Rabies vaccine and vaccination

The outline of a rabies contingency plan in Japan

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By a courtesy, this presentation included the literature and images of the rabies research team in NIID, data and the information from the tuberculosis and infectious disease control division of MHLW, and the other related collaborators.

What is rabies?

- Rabies virus is a member of the Rhabdoviridae family.
- Rabies is a single stranded, negative sense RNA virus which encodes 5 proteins: glycoprotein (G), nucleoprotein (N), matrix protein (M), large protein (L), phosphoprotein (P).
- The mature virus has a bullet shape, a protein coat, and a lipid envelope.

STRUCTURE OF RABIES VIRUS
Message from **Dr. Bernadette Abela**
Team Leader of the Neglected Zoonotic Diseases unit of WHO

The goal for … South East Asia is to attain elimination of human rabies transmitted by dogs by … and 2020.

**Rabies is preventable!**

More than 50,000 people, mostly in Asia and Africa, still die of rabies every year; a large proportion of whom are children. Dog bites are the primary source of human rabies. ……

It also requires strengthened **Health and Veterinary systems**. …… There is still need to improve access and availability of affordable **post-exposure rabies prophylaxis to people** who are bitten in endemic areas. ……
Rabies vaccine and vaccination

**PEP:** Post-exposure Prophylaxis
- Against human rabies

**PreEP:** Preexposure Prophylaxis
- For High risk people
- Against animal rabies for human health

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**Rabies in the World**

- Animal rabies (red)
- Human rabies

Global cases:
- **Asia:** ~31 000 (56%)
- **Africa:** ~24 000 (44%)
- **Other continents:** ~500

(WHO)
November 2006
Two human rabies was imported from the Philippines

Both of patients were late 60s and suspected of having rabies at the hospitals in Kyoto and Yokohama because of the presence of typical clinical symptoms and a history of bites by dogs in the Philippines.
PEP crisis!!

All rabies vaccine for human was consumed in two months!

Shortage ...
WHO APCRI survey

The shortage of RIG in Asia

Category III = 80-85 %

RIG treatment = 2.1 %

Vaccine preventable!!
Regional Vaccine Banks for Asia Rabies

<table>
<thead>
<tr>
<th>Date</th>
<th>Country</th>
<th>Number of doses</th>
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<tbody>
<tr>
<td>28/09/2012</td>
<td>Lao PDR</td>
<td>50,000</td>
</tr>
<tr>
<td>12/12/2012</td>
<td>Viet Nam</td>
<td>200,000</td>
</tr>
<tr>
<td>20/02/2013</td>
<td>The Philippines</td>
<td>500,000</td>
</tr>
<tr>
<td>14 &amp; 17/06/2013</td>
<td>Lao PDR</td>
<td>120,000</td>
</tr>
<tr>
<td>20 &amp; 24/06/2013</td>
<td>Sri Lanka</td>
<td>300,400</td>
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<tr>
<td>19/07/2013</td>
<td>Bangladesh</td>
<td>200,000</td>
</tr>
<tr>
<td>31/07/2013</td>
<td>Indonesia</td>
<td>200,000</td>
</tr>
<tr>
<td>05/09/2013</td>
<td>Bhutan</td>
<td>20,000</td>
</tr>
<tr>
<td>18/09/2012</td>
<td>Myanmar</td>
<td>200,000</td>
</tr>
<tr>
<td></td>
<td><strong>TOTAL DOSES DELIVERED</strong></td>
<td><strong>1,790,400</strong></td>
</tr>
</tbody>
</table>

**Scheduled deliveries for next semester (to date):**

- Cambodia: 50,000
- Afghanistan
- Nepal

Meeting of the OIE Regional Commission for Asia, the Far East and Oceania
Paris, Monday 27 May 2013

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What usage is more preventable?
### Animal Rabies

<table>
<thead>
<tr>
<th>Country</th>
<th>2001</th>
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<th>2003</th>
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<tr>
<td>Cambodia</td>
<td>()+</td>
<td>()+</td>
<td>()+</td>
<td>()+</td>
<td>()+</td>
<td>NR</td>
</tr>
<tr>
<td>Indonesia</td>
<td>65</td>
<td>257</td>
<td>172</td>
<td>578</td>
<td>399</td>
<td>36</td>
</tr>
<tr>
<td>Laos</td>
<td>65</td>
<td>55</td>
<td>37</td>
<td>()+</td>
<td>()+</td>
<td>NR</td>
</tr>
<tr>
<td>Malaysia</td>
<td>No rabies since 1999</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Myanmar</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>7</td>
<td>0</td>
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<tr>
<td>Philippines</td>
<td>()+</td>
<td>981</td>
<td>1475</td>
<td>964</td>
<td>197</td>
<td>568</td>
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<tr>
<td>Singapore</td>
<td>No rabies since 1953</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td>220</td>
<td>531</td>
<td>185</td>
<td>252</td>
<td>163</td>
<td>166</td>
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<td>Vietnam</td>
<td>14</td>
<td>18</td>
<td>5</td>
<td>5</td>
<td>15</td>
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</tr>
</tbody>
</table>

Workshop on Strengthening Cooperation and Sharing Information on Rabies among ASEAN Plus Three Countries.

