Rabies Control in Asia: OIE Perspective

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   • Epidemiological study in Asia

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Rabies virus

- **Genus**
  - Rhabdoviridae
  - *Lyssa virus, Rabies virus* (serotype 1)

- **General Feature**
  - ss RNA (11-12 kb)
  - Helical nucleocapsid
  - Bullet-shaped virion
  - (225 X 60 nm)
  - Isolation only on neurogenic tissue
  - 5 polypeptide (N, P, M, G, L)

  - **G**: determinants of rabies virus pathogenicity and host specificity
  - **N**: plays an important role in the T helper response / highly conserved, most popular target for rabies diagnosis using RT-PCR
  - **Pseudo (ψ)**: highly variable region suitable for sensitive criteria to differentiate virus isolate
Introduction

• Every 10-15 minutes someone dies of rabies in somewhere in the world
• Claim nearly 40,000- 70,000 lives a year
• Dog remains the primary source in Asia, Africa and Latin America – over 96% of human deaths
• Analysts have estimated that just 10% of the financial resources currently used to treat people bitten by potentially rabid dogs would be sufficient to enable national Veterinary Services throughout the world to eradicate rabies at source in domestic animals
Animal rabies cases in the world between Jan and June 2013

Red color means large number of rabies cases
Human rabies cases in the world 2011

Distribution of risk levels for humans contacting rabies, worldwide, 2011

Dark brown color means high rabies risk region corresponding to Asia and Africa
Human death of rabies

Knobel et al., Bulletin WHO, 83: 360-368, 2005

India: > 19,000
China: > 2,500
Human rabies in China in the past 60 years

Since 1949, there have been three rabies epidemics in China. China is currently in the midst of a third epidemic.

Figure 1. The three rabies epidemic waves in Mainland China since 1949. Y-axis shows annual number of human cases in China from 1950 to 2010. Since the foundation of the People's Republic of China, the country has experienced three rabies epidemics. The country is currently in the midst of a third epidemic that began in 1996 (159 cases), peaked in 2007 (3300 cases) and has begun to gradually decrease since this time. Red arrow indicates the beginning of a concerted dog culling program implemented in 1984.

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Regional distribution of human rabies in China since 1999

Since 2008, four laws and plans related to rabies control have been enacted and dog rabies has become the priority animal disease with a planned elimination by 2020. - Zheng Zeng

Source: Dr Xu Zhen (Chinese Center for disease control and prevention)
Introduction – human rabies situation Asia

Approximately 56% of global human deaths

Rabies free:
Japan: 1958-
Singapore: 1953-
Malaysia: 2000-
HK: 1988-
Introduction - *regional comparison*

- Pressure of canine rabies falls most heavily on Asia (E.g. China, India) – experience over ½ of human and cattle deaths, performs >90% PEP administrations and just under ½ of dog vaccination.

Annual direct impacts of canine rabies in terms of human & cattle deaths and PEP cases (in thousands)

<table>
<thead>
<tr>
<th></th>
<th>Latin America</th>
<th>Africa</th>
<th>Asia</th>
<th>Total</th>
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<tr>
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<td>0.002</td>
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<td>69</td>
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<tr>
<td>PEP cases</td>
<td>620</td>
<td>260</td>
<td>8,700</td>
<td>9,000</td>
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<tr>
<td>Cattle deaths</td>
<td>0.002</td>
<td>11</td>
<td>21</td>
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</tbody>
</table>

Stephanie Shwiff et. al., 2013
Animal rabies in Korea since 1907

- 1907: First record of outbreak
- 1907 ~ 1945: Endemic stage (100-900 animal case, annually)
- 1945 ~ 1992: Decrease and elimination stage
- 1985 ~ 1992: No outbreak
• Rabies control program in the world
Vaccinating dogs in Mexico

It is well known that mass vaccination in dogs leads to rapid decrease of rabies cases.
Rabies control in Egypt

• The dog population is estimated at more than 3 million.
• The control measures are aimed mostly to eliminate stray dogs.
• The Trap-Neuter-Release program was used in a pilot phase.
• The stray dog population is eliminated by poisoning with strychnine or by cartridge shooting.

• The limitation in the national budget hindered the expansion of TNR program.
• Elimination by strychnine or cartridge shooting creates many problems with animal welfare organizations.
• Elimination of stray animals (dogs and cats).
• Vaccination of owned dogs by inactivated Rabies Vaccine.
• Vaccination is repeated annually to dogs and cats.
Rabies control in Morocco

• Around 20,000 persons receive yearly PEP treatment after a potential rabies exposure
• 120 PEP Centers present in Morocco
• Dogs remain the main reservoir and transmitter of rabies
• Increase on laboratory diagnostic confirmation
• Local vaccine production

• Inadequate coordination between involved departments due to non clearly defined responsibilities
• Deficiency in public education
• Vaccination coverage is not high enough to break the transmission cycle of the disease
• Insufficient knowledge on rural canine population dynamic.
Implementation of a new rabies control strategy in Morocco in 2003

