virus spillovers**

# Bats & Many Other Agents…

Mortlock M, et al. Novel **paramyxoviruses** in bats from Sub-Saharan Africa, 2007-2012. Emerg Infect Dis. 2015;21:1840-3.

Conrardy C, et al. Molecular detection of **adenoviruses** in bats from Kenya. Am J Trop Med Hyg. 2014;91:258-66.

Gu SH, et al. Molecular phylogeny of **hantaviruses** harbored by insectivorous bats in Côte d'Ivoire and Vietnam. Viruses. 2014;6:1897-910.

Tong S, et al. New world bats harbor diverse **influenza** A viruses. PLoS Pathog. 2013;9:e1003657.

Kading RC, et al. Isolation and molecular characterization of Fikirini **rhabdovirus**, a novel virus from a Kenyan bat. J Gen Virol. 2013;94:2393-8.

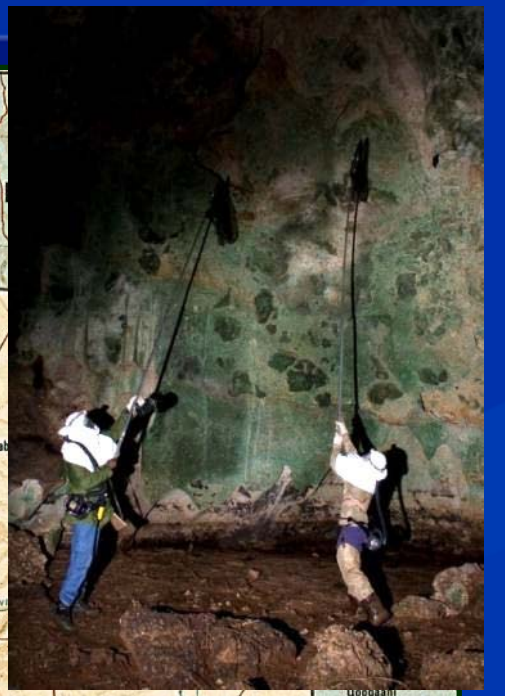
Quan PL, et al. Bats are a major natural reservoir for **hepaciviruses** and **pegiviruses**. Proc Natl Acad Sci U S A. 2013;110:8194-9.

Tao Y, et al. Discovery of diverse **polyomaviruses** in bats and the evolutionary history of the Polyomaviridae. J Gen Virol. 2013;94:738-48.

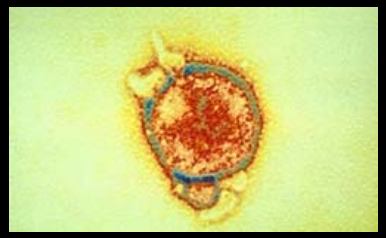
Kosoy M, et al. ***Bartonella*** spp. in bats, Kenya. Emerg Infect Dis. 2010;16:1875-81.

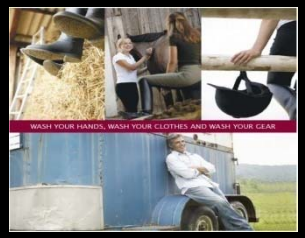
## METHODOLOGICAL EXAMPLES

- Biased surveillance at roost sites.
- These included ~120 ill and dead bats, whereas others appeared healthy.

