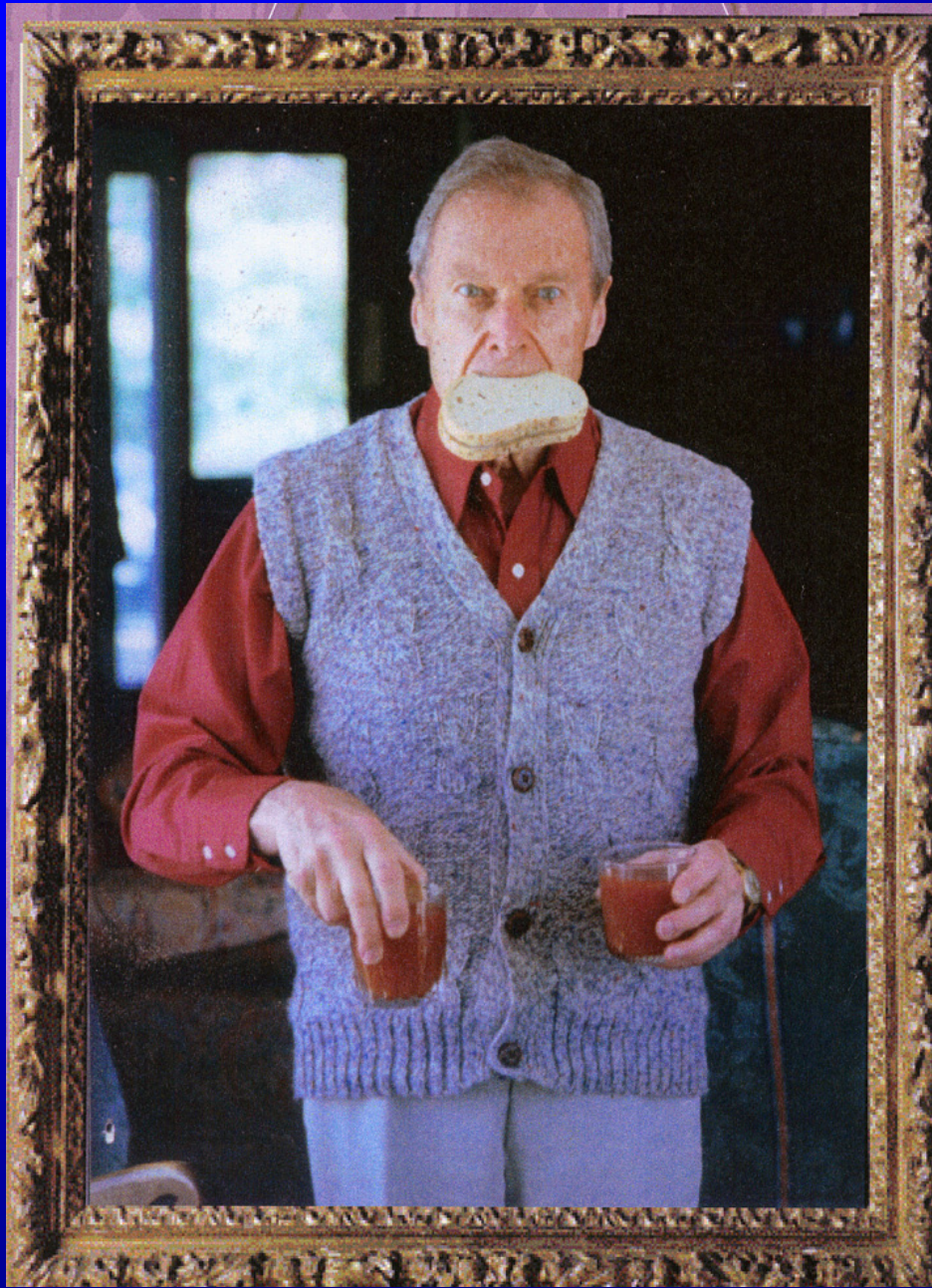


# Current Rabies vaccines, availability, and use in China

