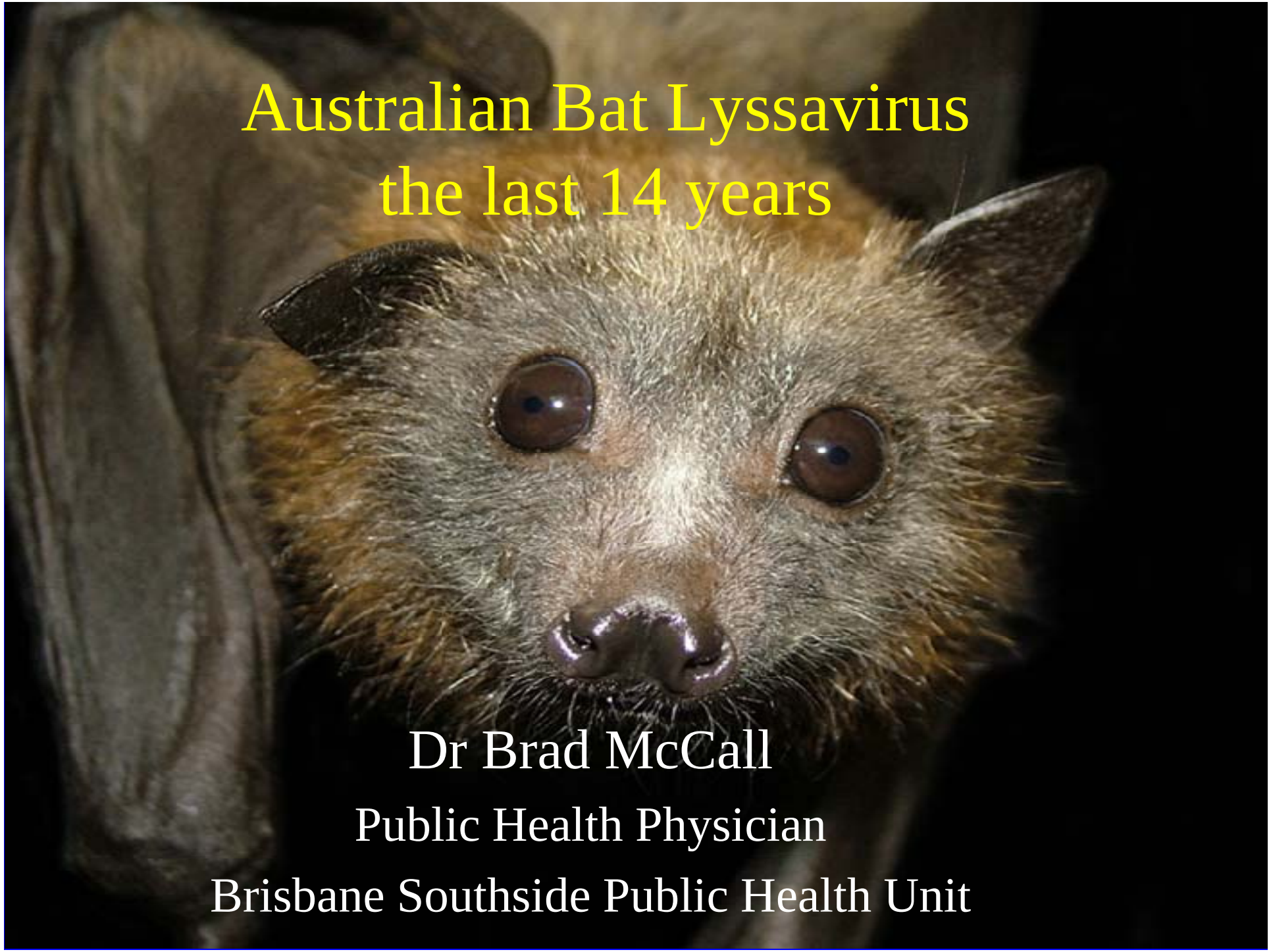

Australian Bat Lyssavirus
the last 14 years

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Outline

- ABLV
  - Surveillance
  - Prevention
  - Public health unit experience
- Current issues
  - RIG shortage
  - Other animals