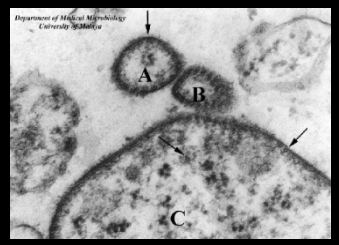


# A Bevy of Bats, Agents, Amplifying Hosts, & Human Infections…

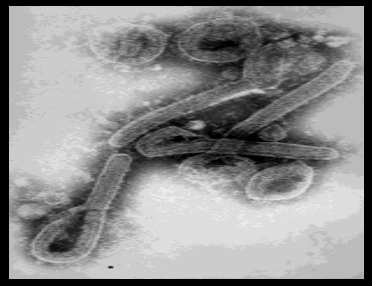




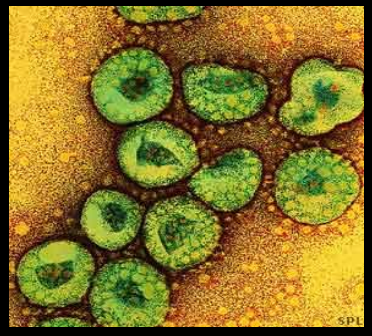

HENDRA




NIPAH

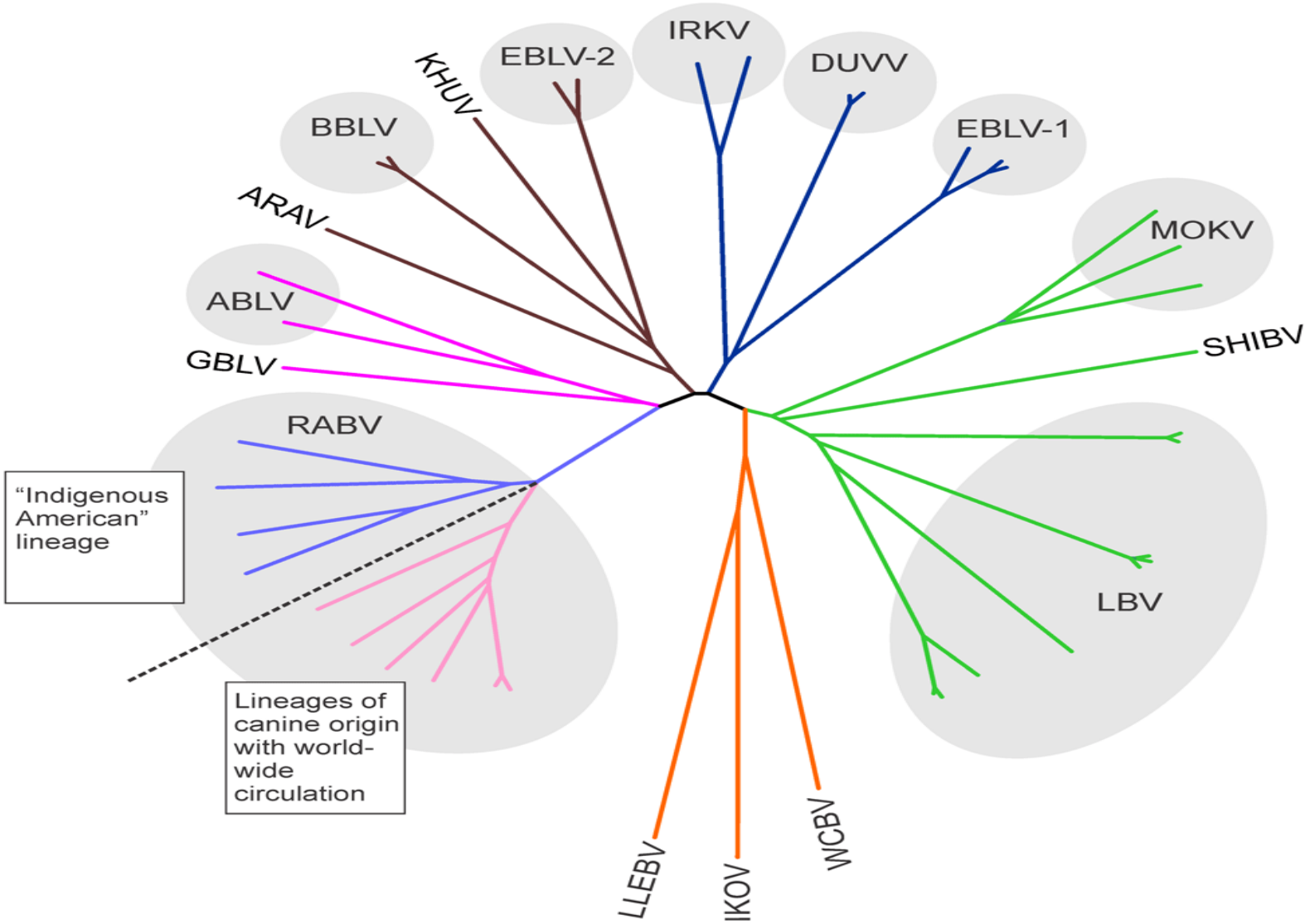


FILOS



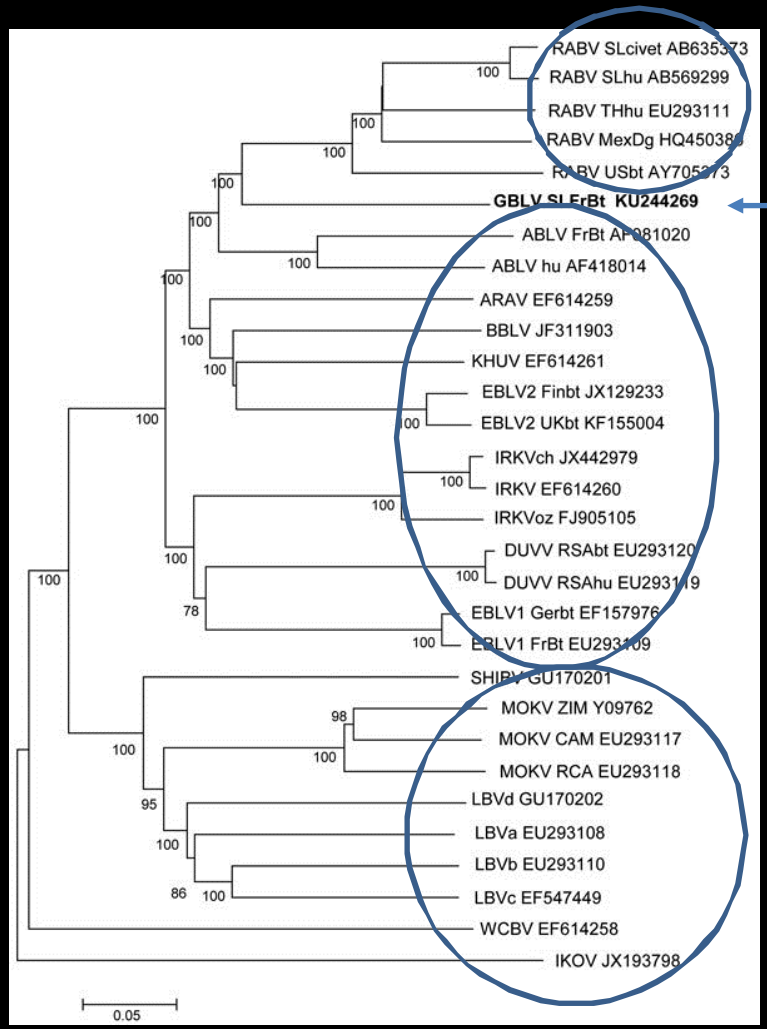

SARS/MERS

**Extant Lyssavirus Phylogeny.**

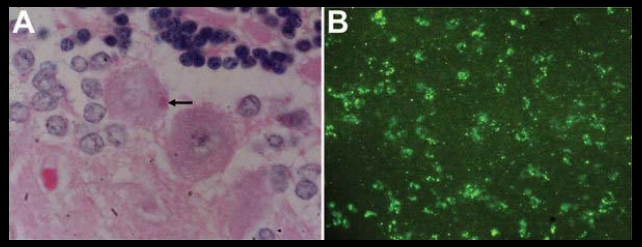



Rupprecht C, Kuzmin I and Meslin F. Lyssaviruses and rabies: current conundrums, concerns, contradictions and controversies [version 1]. F1000Research 2017, 6:184 (doi: 10.12688/f1000research.10416.1)

**A RATHER COMPLICATED PHYLOGENY…**




Phylogenetic relationships between representatives from all classified lyssaviruses and novel **Gannoruwa** bat lyssavirus (GBLV) on the basis of complete genome sequences. Gunawardena et al. Emerg Infect Dis. 2016 Aug; 22(8): 1456–1459.