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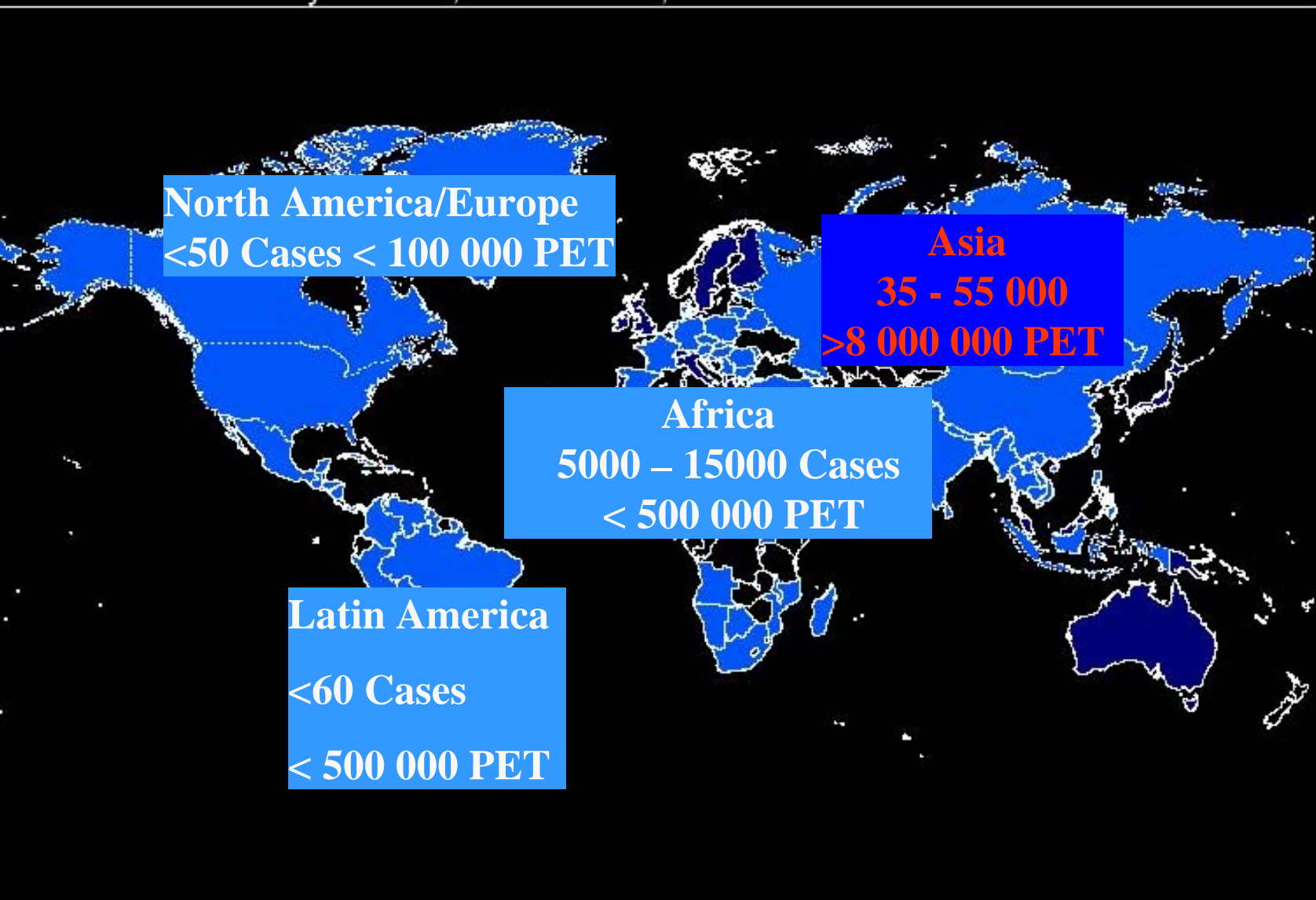