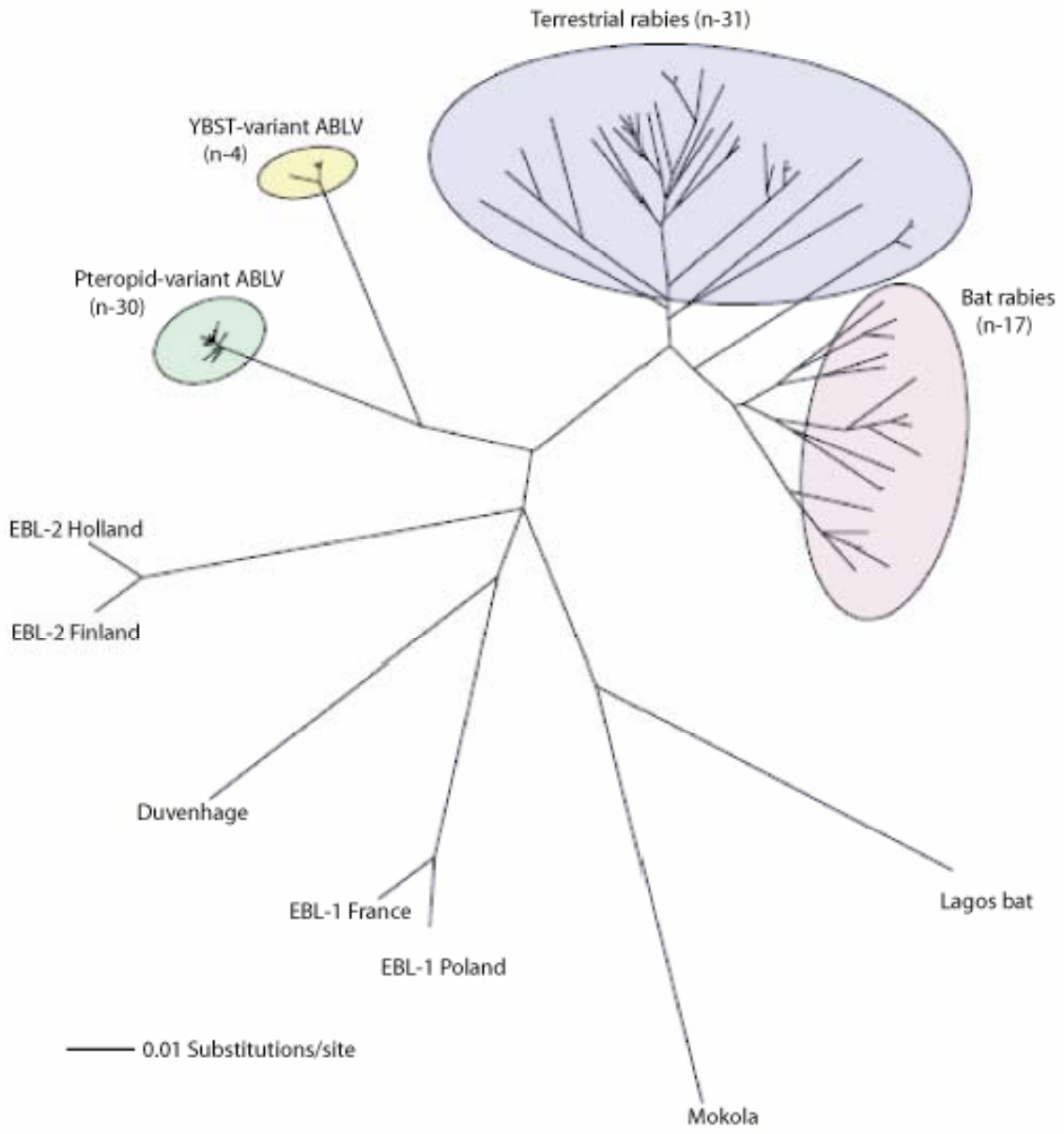
Australian Bat Lyssavirus

- **ABLV is a rabies-*like* rhabdovirus**
- **Known human infection results in clinical disease (encephalitis) that is invariably fatal**
- **First detected in 1996 (bats and a human)**
- **By 2009 181 bats diagnosed and 2 humans (1996 and 1998)**
- **Two variants of the virus in Australia**
- **pteropid-ABLV in the four common flying foxes *Pteropus alecto, P. poliocephalus, P. scapulatus, P. conspicillatus***
- **YBST-ABLV in Yellow-bellied sheathtail bats, an insectivorous microbat *Saccolaimus flaviventris***
- **A person has died from each of the two variants 1996: YBST-ABLV 1998: Pteropid ABLV**