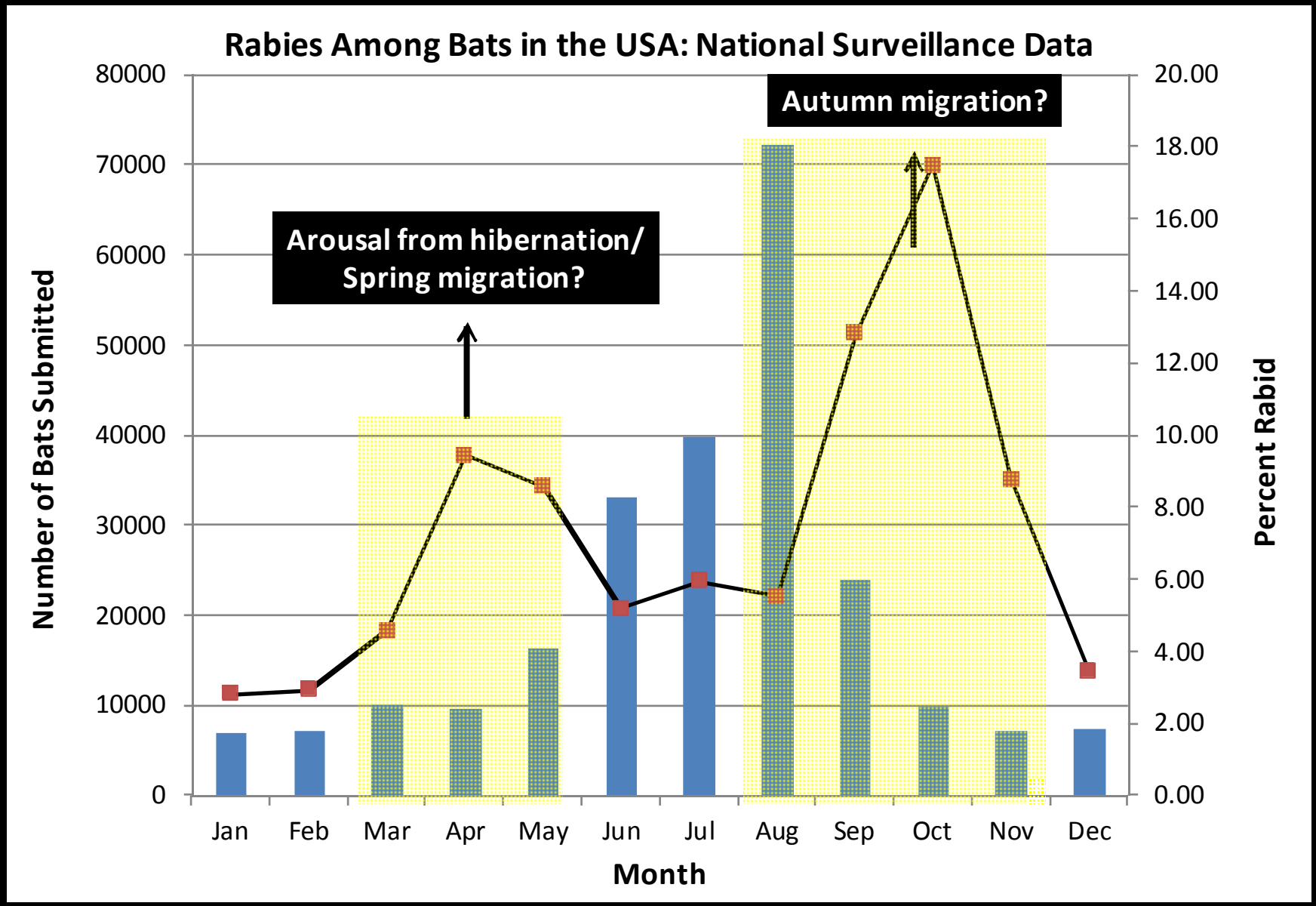

Negri bodies and lyssavirus antigens in brain tissue from an Indian flying fox, Sri Lanka

# Bats and Rabies in the USA

- Between 2001 – 2009, >205,000 bats were submitted for rabies virus diagnosis.
- More than 13,000 (~7%) were found rabid.
- Bats represented ~22% of the 63,356 rabid animals diagnosed.
- All states, with the exception of Hawaii, were represented, but the Southwest had the highest proportionate rabies burden.
- Samples included > 40 native species, but >85% were represented by *Eptesicus* or *Myotis* taxa.
- Bats with the highest % rabid proportion included *Tadarida*, *Lasiurus*, and *Parastrellus*.
- Most bats (~59%) were submitted during summer, but the majority were found rabid during *autumn* (Odds Ratio 5.5)
- Bat species with *less conspicuous* roosting habits were significantly *more likely to be found rabid* (Odds Ratio 13.2)

Patyk et al., 2012

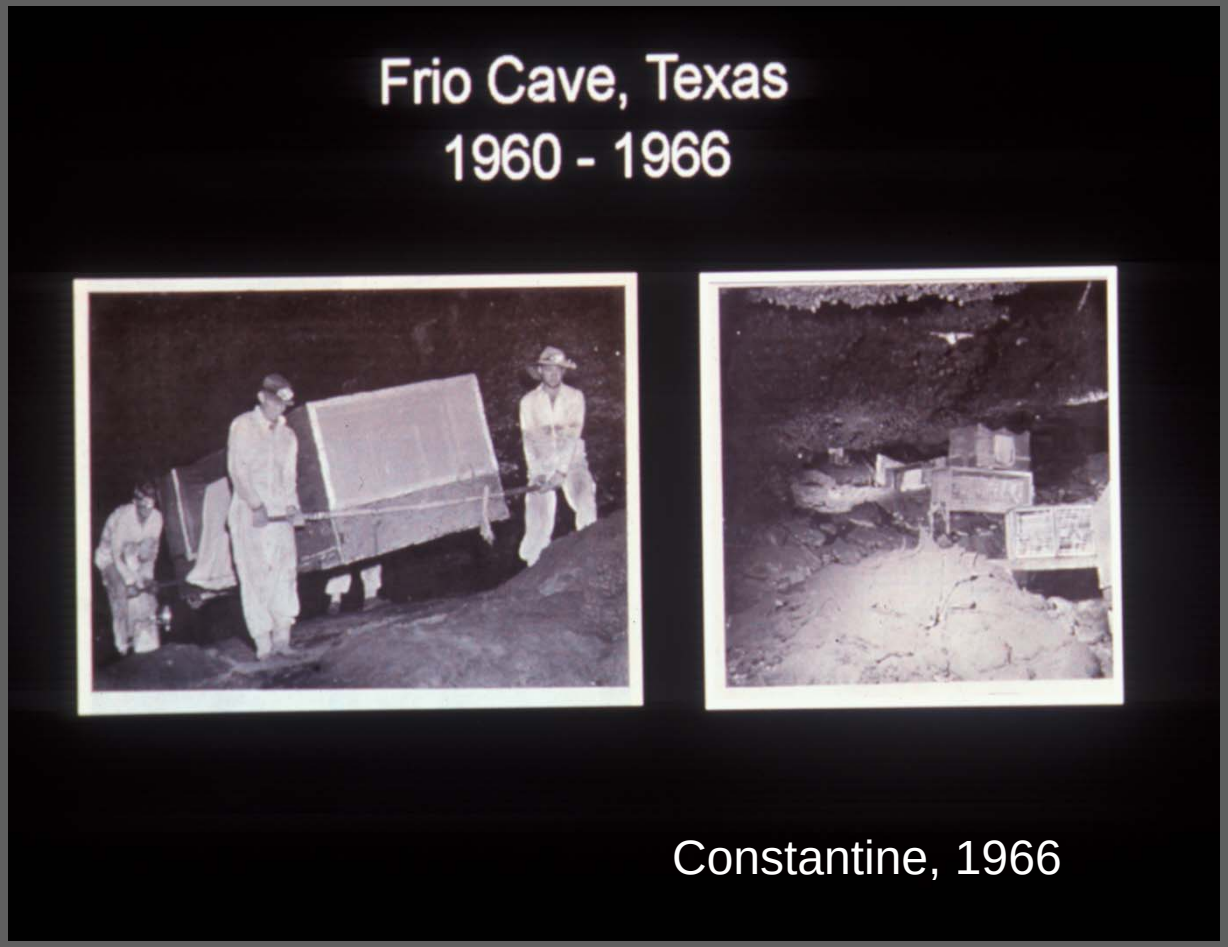
# Bat Biology Influences Disease Patterns



Rabies virus aerosol infection possible under very unique cave environments.