- Organization of sustainable mass dog vaccination campaigns
- Dog population management through reduction of stray dog population, control of movement
- Strengthening the rabies surveillance system
- Training of technical staff
- Coordination between 3 involved departments in rabies control (Agriculture and health ministries and local council)
- Insufficient dog owners participation
- Non-involvement of private vet in vaccination campaigns
- Deficient knowledge on dog population
- A dynamic canine population (30% estimated turnover) leading to an insufficient vaccination coverage
Rabies control in Indonesia

- Indonesia has a goal to eradicate rabies by 2020
- Rabies control program has been expanded (Bali success story)
- Human resources and community empowerment
- Eradication of rabies in 4 provinces (Jakarta, Central Java, East Java, Yogyakarta) and maintaining 5 provinces as free area

- Surveillance and response (integrated bite case management)
- Integration (training, surveillance, evaluation)
- Mass vaccination
Keys to successful program implementation in Bali

- The focus on a clear operational goal of vaccinating 70% of dogs
- Daily short message service (SMS) reporting of all vaccination and PEP results
- Daily, weekly, monthly government coordination meeting
- Development of campaign-specific standard operating procedures (SOP)
- Single dose vaccine, dog catching nets and long-lasting collars are required
Rabies control in Thailand

- Dogs are still main reservoir
- Most animals involved in rabies were not vaccinated
- Socio-cultural activity: raise public awareness through media
- Develop national rabies control strategy in 2010
- Transfer rabies control strategy to local organization

- Survey and registration of dogs and cats
- Immunization
- Dogs and cats population control
- Outbreak management and animal shelter
The main problems in rabies control in Viet Nam

- Dogs are breed for four reasons; as guard dogs, pets, for meat and export
- The large dog population with inadequate measurers
- The long established presence of stray dogs
- The limited system for surveillance of rabies
- The small amount of vaccine available and its unequal distribution
- The inadequate of the national rabies program
Human rabies cases in 5 Asian countries

The national rabies control and prevention program of the Philippines set a target of 2020 for the elimination of rabies. It is noted that RABVs in the country have an independent evolution in each area without frequent introduction into other areas.
Animal rabies cases in 5 Asian countries

- Thailand
- Philippines
- Indonesia
- Korea
- Lao PDR

No. of rabies cases

- 2008: Thailand - 289, Philippines - 14, Indonesia - 109
- 2009: Thailand - 250, Philippines - 18, Indonesia - 74
- 2010: Thailand - 611, Philippines - 10, Indonesia - 10
- 2011: Thailand - 695, Philippines - 4, Indonesia - 4
- 2012: Thailand - 825, Philippines - 596, Indonesia - 512
- 2013: Thailand - 594, Philippines - 473, Indonesia - 475
Innate immune response in raccoons

- 5-40% of raccoons survive RABV challenge
- Incubation period can vary among raccoons
- In a few cases, vaccinated raccoon dogs have not demonstrated sero-conversion
Innate immune responses in raccoons after raccoon rabies virus infection

Table 1. Time course of RRV infection in raccoons

Viral detection data was obtained from the doctoral thesis of Szanto (2009).

<table>
<thead>
<tr>
<th>Sample*</th>
<th>Days p.i.</th>
<th>Clinical signs</th>
<th>Viral RNA in brain†</th>
<th>Viral RNA in salivary glands</th>
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<tr>
<td>Control 1</td>
<td>-4</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Control 2</td>
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<td>-</td>
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</tbody>
</table>

*Sample shows days p.i. and the sample numbers that were euthanized that day.
†Viral RNA detected by quantitative PCR <45 C₀.

Four of 20 raccoon dogs inoculated RABV (10.6.5 TCID₅₀/ml) IM were survived.
Host transcriptional response to infection with RABV within raccoons in the Brain. Once the clinical signs of rabies were apparent (20–24 days), expression of all genes under investigation increased significantly. Especially IFN-r demonstrated a 130-fold increase in the brain, and this increase was much higher than that noted for other genes.

I guess rabies will occur again in the rabies risk region sometime.
3

• Activities of OIE, FAO and WHO on rabies
OIE organized three conferences on rabies

- OIE organized two regional conferences on rabies in 2005 (Kiev), 2007 (Paris) and one global conference (Seoul 2011)
- OIE-WHO-FAO Tripartite meeting: Mexico City, November 2011
- High Level Technical Meeting to Address Health Risks at the Human-Animal-Ecosystem Interface
- Need for common actions Three “flagship” topics:
  - Rabies
  - Antimicrobial resistance (AMR)
  - Zoonotic influenza
A long term and consistent rabies control strategy must be prepared and revised at regular intervals.

An integrated international approach including financial support for rabies control should be a high priority.

Canine rabies can be eliminated with mass vaccination. Stray dog destruction alone is not fully effective in rabies control.

Oral vaccination should be also considered as complementary measures for interrupting the rabies cycle.

Reservoir species should be monitored in countries where a risk of re-emergence should be strengthened.