Family Rhabdoviridae
Genus *Lyssavirus*

- Phylogroup 1
  - RABV (genotype 1)
  - Duvenhage (genotype 4)
  - EBLV 1 and 2 (genotypes 5 and 6)
  - Australian bat Lyssavirus (genotype 7)
- Phylogroup 2
  - Lagos bat Virus (genotype 2)
  - Mokola virus (genotype 3)

  4 unclassified lyssaviruses from bats in Eurasia


Terrestrial rabies (n-31)
YBST-variant ABLV
(n-4)
Pteropid-variant ABLV
(n-30)
Bat rabies
(n-17)
EBL-2 Holland
EBL-2 Finland
Duvenhage
EBL-1 France
EBL-1 Poland
Lagos bat
Mokola
0.01 Substitutions/site

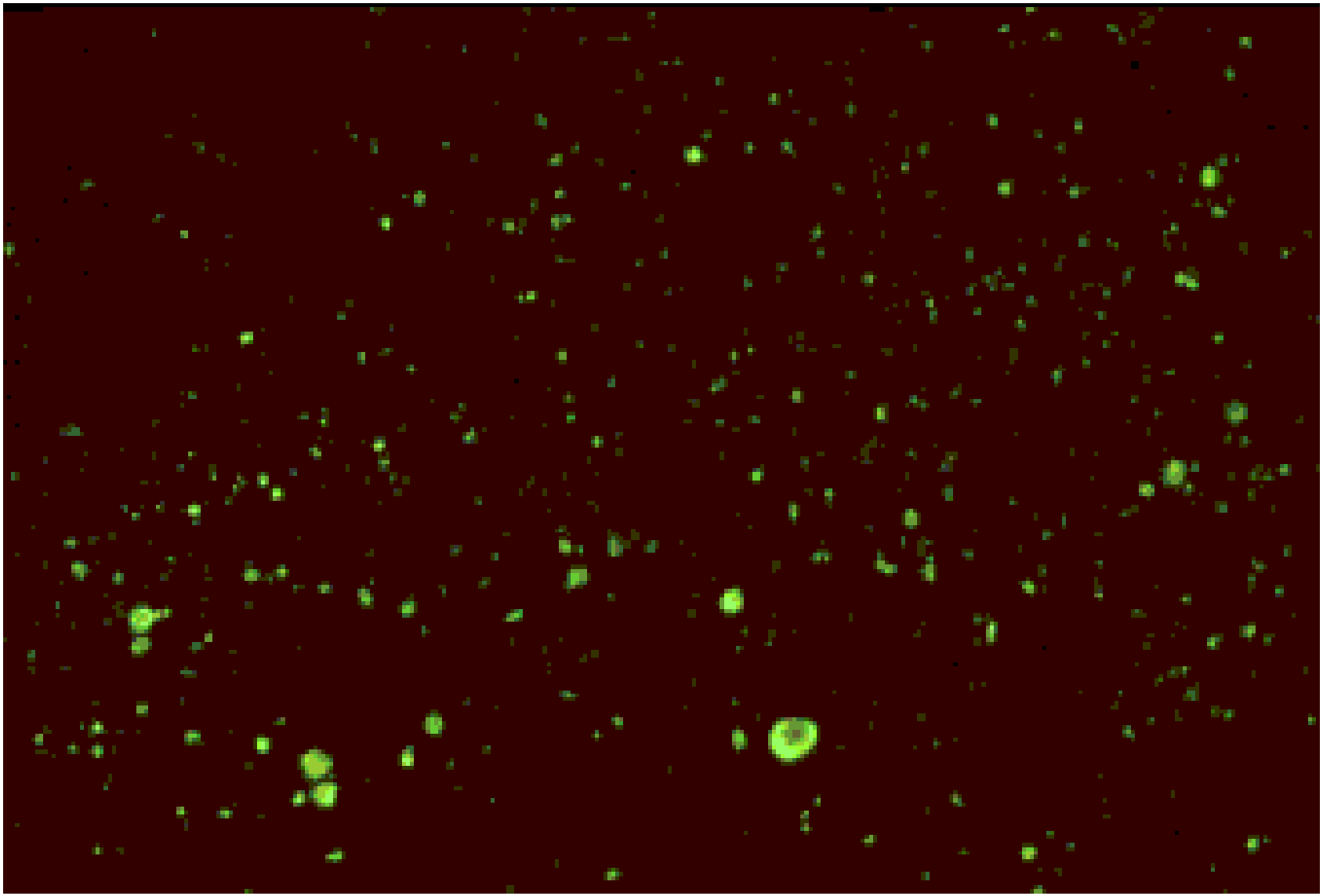
Name	Genotype designation	Locality	Principal hosts	Spillover hosts reported
Rabies virus	1	Worldwide (with exceptions) Bat variants are confined to the American continents: insectivorous bat strains mainly in North America, haematophagous bat rabies in South and Central America and the Caribbean.	Multiple American insectivorous bats: highest frequency in *Eptesicus fuscus*, *Lasionycteris noctivagens*, *Lasiuris* spp., *Myotis* spp., *Pipistrellus* spp., *Tadarida brasiliensis* Haematophagous (vampire) bats: *Desmodus* spp.	Insectivorous bat strains to human, fox, skunk. Vampire bat rabies mainly to cattle, horse, human.
Lagos bat virus	2	Sub-Saharan Africa. One case from France in a fruit bat imported from West Africa (1999).	Fruit bats: *Eidolon helvum*, *Micropterus pusillus*, *Epomophorus wahlbergi* Single isolate from insectivorous bat: *Nycteris gambiensis*	Cat, dog, *Atilax paludinosus* (water mongoose)
Mokola virus	3	Sub-Saharan Africa	Not known. Has been isolated from shrews (*Crocidura* spp.)	Cat, dog, human, shrew
Duvenhage virus	4	Southern and East Africa	Insectivorous bats: *Nycteris thebaica*, possible *Miniopterus schreibersi*	Human