Human  
rabies is an  
**almost**  
completely  
preventable  
disease



# Occurrence of Rabies in Countries

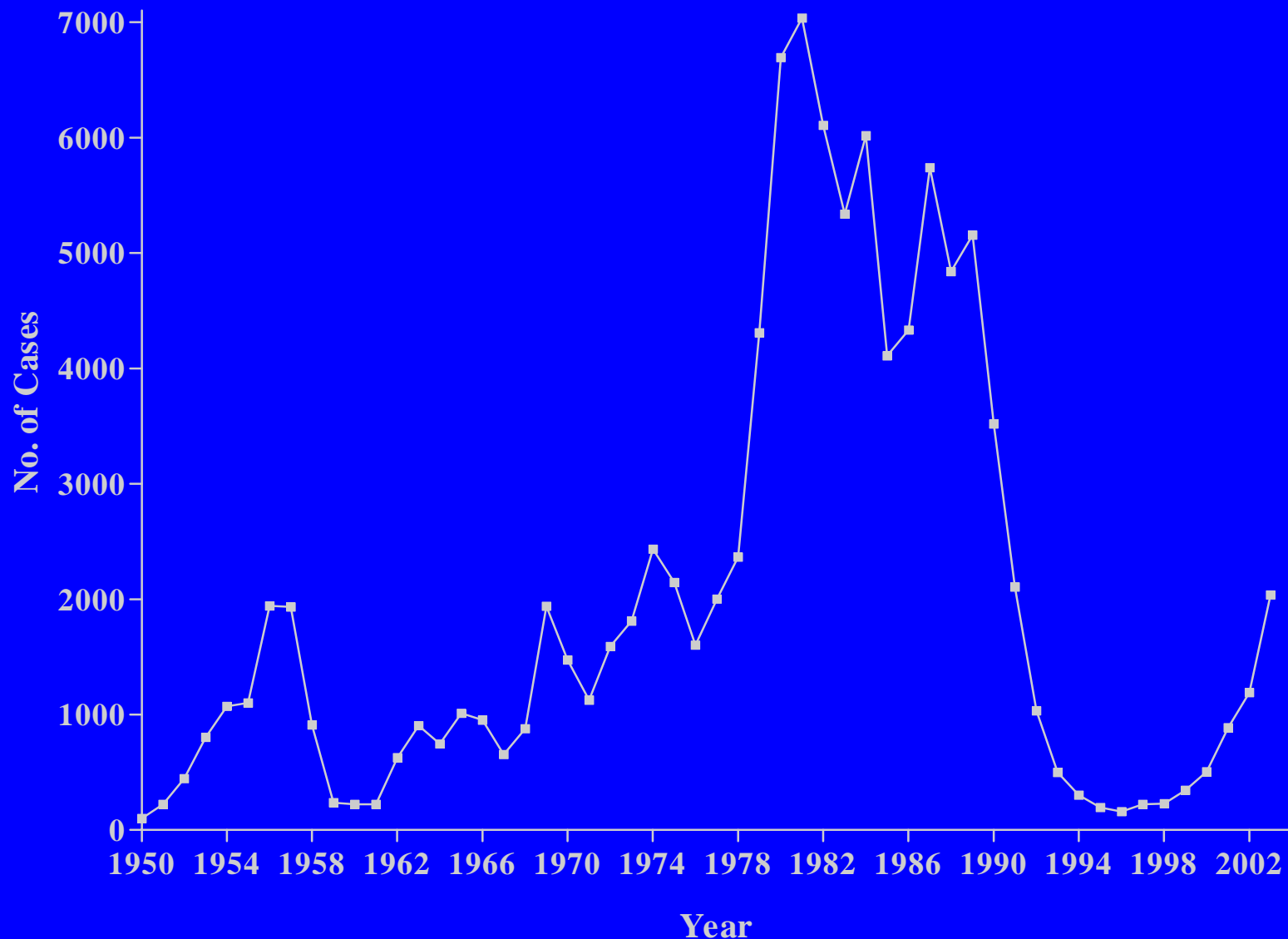
## Rabies endemicity status, worldwide, 2000



The presentation of material on the maps contained herein does not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or areas or of its authorities, or concerning the delineation of its frontiers or boundaries.