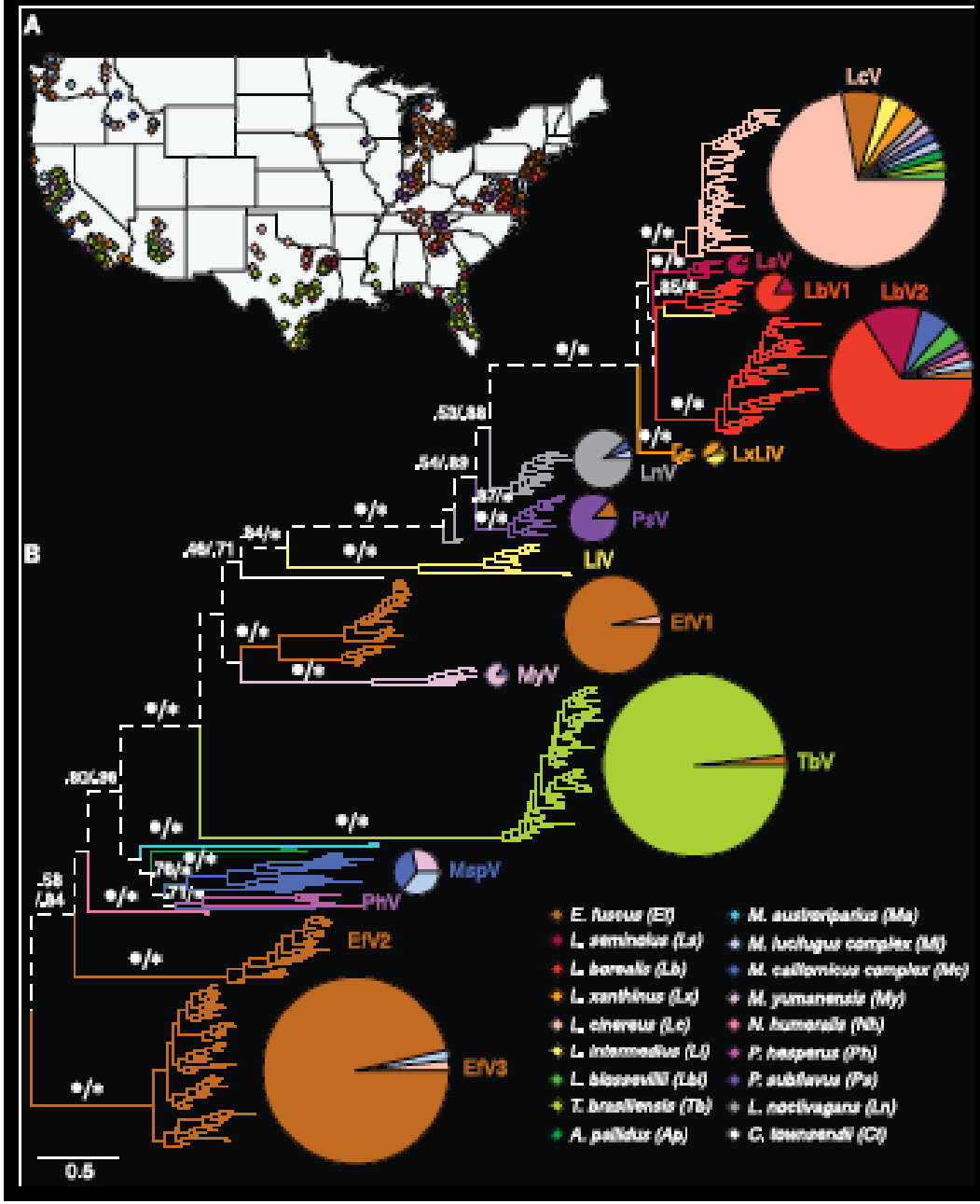
Has not been documented under routine house-hold conditions with bats.

Mechanisms of likely infection or resultant immunity not well understood.




UNUSUAL FACETS OF BAT RABIES PATHOBIOLOGY?