There is a requirement for rapid and accurate serological methods (i.e. ELISA) to replace FAVN/RFFIT

Development in Biologicals- Dodet et al., p525-527

Acknowledged that:
• Rabies in wildlife remains a serious problem in the Northern hemisphere and, although fox rabies has been eliminated successfully in many western European countries by oral vaccination programmes, the disease in foxes and other terrestrial species (eg raccoon-dogs) is still present and is increasing in Eurasia.

• Immunization is the method of choice for controlling and eliminating rabies in its main animal reservoirs, as reduction of the wild animal population by culling has been shown not to be effective for controlling

Recommendations:
• Design and implementation of sustainable national programmes for rabies control
• Good governance of veterinary services
• Improved surveillance and reporting
• Standardisation of diagnostic techniques in line with OIE manual
• Oral and parenteral vaccination campaigns strongly recommended especially
  • for wildlife and canine rabies control
• **Global Conference on Rabies Control: Towards Sustainable Prevention at the Source**”

• The OIE, WHO and FAO should consider rabies a priority and should encourage international solidarity and donor support for countries in need of funding to initiate and sustain control programmes for rabies.

• Adoption of recommendations on a global strategy for controlling rabies in dogs worldwide.
Key recommendations of the Conference

• Control programme should support effective public and private component of national Vet Services
• Vaccination of dogs is the preferred method
• More research on practical and feasible chemical or immuno-contraception is encouraged
• Dog population management, rabies control and animal welfare should be included in the basic core curriculum of vet education
• All stakeholders should be involved under “One-health” concept
• Public awareness and education
Revised OIE standards on rabies

Main considerations:

- In large part of the world dogs are the main source of human rabies infection
- High number of non-commercial movements
- Endemic or sporadic rabies in wildlife or stray animals can easily spill over to domestic animals and humans
- Animal welfare considerations for stray dog population control programs
- Immunization is the method of choice for controlling or eliminating the disease, use of quality vaccines
- International standards for diagnosis of rabies are approved by OIE and WHO, if applicable
- Quality of Veterinary Services
Revision of Terrestrial Code chapter

• Change in virus taxonomy: Genotype-1 Lyssavirus-> Rabies Virus
• Focus on ‘high risk animals’ for rabies transmission: Dogs, cats and wild captive carnivores
• Omission of bat lyssaviruses, but provisions for Chiroptera
• Intermediate step: Country free from dog rabies, versus rabies free country (in all animals)
• Emphasis on rabies surveillance (particularly on early detection), identification and stray dog population control programs
• Re-grouping of animal species traded that pose a lower risk to humans and spread of rabies
• More flexible timeframes for re-vaccination (broader range of vaccines available now)
Revision of Terrestrial Code chapter
Chapter 7.7.7 on Stray dog population control

- Improve health and welfare
- Reduce numbers
- Promote responsible ownership
- Creation and maintenance of a rabies free dog population
- Reduce the risk of other zoonotic diseases
- Manage other human health risks
- Prevent harm to the environment and biodiversity
- Prevent illegal trade
Revision of Terrestrial Manual chapter

• The quality standards for rabies diagnostic tests and vaccines have been updated to include the most recent evolution of scientific concepts

• The production and use of both injectable and oral vaccines has been extensively revised

• For injectable vaccines, the utilization of live animals to test the potency of batches is discouraged and alternative tests have been included

• The new Manual has created a special chapter for the necessary tests for registration of rabies vaccines, a chapter describing reduced control tests for commercial batch release
At present there are 10 Reference Laboratories – 5 of them are WHO Collaborating Centers.

OIE RL & WHO CC are working together to achieve an International harmonization of laboratory methods for diagnosing rabies and conducting the quality control of vaccines.

Laboratory twinning projects on rabies have been successfully completed in Turkey, Nigeria & China (OIE RL since May 2012), another labs in RO Korea and China were also selected as an OIE RL for rabies (May 2012).
OIE Rabies vaccine bank for dog vaccination

- EU funded HPED in Asia expanded to FMD and Rabies – now extended to Dec 2014
- To facilitate high quality vaccine procurement and deliveries, complying with international standards, at low cost, with rapid dispatch and reduced administrative delays
- Supply in 10 ml and 1 ml vials
- OIE deliveries to Asian countries up to Jan. 2014 were 2,690,400 doses of rabies vaccines for dog vaccination
Rabies Regional Vaccine Bank
Number of doses delivered – June 2014

<table>
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<tr>
<th>Date</th>
<th>Country</th>
<th>Number of doses</th>
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<tbody>
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<td>26/09/2012</td>
<td>Lao PDR</td>
<td>50,000</td>
</tr>
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<td>12/12/2012</td>
<td>Viet Nam</td>
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<td>20/02/2013</td>
<td>The Philippines</td>
<td>500,000</td>
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<tr>
<td>14 &amp; 17/06/2013</td>
<td>Lao PDR</td>
<td>120,000</td>
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<td>20 &amp; 24/06/2013</td>
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