Data Source: World Survey of Rabies, Bulletin of the World Health Organization, 1996; Bulletin of the World Health Organization, 1997; Bulletin of the World Health Organization, 1998; Bulletin of the World Health Organization, 1999; Bulletin of the World Health Organization, 2000.

Map Production:  
Public Health Mapping & Rabies  
Communicable Diseases (C)  
World Health Organization  
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**The number of human rabies cases in China during the past 50 years**

**Zhang, Xiong, Xiao, Jiang, Wang, Zhang, and Fu: Emerging Infectious Disease, 2005**





**Representative human rabies cases in China**



**Representative human rabies cases in China**





Human  
Rabies  
cases in  
2004

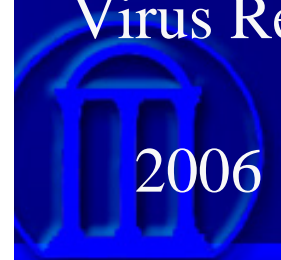
Total:  
2561

**Zhang,**

...  
**Yu**  
**Fu**

Virus Res.

2006



**To investigate if viruses from the current epidemic are similar to viruses found previously in China or around the world:**

**RV was detected from canine brains. The complete N gene sequences were obtained from 38 samples (36 from dogs and 2 from humans).**

**Compared these N sequences with those isolated around the world.**

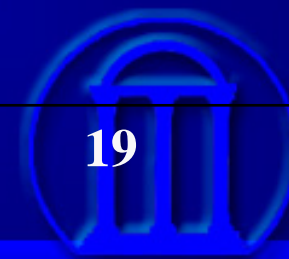
**Compared with those isolated in China during earlier epidemics (1969-1997).**