# Bats and Rabies

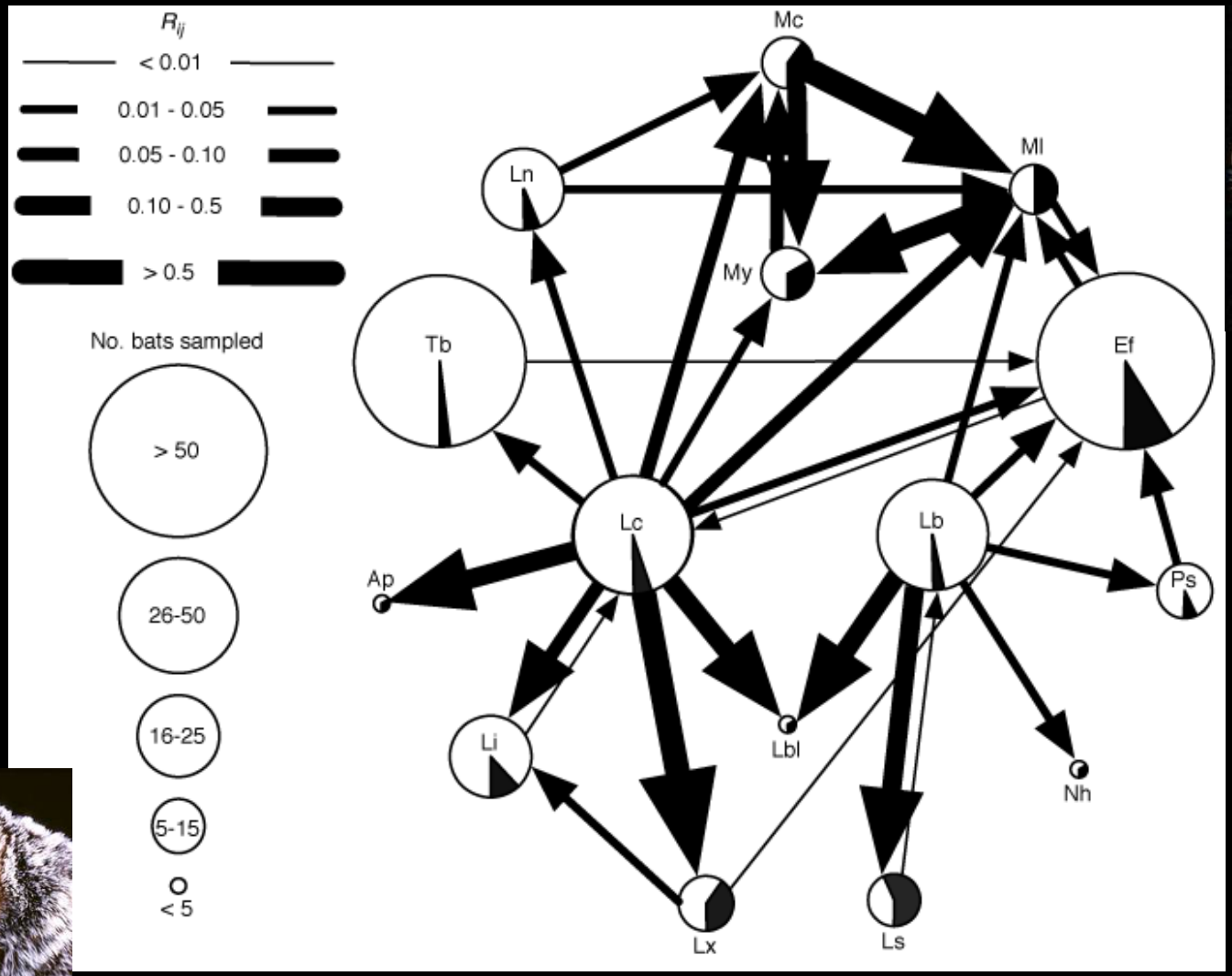



In the New World, only one lyssavirus, rabies virus, has been detected to date.

Among bats, evidence of many species-specific variants perpetuated in given taxa, but varying levels of inter-specific spillover events

Streicker et al. Science 2010

# Community Ecology of Bat Pathogens




Streicker et al. Science 2010

# Lyssavirus Dynamics: Host Spillover, Switches, & Shifts

*ectodomain G; neighbour-joining*

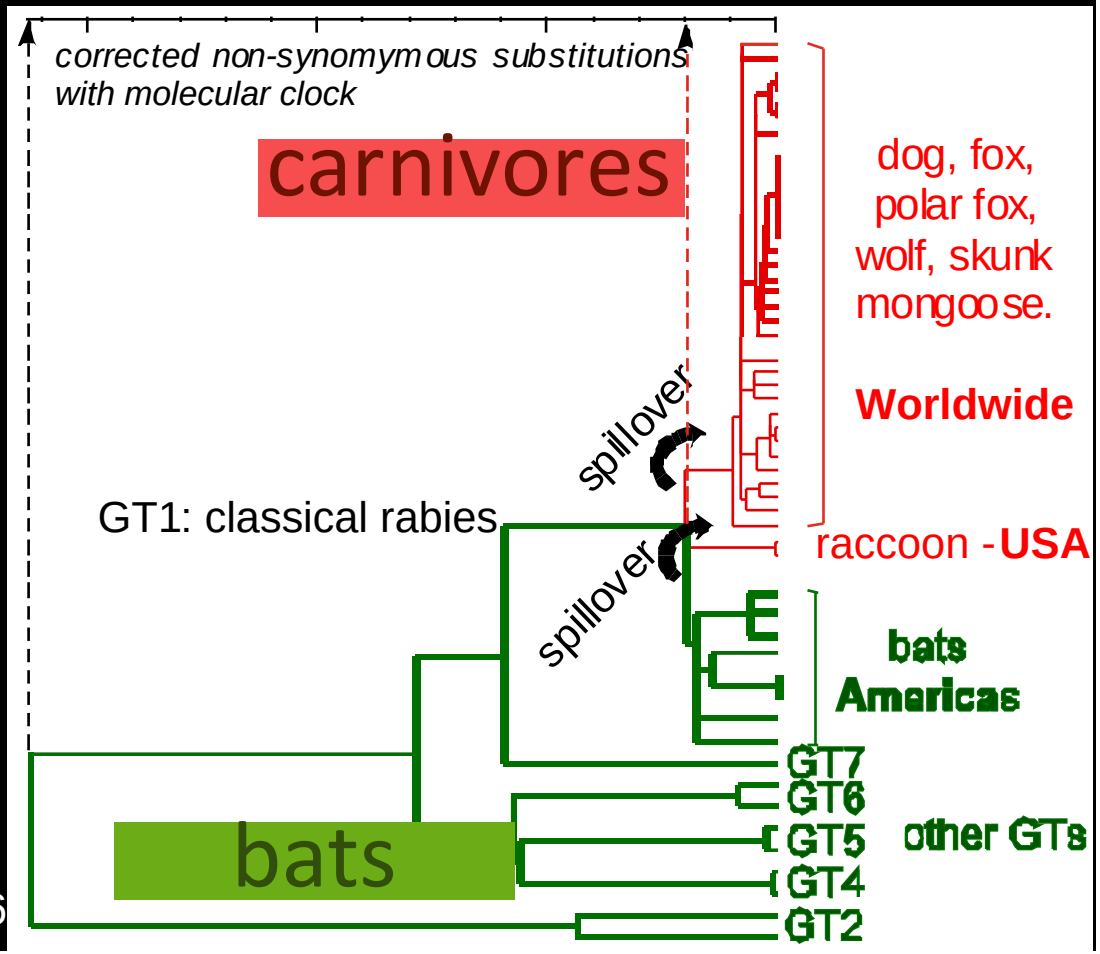
*Bat lyssaviruses arose before carnivore rabies viruses*

-9000 / -5000

600 / 1600

*«Predicted» host-changes bat->carnivore*

- ↓ raccoon lineage (E. USA)?
- ↓ skunk lineage (S.Cent. USA)?
- ↓ skunk lineage (N.Cent. Mexico)?





*Badrane & Tordo 2001, JVirol 75:8096-104*

*Holmes et al., 2002, Virology 292:247-57*

*Hughes et al., 2005, J. Gen. Virol. 86: 1467-74*

*Kuzmin et al., 2012, PLoS Path*8(6): e1002786

## Dimensions at the Bat/Carnivore Interface…?










# Questions:

- Where did the host shift/switch of bat rabies virus to carnivores occur?
- When did it happen?
- Why did it result in sustained transmission?
- How frequently may it be going on today?

