Animal rabies: BATS

- Primary reservoirs for all except Mokola
- Wide diversity of species, large numbers, widespread, often protected
- Human rabies bat origin only in Americas

Rupprecht *Lancet Infect Dis* 2002 2: 327-43
Messenger *Clin Infect Dis* 2002 35: 738-47
The African lyssaviruses

- Lagos bat, Mokola, Duvenhage
- Epidemiology poorly studied
- Human case numbers small, ? underreported
- Last human case Duvenhage S Africa 2006: scratch face by bat, no medical attention, died

Rupprecht *Lancet Infect Dis* 2002 2: 327-43
Paweska *Emerg Infect Dis* 2006 12: 1965-7
European bat lyssaviruses

- EBLV 1 predominant
- Geographic variability eg Germany only type 1; UK only type 2
- Spillover from bats to mammals inc livestock, humans, wildlife but no reservoir roles
- 4 human cases (1997 +)
  - Ukraine, Russia (EBLV 1); Finland, Scotland (EBLV 2) – all died
  - 3 bat bites, 1 bat conservationist; no vaccination

Australian bat lyssavirus

- Pteropus alecto (black flying fox) 1996
- Ag in brains of 7% of bats submitted for testing following human contact
- Seropositivity rates 6-7%: Qld
- Rabies found in bats in Philippines with cross-reactivity to ABL
- Two human cases: Qld & NSW – occupational & bite (27 mos earlier!)

ABL in the Philippines

- Neutralizing antibody 22/1998 bats
- One species *Miniopterus schreibersi*
- No active infections found
- (350 cases human rabies yearly)

Arguin *Emerg Infect Dis* 2002 8: 258-62
Rabies transmission

- Bite from rabid dog or bat
- Scratch or lick: broken skin or mucosa
- Not always a clear history (20/32 in USA)
- Aerosolization: lab accidents 2 human cases; experimental in bats & mice
- Organ donor: 4 recipients kidneys, liver and arterial graft – all died [donor SAH; rabies antibodies, bat bite]

Lyssavirus lab diagnosis

- Culture: saliva, CSF – neuroblastoma cell line or ic inoculation of mice [several]
- Direct FAT using anti-N antibody, corneal impressions & skin biopsies. Animals.
- Immunohistochemistry of skin biopsies
- RT-PCR (real time) using N gene: saliva, CSF, skin. Epidemiologic investigations.
- Serum/CSF antibody in unvaccinated (neut, IFA)
- Brain FAT, Negri bodies, immunohistochem, culture, RT-PCR

Clinical features: rabies

- Incubation 1-3 months, up to 6 years
- Prodromal flu-like, several days +/- local pain, itch, paresthesiae
- Encephalitic: salivation, spasms, LOC, convulsions, coma, death
- Paralytic: Guillain Barre-like, sphincter loss, sensory preservation, myoedema
- Atypical: neuropathic pain, sensory/motor, chorea, brainstem, cranial ns, myoclonus, psychiatric disturbance

Clinical features: other lyssaviruses

- Not well characterized
- Lagos bat virus no human disease
- EBLV (4 pts) local pain/itch/paresthesiae with encephalitic sequelae
- ABLV (2 pts) encephalitis, 1st case initial weakness arm

Rabies: 6 survivors (1)

[Highest case fatality of any ID in humans]

- Dog (3), bat (2), lab accident (1)
- USA (3), Mexico, Argentina, India
- 9 yo boy complete recovery; others significant sequelae; 1 died 23 ys later
- 5 received vaccine prior to onset of symptoms; none received RIG

Rabies: 6 survivors (2)

- 15 yo girl Wisconsin, no vaccine, coma induced by ketamine + amantididine, ribavirin
- Acquired rabies antibodies
- Residual choreoathetosis, dysarthria, ataxia
- Subsequent Thai pt similar treatment without vaccine – died

Willoughby *NEJM* 2005 352: 2508-14
Prevention in animals

- 50 million dogs vaccinated/year – public health programmes or by private owners
- Vaccination effective eg Morocco, Tunisia, Sri Lanka
- Oral live vaccines advocated by WHO eg foxes & coyotes Europe & N America
- Fertility control; clearance of rubbish

www.who.int/rabies/animal/en/
Wandeler Rev Sci Tech 1993 12: 51-71
Prevention in humans

- Pre-exposure prophylaxis
- Post-exposure prophylaxis
- Wound care: soap and water reduces mortality (Kaplan Bull WHO 1962 29: 765-75)

www.who.int/rabies/vaccines/en/
Pre-exposure (1)

- No rabies deaths reported following admin of appropriate vaccine regimen
- Obviates need for RIG
- Boosting recommended with monitoring of neut Ab levels; 1 y boost assoc Ab for 10 y
- ID route immunogenic but lower Ab levels & involves use of multi-dose vials
- Reduced response in HIV pos children

Pre-exposure (2)

- HDCV & others from genotype 1
- Not protective Lagos bat, Mokola, Duvenhage
- Protective EBLV 1, partially EBLV 2
- HDCV 79% protective vs ABLV challenge in mouse model [100% RABV & EBLV]
- ABLV vaccine likely to be more successful if local strains used in development
- Encouraging results for new Eurasian strains

Post-exposure (1)

**RIG**: human source
- Horse, sheep, goat
- Rodent sources
- Monoclonal products in development

**HDCV**
- Chick embryo, duck embryo, rhesus cell & vero cell vaccines considered equivalent
- DNA or recombinant vaccines + use of plant technology in future


Post-exposure (2)

- Failures usually assoc with deviations from protocol or poor availability or quality: Thai study 7/15 represented true failures
- No failures of RIG + vacc for EBLV; animal studies: neutralizing effect of RIG variable
- ABLV more closely related to rabies than EBLV so RIG + vacc hopefully effective

The number of annual human deaths from rabies in the world is:

- 25,000
- 35,000
- 45,000
- 55,000
- 65,000
Rabies: true/false

- Transmitted as a lab accident in 1 person: 2
- Transmitted from cornea of an organ donor: kidneys, liver, arterial graft
- There have been only 4 survivors: 6
- Axonal transmission occurs at 20 mm/day: 50-100
- Phylogenetic classification is based on G protein: N protein
European bat lyssavirus: true/false

- Has been found in a human in northern England: **Scotland**
- Only 5 human cases have been described: **4**
Where outside Australia has ABL been found?

- New Zealand
- New Caledonia
- Papua New Guinea
- Malaysia
- Vietnam
- Philippines
Advances

- Virology: proteins, virulence, pathogenesis
- Neuroinvasiveness
- Transmission
- Diagnostic tools
- Global surveillance of animals and humans
- Reduction in animal cases in some countries
- Effectiveness of preventive measures
However....

- 55,000 humans/ year develop rabies
- They almost all die
- Prophylactic measures very effective
- The old problem between rich and poor countries applies
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