Rabies situation in Eastern Europe
(a molecular epidemiological perspective)

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This Is Not An Option  Courtesy of Corrie Brown

Rabies is an under-reported disease

In a cohort of 133 children with CNS-related diseases
- 14 (10.5%) – rabies
- Three of 26 (11.5%) clinically diagnosed cases of cerebral malaria were laboratory-confirmed as rabies

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In a malaria-endemic area of Africa, rabies was an important cause of fatal central nervous system infection, responsible for 14 (10.5%) of 133 cases. Four patients had unusual clinical manifestations, and rabies was only diagnosed post-mortem. Three (11.5%) of 26 fatal cases originally attributed to cerebral malaria were due to rabies.

What are the major risk factors in Europe?

- **Sylvatic rabies**
  - Foxes / raccoon-dogs likely to be serious problem
  - Emerging lyssaviruses – bats?
    1. Bat virus ➔ wildlife reservoir ➔ cat
    2. Other bat-adapted variants of rabies virus (gt.1)

- **Urban rabies**
  - Other imported carnivores (ferrets)

- **Accidental / deliberate release of imported wildlife**
  - Non-indigenous species
    1. Raccoon-dogs; raccoons (Germany!)
  - Agro-terrorism
  - Political instability
  - Complacency through lack of border control
Epidemiological situation of rabies in Europe

- **Vectors / reservoirs**
  - Red fox
  - Dog / cat
  - Raccoon dogs
  - Arctic foxes
  - Wolves
  - Badger!

- **European bat lyssavirus type-1**
  - *Eptesicus serotinus*; man; sheep; stone-marten, cat

- **European bat lyssavirus type-2**
  - *Myotis daubentonii / Myotis dascyneme*; man

- **Eurasia - ARAV, KHUV, IRKV, WCBV**
  - Aravan Virus - Kyrgyzstan (1991)
    - Lesser Mouse Eared bat (*Myotis blythi*)
  - Khujand – (Tajikistan 2001)
    - Whiskered bat (*Myotis mystacinus*)
  - Irkut - East Siberia (2002)
    - Greater tube-nosed bat (*Murina leucogaster*)
  - Western Caucasian bat virus – Krasnodar (2002)
    - Schreiber’s bat (*Miniopterus schreibersii*)

Bat rabies (1977 – 2007)

positive = 860
Bat rabies (1977 – 2007)

EBLV-2
EBLV-1a
EBLV-1b

Europe – Spread of fox rabies
Spread of rabies

- Dogs to Foxes (Western Russia / Poland)

- Foxes / Dogs to Raccoon Dogs (NE Europe)
- Dogs to foxes (Turkey)
- **No** evidence for bat spill-over / adaptation to a terrestrial mammal with sustained species – species transmission in Europe
- Evidence for occasional bat spill-over cases only
Rabies situation in Europe - 2008

RABIES CASES EUROPE
1st QUARTER 2008
3715 CASES REPORTED
2 BAT RABIES CASES INCLUDED
3 HUMAN RABIES CASES INCLUDED

- Rabies free (terrestrial rabies)
- No data
Impact of ORV on Rabies

1980-2007
Reasons for setbacks

- limited financial resources
- lack of long-term planning
- missing cross-border activities
- small-scale vaccination
- other disease priorities
- increasing fox densities
- inadequate bait distribution
- premature declaration of areas as being “rabies free”
- inferior adaptation of vaccination strategies
- decreasing awareness
- violation of elementary principles of rabies control
- absence of complementary measures
- no epidemiological analysis
- deficient surveillance
- cold-chain of vaccines
Species barrier: practical consequences

- Target the vector, not the victim
- To eliminate human rabies - dogs must be the principal target
  - Human rabies pre-immunization and prophylaxis provided in rabies-endemic regions
Destruction of ‘stray’ dogs

- Strategy provides short-term respite to the rabies problem
  - Ecological vacuum soon filled by naïve animals
- Lack of understanding between veterinary and medical authorities
  - Undertaken in response to human cases
- Vaccination of dogs preferential
  - Animal Birth Control (ABC)
- Population reduction
  - Not socially acceptable
  - Not economically viable
Oral vaccination of dogs

- Considered as a supplement to parenteral vaccination
- Could be applied on a larger scale
  - A tool of rabies control in dogs

Radial Tree of European RABV

N gene (400bp)

n=198
North East Europe (NEE) Isolates

Raccoon Dog, Fox, Badger, Dog, Cat, Polecat, Rat, Cow
East Europe (EE) Isolates

Serbia, Hungary, Bosnia, Montenegro, Bulgaria, Poland, & Czech Republic

Dog, cat, fox, horse, cattle, deer
Central Europe (CE) Isolates

Fox n=19, Raccoon Dog n=3, Water Rat n=1, Marten n=1
East
Turkey/Georgia/Russia
Fox n=4, Cow n=2
Dog n=2, Cat n=2
Human n=1, Wolf n=1
Close to Iranian isolates

West Turkey/Russia/Hungary
Dog n=8, Fox n=6, Human n=2
Intermediate Dog/Fox ?