?

# Recent host shifts of bat rabies viruses in North America:

**AZ, 2001-2009**

Outbreaks in striped skunks in Flagstaff area (2001; 2004-2005), and in gray foxes (2008-2009), caused by the big brown bat RABV.

**USA, Mexico: 2008**

Outbreak in white-nosed coatis in Cancun, Mexico. The same virus variant was detected in an immigrant in CA, who was exposed to a coati or fox in Oaxaca, Mexico. The virus was close but not identical to the *Tadarida brasiliensis* variant.

**OR, 2009-2010**

Two gray foxes and a goat at the end of winter, were infected with the same RABV variants, associated with *Myotis* bats and with big brown bats.

# Human Rabies in the USA

- In ~ 21 of 36 cases where a bat virus variant was identified, it was the variant associated with silver-haired (*Lasionycteris noctivagans*) and eastern tri-colored (*Perimyotis subflavus*) bats.

- The rabies virus associated with Mexican free-tailed bats (*Tadarida brasiliensis*) was identified in ~10 cases.

- The viruses associated with big brown bat (*Eptesicus fuscus*) and *Myotis* spp bats caused human rabies in at least one case each.

Greater susceptibility?

Ability of the virus to replicate in fibroblasts and epithelial cells? (*Morimoto et al., 1996*)

# REPERCUSSIONS OF MIS-DIAGNOSIS: HUMAN TO HUMAN TRANSMISSION

Burton et al.

Arch Neurol. 2005 Jun;62(6):873-82.

Rabies encephalomyelitis: clinical, neuroradiological, and pathological findings in 4 transplant recipients.

## BAT RABIES MANAGEMENT WITH POTENTIAL APPLICABILITY TO OTHER PATHOGENS?

**Focused studies to understand transmission, perpetuation, and exacerbation**

**Public education concerning health risks and defining exposures**

**Outreach focusing upon ecological benefits, and detriments from population reduction**

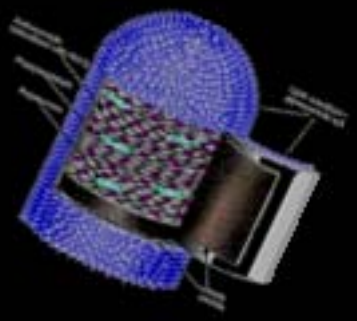
**Training, PPE, and pre-exposure immunization for those at risk of exposure**

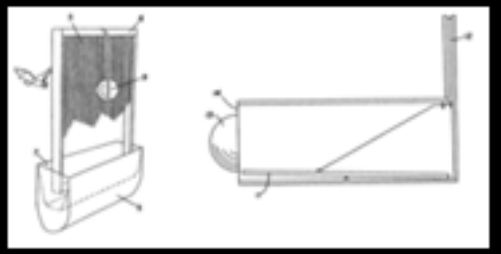
**Euthanasia of suspect animals and prophylaxis of exposed humans and other mammals**

**Community planning to mitigate impacts from inappropriate development**

**Exclusion of bats from human dwellings using appropriate methods**

**Syndrome-specific techniques to enhance local surveillance /control**





D. Constantine 2006

# Epizootiological Outcomes…?

AB –
Population at large

AB +(?)
Non-specific viral inhibition

Non-exposed

Bat population

Exposed survivors
Rabid ±
AB ±

Exposed to *lyssavirus*

Non-rabid

Carrier?
Hypothetical group

AB +

Susceptible
(insufficient
immunity)

Immune

RABID (ill)

AB -

Terminal AB +

Terminal AB -

Recovery AB ±

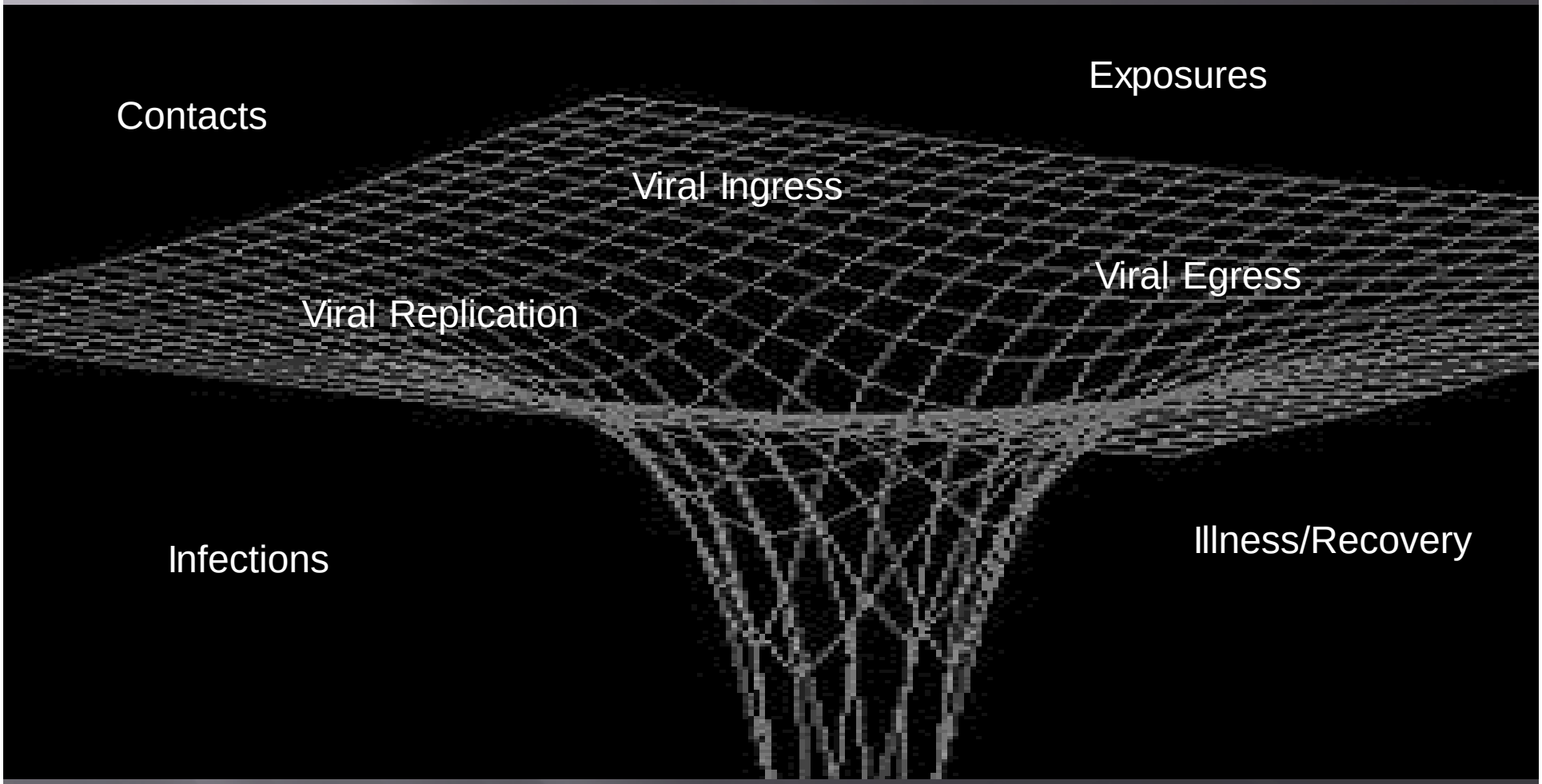
Susceptible
(non-productive
infection)