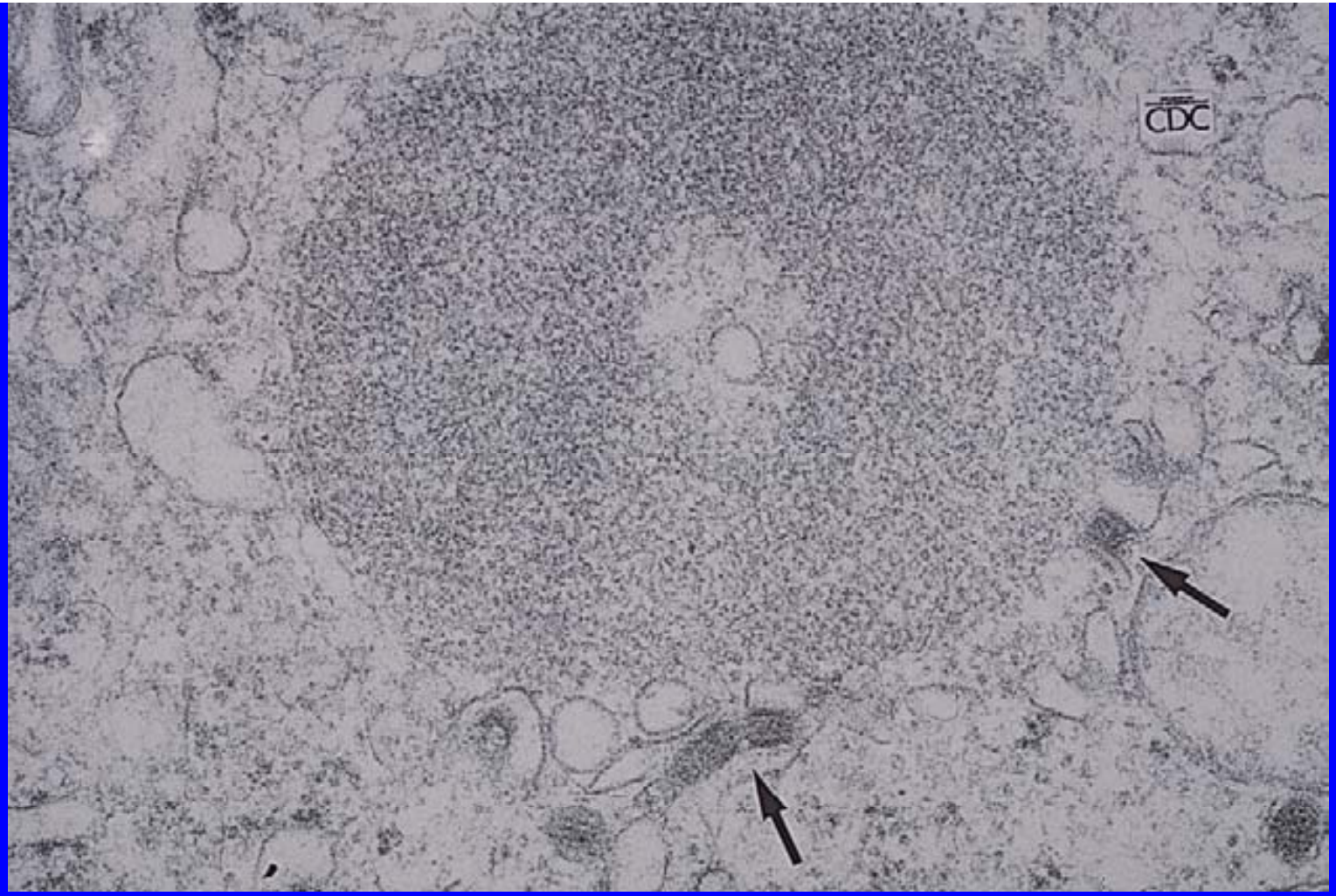
Name	Genotype designation	Locality	Principal hosts	Spillover hosts reported
European bat lyssavirus 1	5	Europe (continental)	Insectivorous bats, particularly *Eptesicus serotinus*	Sheep, stone marten (*Martes foina*), cat, human
European bat lyssavirus 2	6	Europe (continental, UK)	Insectivorous bats, particularly *Myotis daubentonii*, *Myotis dasycneme*	Human
Australian bat lyssavirus	7	Australia	Flying foxes (*Pteropus* spp.) Insectivorous bat: *Saccolaimus flaviventris*	Human
Aravan, Khujand, Irkut, West Caucasian bat virus	Undesignated. Proposed new genotypes.	Central Asia	Single isolates from insectivorous bats: *Myotis blythi* (Aravan virus), *Myotis mystacinus* (Khujand virus), *Murina leucogaster* (Irkut virus), *Miniopterus schreibersi* (West Caucasian bat virus)	None recorded