North East
Turkey/Georgia
Dog n=2, Human n=1

Working for public and animal health
Serbia Fox Group

N East Serbia 1972-1977

N Serbia 1986-1997
FRY – Bovine isolates

RV1185 - Montenegro Bovine 1978
8658YOU - FRY Bovine 1981

Divergent Isolates – 100% bootstrap support
# Epidemiology of Rabies in Balkan Peninsular

- FLI-Wusterhausen (Germany) | T Muller, C Freuling
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- Vet. Inst. Of Republika of Srpska | V Sandrac
Southeast Europe (the Balkans)

- Rabies is endemic within many countries of south east Europe
- The fox is the principal reservoir species but dog rabies cases still reported
- Few epidemiological studies reported from the region
- Lack of knowledge hampers vaccination programmes
The Balkan Peninsular
## Cohort Details

<table>
<thead>
<tr>
<th>Country (Cases 2005)</th>
<th>Fox</th>
<th>Dog</th>
<th>Jackal</th>
<th>Human</th>
<th>Other</th>
<th>Not recorded</th>
<th>[Total]</th>
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<tr>
<td>Bosnia-Herzegovina (36)</td>
<td>10</td>
<td>3</td>
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<td>4</td>
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<td>17</td>
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<td>Bulgaria (8)</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td></td>
<td>12</td>
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<tr>
<td>Georgia</td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>Serbia &amp; Montenegro (101)</td>
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<td></td>
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<td>2</td>
</tr>
<tr>
<td>Hungary (9)</td>
<td>3</td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Poland (138)</td>
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<td></td>
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<td>2</td>
</tr>
<tr>
<td>Romania (530)</td>
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<td>2</td>
<td>1</td>
<td></td>
<td>1</td>
<td>2</td>
<td>9</td>
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<tr>
<td>Russia (3087)</td>
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<td>5</td>
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<tr>
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<td>9</td>
<td>4</td>
<td></td>
<td>1</td>
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<td>21</td>
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Phylogenetic analysis of RABV sequences from Southeastern Europe
Romania
Bulgaria
Bosnia-Herzegovina
Conclusions

- Most isolates fall into the East European (EE) group of viruses
- Geography dominates isolate clustering
- Evidence for host switching
- Topography may play a significant role in preventing spread of fox-rabies
  - The Danube appears to block movement between Romania and Bulgaria
  - Such natural / artificial factors should be used to assist future vaccination campaigns
Biotypes by Country
(Geographical determinant)
Can rabies be eliminated from wildlife?

- **Wildlife rabies** can be controlled
  - Intensive culling / hormonal sterilization have failed to reduce the fox population below an endemic threshold ($R_0$)
  - Mass vaccination of primary reservoir
    1. Oral rabies vaccination (ORV)
  - **Within 25 years of introduction of ORV**
    1. Elimination of fox rabies in Western Europe
  - ORV is most effective with complementation
    1. Public health strategies / education
    2. Agricultural and wildlife management
  - ORV has become the pre-eminent example of a modern and innovative method of disease control among free-ranging wildlife

Rabies elimination from ‘man’s best friend’

- Estimated dog to human ratios range typically between 1:8 and 1:40
  - Dog population densities may reach several thousand per km²
  - High rate of exposure to biting dogs in developing countries
    1. Southern Asia – annual human exposure to dog bites is between 0.1 – 2% of the population
    2. >99% human rabies caused from rabid dogs
- Dog vaccination is recommended or compulsory in rabies-endemic areas
  - Dog registration
  - Commercial veterinary vaccines are pure, potent, safe, efficacious and provide long-lasting immunity (3 – 4 yrs)
  - Reduction in dog rabies will provide a concomitant reduction in human rabies

Can rabies be ‘eradicated’?

- Rabies is the most significant viral zoonosis in the world today
- Need for a ‘One Health’ approach
  - Public health
  - Veterinary
  - Economic standpoint
- Given the distribution and abundance of bats as reservoir hosts
  - Rabies is not a candidate for true eradication
- Human rabies can be eradicated
  - Eliminating exposures
  - Proper, timely application of modern PEP
- Canine rabies transmission can be eliminated
- Wildlife rabies can be controlled
  - ORV

Conclusions

- Comprehensive knowledge of rabies epidemiology in a specific region / country
  - Reservoir species
  - Other hosts
  - Virus spread across borders
- Harmonization of control efforts with bordering countries
  - Border control
  - Government support (financial backing)
- Appropriate control strategy linked to epidemiological knowledge of rabies
  - Which animals to target!
  - Vaccine type
  - Other control strategies
- Sustainability!
- “Making a paradigm shift!”
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