Immune
VNA undetected
Th?, CTL?

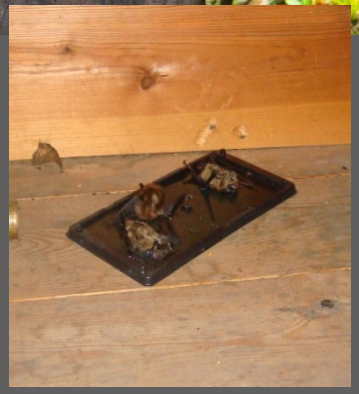
VNA concomitant
With clinical signs

Insufficient
antigenic mass

## Bats, EIDs and Rabies: Infection and Immunity Fall Along a Continuum …



# Anthropogenic Stress & Limitations To Ecological Resilience?



# EIDs Impact Bat Populations

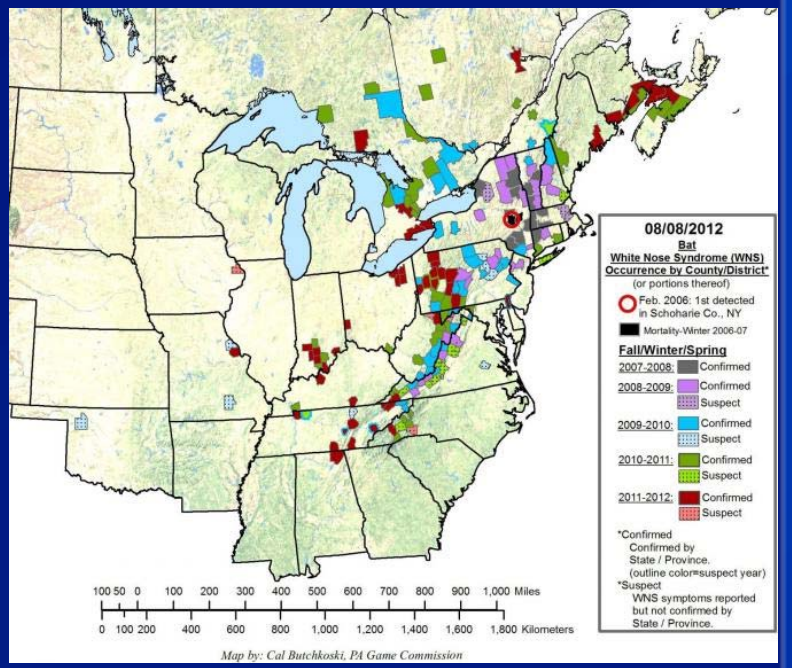
- Factors which compromise metabolism, and increase mortality, may exacerbate the effects of climate change on temperate bat populations, such as WNS

Sciencexpress Brevia

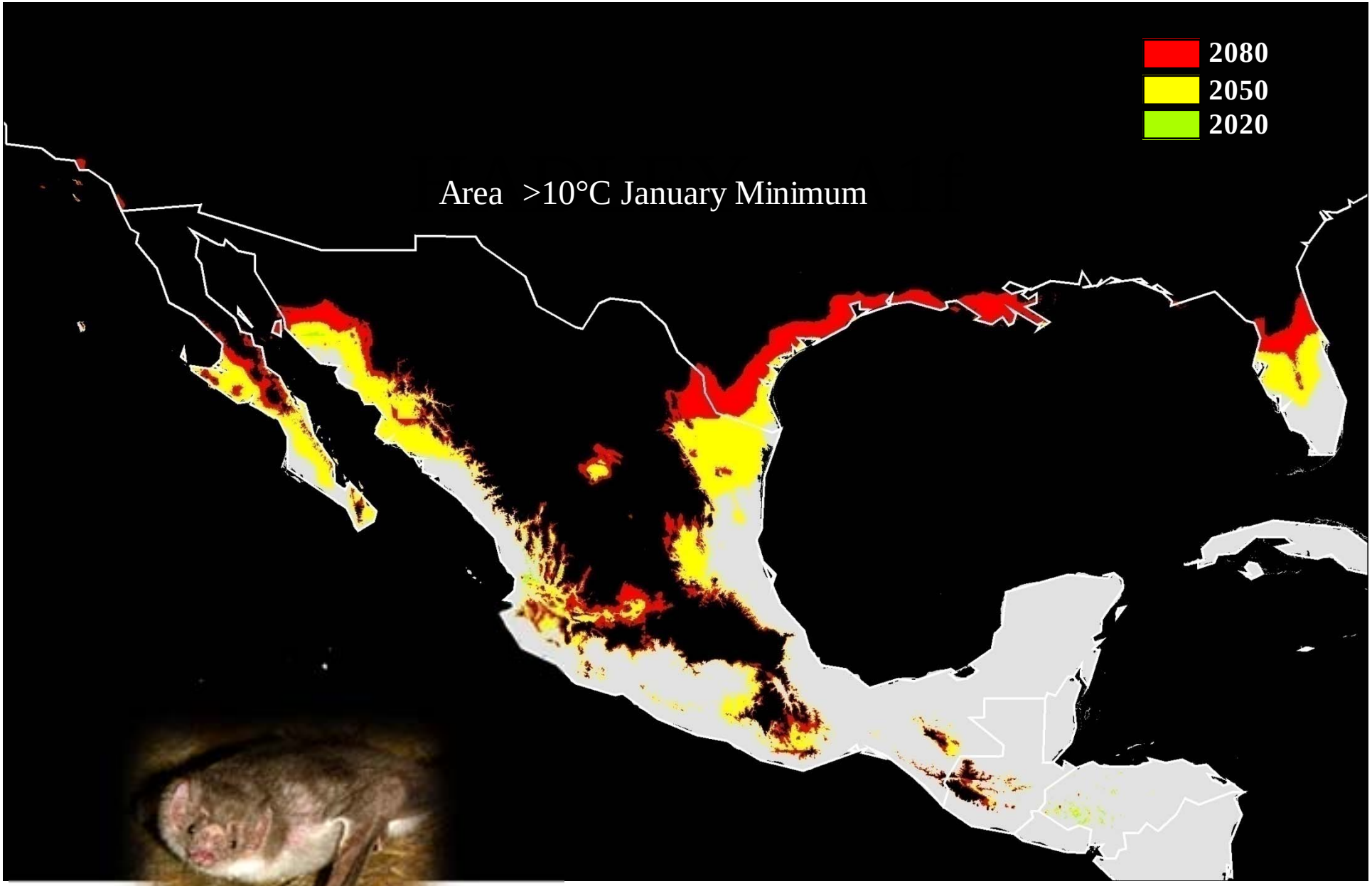
**Bat White-Nose Syndrome: An Emerging Fungal Pathogen?**