Diagnosis

- Standard diagnostic test is the Fluorescent antibody test (FAT)
- Usual sample is fresh brain impression smears however other nervous system tissues can be used (brain is best but test can be done if there is no head e.g. using spinal cord, ganglia etc)
- Blood tests: serological results are interesting but meaningless in terms of determining if a clinically well animal will become ill with ABLV
  i.e. not a suitable test for diagnosis or risk assessment, is useful for epidemiological research
- Confirmation and typing ABLV may be done with other tests
  - PCR and Sequencing (pteropid v YBST-bat variant)
  - Antigenic typing with monoclonal antibodies (mAb)
- Immunohistochemistry - using monoclonal antibodies to detect antigen in formalin fixed tissues – most useful when no fresh tissue is available e.g. for testing archive material

Positive Flourescent antibody test





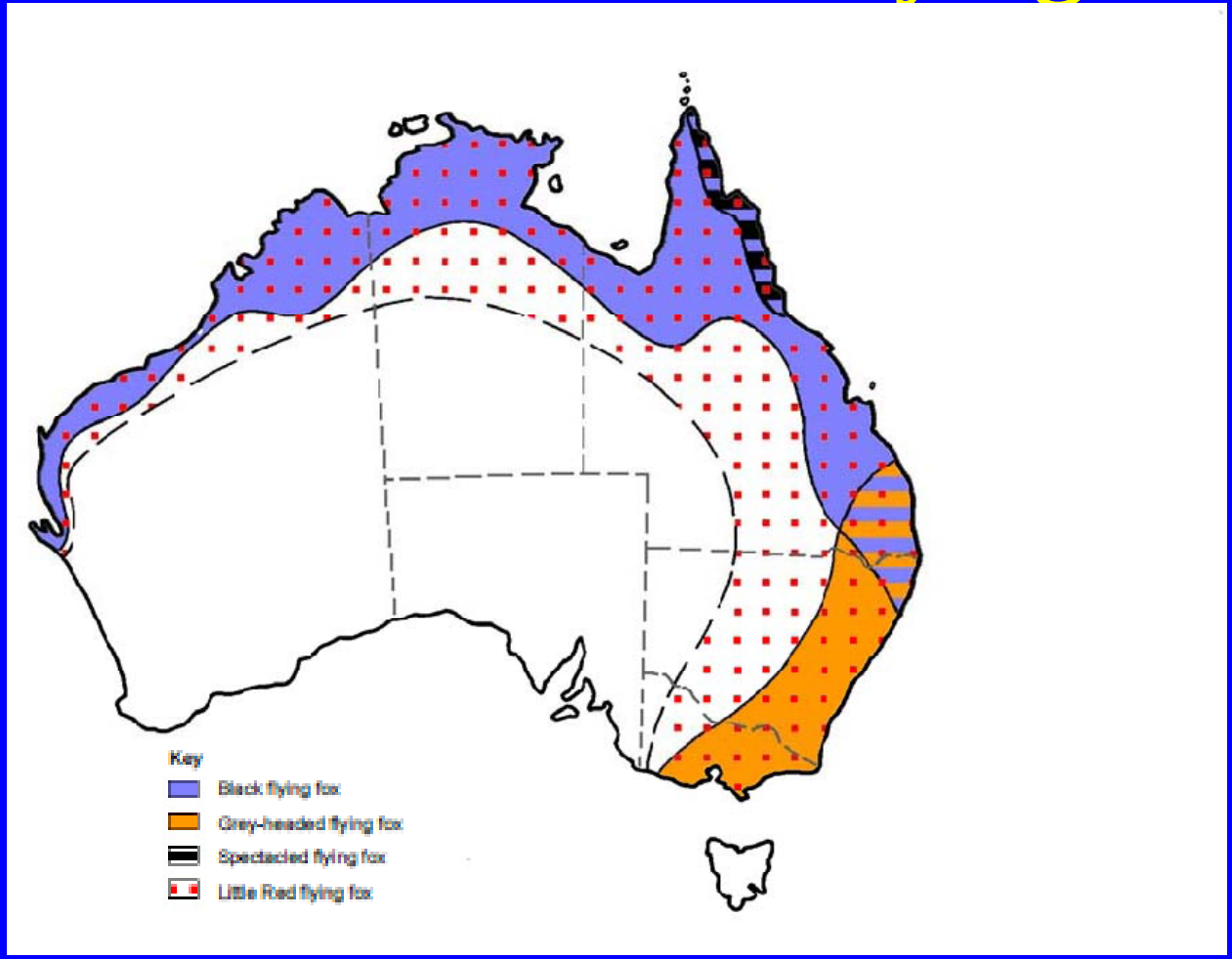
Electron micrograph of an Australian bat virus isolate (family Rhabdoviridae, genus Lyssavirus), showing the typical rod-shaped morphology (arrows) of virions in the cell cytosol.

Rupprecht C et al, Lancet Infect Dis 2002; **2:** 327–43

Table 1.3 Tests currently available for ABLV

Test	Specimen	Test detects	Time taken to obtain result
FAT	Fresh brain	Lyssavirus antigen	0.5 days[a]
TaqMan assay (separate assays for pteropid and insectivorous ABLV)	Fresh brain	Viral genome	1 day[a]
PCR for generic lyssavirus (nested RT-PCR and sequencing)	Fresh brain	Viral genome	2–3 days
Competitive ELISA	Serum and plasma	Rabies neutralising antibody	2 days
Virus isolation using neuroblastoma cell cultures	Fresh brain	Live virus	5 days
Immunohistochemistry	Formalin-fixed brain	Lyssavirus antigen	2 days
Serum neutralisation test (rabies RFFIT)	Serum	Rabies neutralising antibody	3 days
Serum neutralisation test (ABLV FAVN)	Serum	ABLV neutralising antibody	5 days