Evidence based measures has been done correctly?
We have been doing ...

Laboratory network in Asia

- Epidemiological data of rabies
- Molecular analysis
- Understanding of rabies etiology

Laboratory works on Diagnostics, Geography, Ecology of host species, Genetics and Pathogenicity.
Rapid Detection of Rabies Virus by Reverse Transcription Loop-Mediated Isothermal Amplification

Bazartser Boldbaatar1,2, Satoshi Inoue1,2, Naoko Sugiyama1, Akira Noguchi1, Jun Ryan C. Orbina1, Catalino Demetria1, Mary Elizabeth Miranda1, and Akio Yamada1,2

1Department of Veterinary Science, National Institute of Infectious Diseases, Tokyo 162-8640; 2The University Graduate School of Veterinary Science, Gifu University, Gifu, Japan; and 3Department of Public Health and Environmental Science, University of the Philippines

SUMMARY: In this study, reverse transcription loop-mediated isothermal amplification (RT-LAMP) was established which can detect 10^5 copies of viral RNA corresponding to approximately 5 fg of RNA. RT-LAMP with the Phil primer set designed according to the nucleotide sequences obtained from a Kyoto patient who contracted rabies in the Philippines was able to amplify all 16 street viral sequences derived from the Philippines. The specificity of RT-LAMP products was easily confirmed by digestion with Rsal restriction enzyme. The reaction of RFLP-LAMP could be completed within 1 hr and could be conducted under isothermal conditions using a conventional water bath or heat blocks, indicating that RT-LAMP is ideal for the diagnosis of rabies in developing countries. Although further study is required to establish more universal RT-LAMP primers applicable to viruses from other regions or countries, the fast, easy, simple, sensitive and specific RT-LAMP method established here might be useful for rabies diagnosis and can facilitate studies of rabies epidemiology where rabies is enzootic, particularly in developing countries.

Phylogenetic tree of Philippine RABV glycoprotein

- Samples collected during period of 2004-2013
- All 235 samples are dog derived
- Rabies status confirmed by DFA
- RT-PCR sequencing performed on RABV glycoprotein
History of rabid animal exposure among the rabies confirmed patients

- Unknown: (6) 26%
- Dog, cat butchering: (5) 22%
- Dog bite: (12) 52%

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**Furious Rabies after an Atypical Exposure**


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**Original Article**


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※ Border between VN and China

**VN:** H130108, Human (2008)
**China:** EF555106, Quangxi (2007)

Rabid dogs as food in the slaughterhouses
Need a criteria of free zones.
✓ Preparedness against rabies in Japan

The last indigenous rabies cases in Japan

1956 Human
1957 Cat

The imported rabies cases in Japan

1970 A student infected at Nepal
2006 Two retired men exposed at the Philippines
Control and prevention of rabies in Japan

Rabies Prevention Law
MHLW, 1950

Domestic Animal Infectious Diseases Control Law
MAFF, 1951

Infectious Diseases Control Law
MHLW, 1998


Rabies prevention officer: veterinarians

- Registration of domestic dogs
- Immunization of domestic dogs, periodically
- Eradication of stray dogs
- Quarantine of dogs exported and imported
- Duty to report of rabid-dogs, by veterinarians

- handing of carcass for the examination or autopsy by the prevention officer
- surveillance, periodically and geographically
- a temporary immunization.
- ….. etc.
The schema of rabies confirmation

**National government**
- National Institute of Infectious Diseases
  - Department of veterinary science (Definite diagnosis of human/animals)
  - Department of pathology (Post-mortem diagnosis of human)
  - Department of virology I (Quality control of rabies vaccine)

**Local government**
- Public health center
- Institute for health
- Municipal animal control facility
- Institute for health

**Medical Hospital**

**Veterinary Hospital**

**Public health center**

**Institute for health**

**Municipal animal control facility**

**Institute for health**

**Med**

**Vet**

**Human health**
Keys for Strengthening Rabies Control

1. Laboratory network
2. Evaluation of diagnostics
3. Establishing free zones
4. Border control by the cooperation

Thank you for your attention!