David S. Blehert,[1]* Alan C. Hicks,[2] Melissa Behr,[3]† Carol U. Meteyer,[1] Brenda M. Berlowski-Zier,[1] Elizabeth L. Buckles,[4] Jeremy T. H. Coleman,[5] Scott R. Darling,[6] Andrea Gargas,[7] Robyn Niver,[5] Joseph C. Okoniewski,[2] Robert J. Rudd,[3] Ward B. Stone[2]






http://whitenosesyndrome.org/resources/map



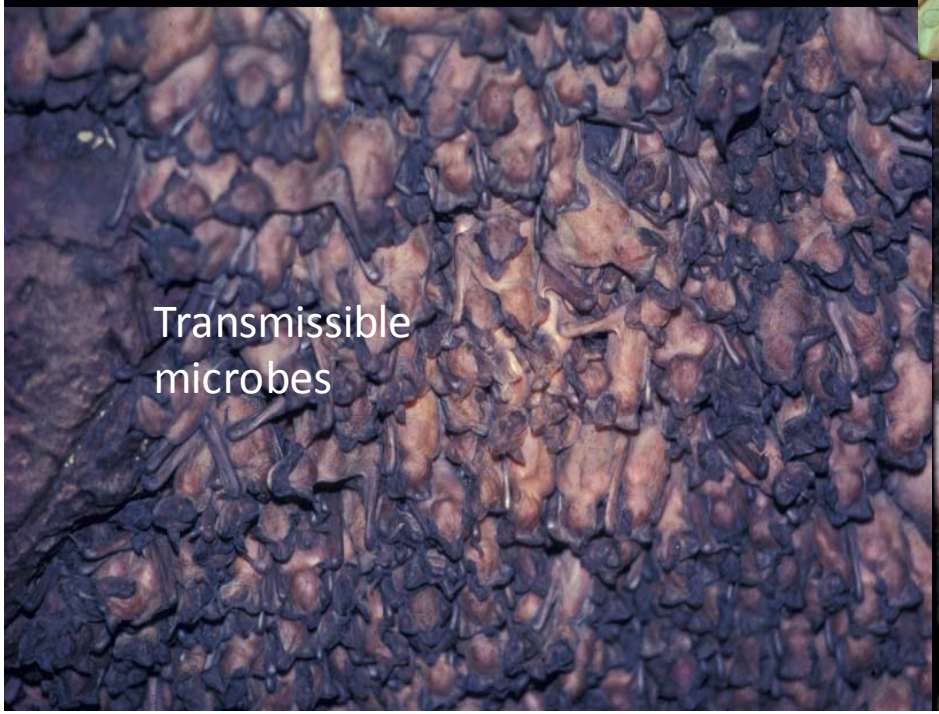



Common Vampire Bat

**ALTERED DISTRIBUTION OF VAMPIRE BATS?**

# BENEFITS & TRADEOFFS OF GREGARIOUS LIFE STYLES!






## CONCLUSIONS?

-Several newly appreciated emerging infectious diseases are associated with bats, due in part to their *distribution, abundance, diversity and vagility*.

-Bats are '*special*' biologically, in their capacity to orchestrate various disease ensembles, compared to other mammals, such as rodents.

- Given their comparatively low reproductive potential, various '*stressors*' on extant bat communities may result in unpredictable ecological repercussions, due to their critical role in arthropod suppression, pollination, seed dispersal, and forest regeneration with unexpected consequences.

- *Rabies is the oldest known bat zoonosis* and multiple public health, agricultural, and wildlife biology 'lessons learned' historically from this disease may be applicable directly to other emerging bat pathogens.

- A modern holistic *One Health strategy* integrating epidemiologically relevant best practices of disease prevention and control with the essential elements of conservation biology for wildlife management in general and for bats specifically often seems as elusive as "the undiscovered country".

**ACKNOWLEDGEMENTS**

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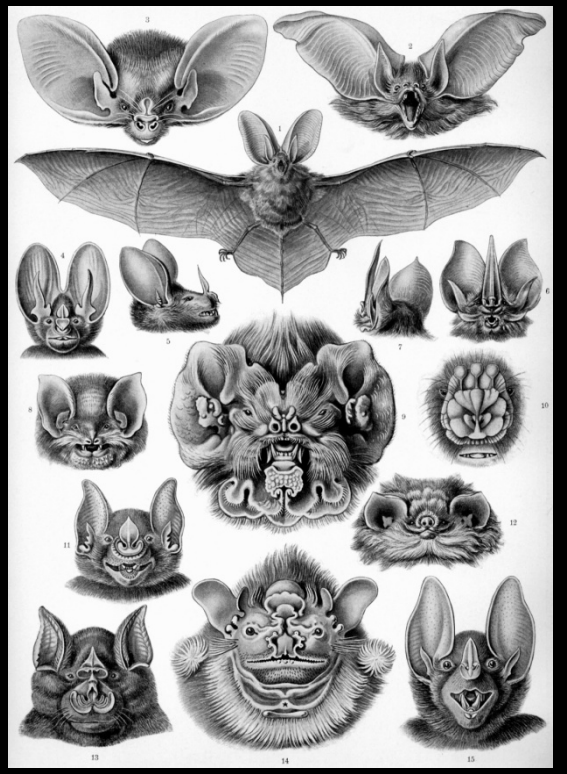
CDC, OIE & WHO, *MANY* COLLEAGUES



# QUESTIONS?

charleserupprechtii@gmail.com

Honduran white bat
*Ectophylla alba*
Photo: Jose Martinez