Distribution of the four common species of Australian flying fox

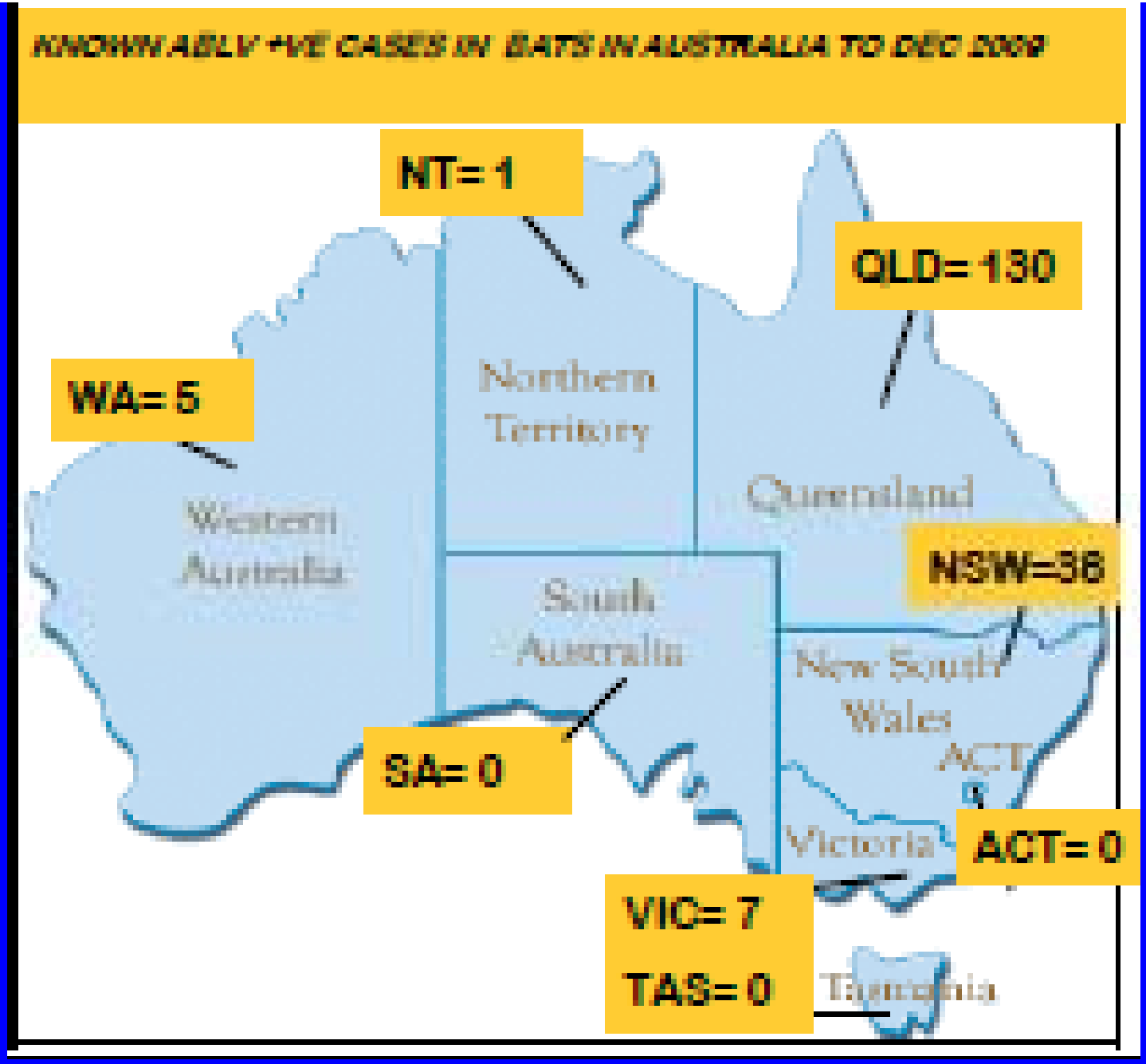


Barrett J, ABLV Thesis, University of Queensland

Table 2: Confirmed ABLV cases in bats (as confirmed by FAT, PCR, IHC and/or Virus Isolation^) for Australia in the period Jan 1996 – Dec 2009.

	NSW	NT	QLD**	VIC	WA	TOTALS (BY YEAR)
1996	1	0	10*	1	0	12
1997	7	1	27	0	0	35
1998	1	0	26	0	0	27
1999	0	0	6	0	0	6
2000	1	0	14	0	0	15
2001	0	0	9	1	4	14
2002	4	0	10	2	1	17
2003	3	0	3	2	0	8
2004	5	0	6	1	0	12
2005	6	0	5	0	0	11
2006	2	0	4	0	0	6
2007	6	0	2	0	0	8
2008	0	0	0	0	0	0
2009	2	0	8	0	0	10
TOTALS	38	1	130	7	5	181

ABLV Quarterly Report, AWHN, Apr 2010



ABLV Quarterly Report, AWHN, Apr 2010

Bat testing

- Prevalence in submitted sick, injured, orphaned bats ranges from 1- 17%, typically 5 -10%
- None of 475 wild caught megachiroptera had evidence of ABLV (prevalence in healthy wild bats < 1%

Human cases of ABL infection

- May 1996 Australian Bat Lyssavirus (ABL) discovered in Australian bat population

- Nov 1996 -female bat/animal carer, Rockhampton
  - Uncertain exposure history-Scratched, ? Bitten
  - Incubation – several weeks
  - Clinical course 20 days

- Dec 1998 - female, Mackay
  - bitten by bat while removing it from child
  - Incubation 27 months
  - Clinical course 19 days

- Symptoms and clinical course very similar to rabies (pain, parasthesia, headaches, non supperative meningoencephalitis, coma, death)

- Post exposure prophylaxis given to family/close contacts and health care workers

The Public Health response

- Initially focused on extensive program of catch up post exposure prophylaxis
- Interagency collaboration (QH, DPI, QPWS)
- Education
- Surveillance PHUs
- Research (AAHL, QHFSS)

Since then….

- Many hundreds of people have come forward with history of exposure to bats
- Reports of exposure clustered around publicity of cases but exposures may have occurred some months or years earlier
- There is still not good knowledge among the public about the dangers of handling bats
- Any bat/flying fox is considered ABL positive until proven otherwise

A potential human exposure (C3)

- Bat bite or scratch
- Percutaneous or permucosal exposure to bat saliva or neural tissue
- Behaviour/condition of the bat is not 100% predictive of ABL status

Risk Categories of bats

- **Category 3** (high human health risk). Bat that is known or reasonably suspected to have had potentially infectious contact with a human (eg has bitten or scratched a person). Within Category 3, bats with clinical signs suggestive of ABLV (see Table 1.2) are of highest risk.
- **Category 2** (high animal health risk, medium human health risk). Bat that poses a potential risk of infection to humans. Disease investigation and exclusion testing is recommended due to either:
  - history or clinical signs suggestive of ABLV without a history of a potentially infectious contact with a human (Category 2a)
  - history of known or suspected contact with another animal (other animal potentially exposed to ABLV via bat) (Category 2b).
- **Category 1** (low risk). Bat that is neither Category 2 nor Category 3 – that is, bat that has no history of known or suspected contact with another animal or person and for which the index of suspicion for ABLV infection is low (eg no clinical signs consistent with ABLV) (see Table 1.2).

Prevention

- Education – GPs, Bat care organisations, public
- Pre-exposure vaccination (lab workers, bat carers, researchers)
  - 3 doses rabies vaccine, IM days 0, 7, 28
- Post exposure vaccination
  - Immediate first aid (soap and water), antiseptic
  - Rabies Immune Globulin 20 IU/kg (150IU/mL) into the wound (passive immunity – half life 21 days)
  - 5 doses rabies vaccine, IM days 0, 3, 7, 14, 28-30
  - Consider tetanus prophylaxis

Policy re C3 bats

- Any bat involved in a C3 exposure should be submitted for testing to exclude ABL
- If the bat has flown away it is regarded as positive and the person is treated with full Post Exposure Prophylaxis (PEP)
- Rabies Immune Globulin and 5 doses of HDCV if not previously immune
- 2 doses of vaccine if previously immune
- **May defer vaccination for 48 hours pending test results**
- **5 x HDCV if exposure > 1 year ago**

PHU-Lab role

- Public Health Units will coordinate the retrieval and testing of the bat/flying fox and provision of post exposure treatment
- Rely to a large extent on the support of existing networks of animal carers, QPWS, RSPCA and veterinarians
- A result will usually be available within 24 hours of receiving the bat (prefer bat to be euthanased before arriving at lab)

Role of Vaccine

- 1996 CDC studies[1]
  - Human and animal rabies vaccines completely protected mice against intracerebral challenge with ABL
- 2005 studies[2]
  - Human sera used in FA virus neutralisation assays 48/50 cross neutralised ABLV
  - ABLV least invasive (cf EBLV>wRABV)
  - Cross protection peripheral challenge 80%

1. Bull Inst Pasteur, 1997, 95: 209-218

2. Brookes S. et al. Vaccine 2005; 23: 4101-4109

What about domestic animals?

- So far, no evidence that ABL causes symptoms in naturally exposed dogs and cats (< 10 mammals involved in C2 exposures to +ve bats)
- No recommendation to destroy dogs/cats involved in C2 exposures
- Monitor, observe, consult vet if worried

- Lyssavirus infections host specific, rare spillover events
- No contemporary evidence of ABLV infection in dogs/cats/possums
- AAHL experiments*
  - Transient behavioural changes 2 – 3 wks post innoculation ABLV in 3/5 dogs (puppies)
  - No observed clinical disease, all seroconverted
  - No virus in saliva???
  - CSF (3/12) +ve for rabies virus neutralising ab in 2 dogs

* McColl, K, et al, Veterinary Microbiology 2007; 123:15-25

AUSVETPLAN

- Management of in contact domestic animals
- Risk assessment
- Testing if bat available
- Options
  - Vaccination
  - Observation
  - Euthenasia

Conclusion

- Human potential exposures continue to occur (last +ve bat in Qld in 2009)
- Considerable resources in managing post exposure prophylaxis
- Ongoing requirement for education and further research