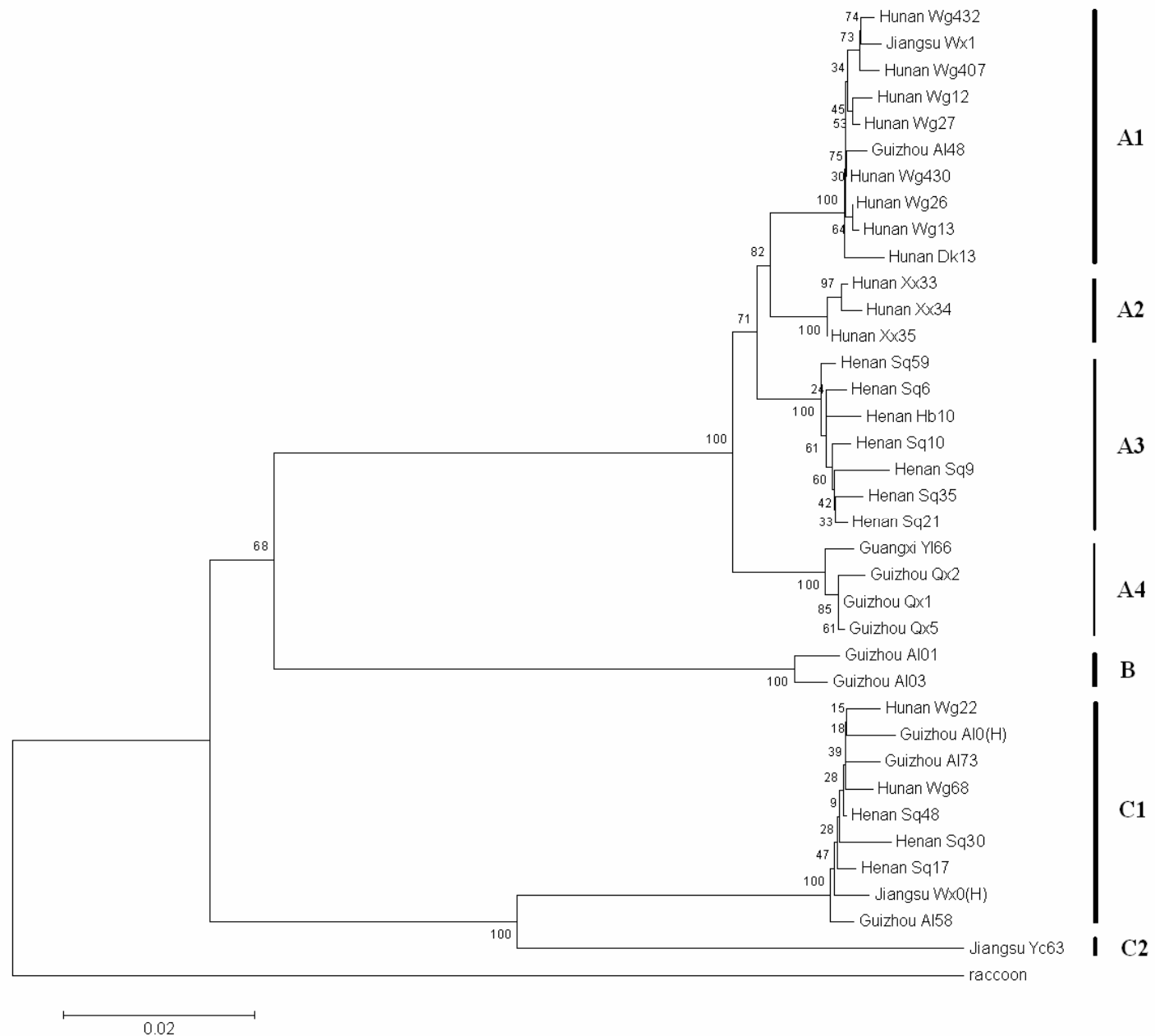
**Zhang, ...Yu, Fu: Virus Res. 2006**

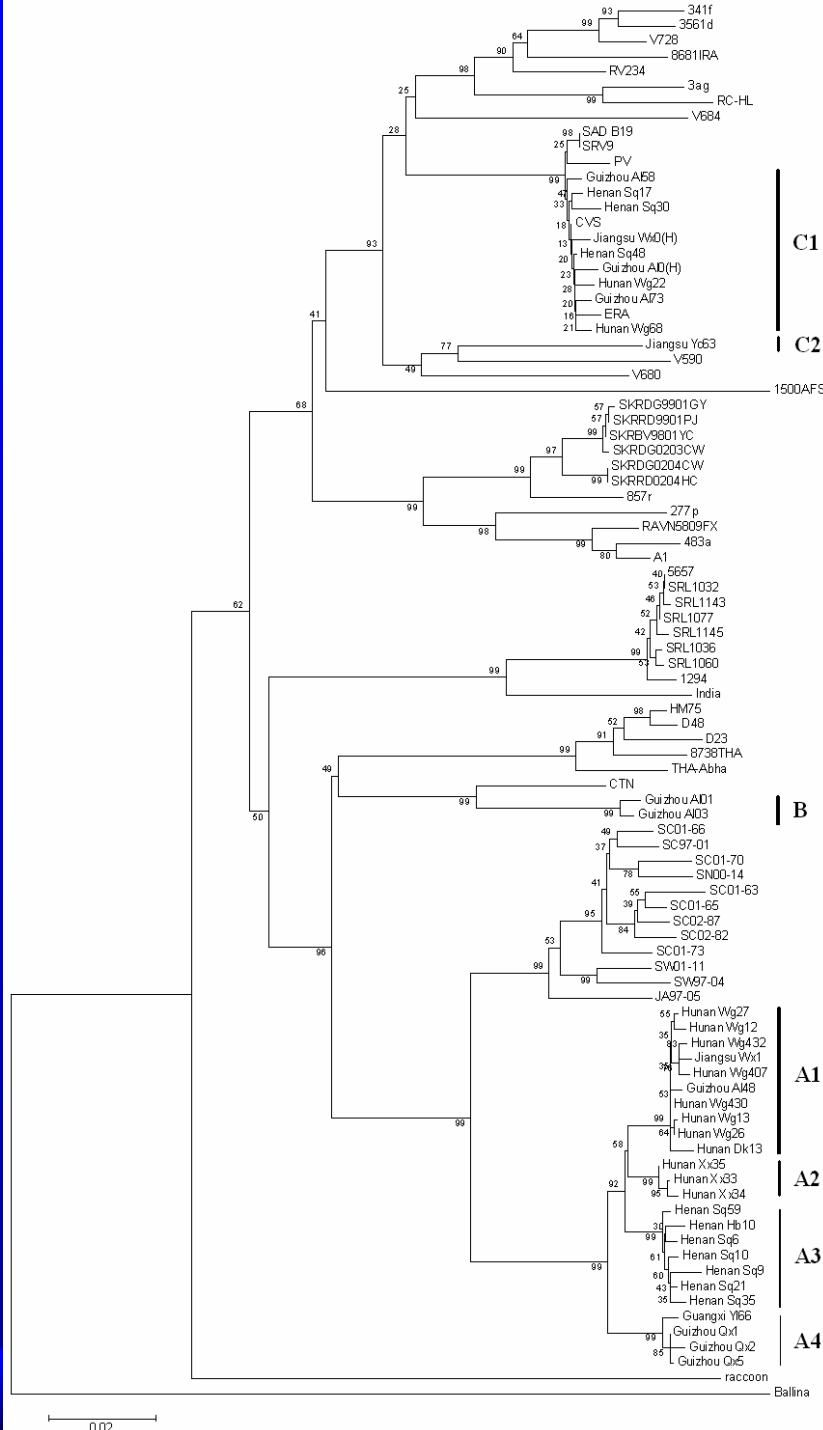




<b>Province</b>	<b>Total sample number</b>	<b>IFA positive</b>	<b>RT-PCR positive</b>	<b>Virus Isolation</b>
<b>Hunan</b>	<b>270</b>	<b>20</b>	<b>13</b>	<b>9</b>
<b>Henan</b>	<b>100</b>	<b>5</b>	<b>10</b>	<b>4</b>
<b>Guizhou</b>	<b>175</b>	<b>18</b>	<b>9</b>	<b>4</b>
<b>Guangxi</b>	<b>139</b>	<b>14</b>	<b>1</b>	<b>1</b>
<b>Jiangsu</b>	<b>154</b>	<b>19</b>	<b>3</b>	<b>1</b>
<b>Total</b>	<b>838</b>	<b>76</b>	<b>36</b>	<b>19</b>







The A lineage is similar to dog rabies virus isolated in Indonesia.

The B lineage is similar to Chinese vaccine strains CTN and dog viruses isolated in Thailand.

The C1 sub-lineage is similar to classical vaccine strain CVS and ERA.

The C2 sub-lineage is similar to dog virus isolated in Mexico.

These demonstrate that basically the viruses are dog rabies virus.





# Factors contributing to the third rabies epidemic in China

## 1, Sources of infection – dogs (93%) and cats (7%).

Increased numbers of dogs

No immunization of dogs (<3%)

## 2, Surveillance of animal rabies.

Inadequate surveillance of animal rabies

No diagnostic facilities for animal rabies

## 3, Diagnosis for humans.

Rely only on exposure history and clinical signs

No laboratory diagnosis performed

Very little supportive therapy

## 4, Post-exposure treatment

Awareness

Vaccine cost and quality

Incomplete immunization

Shortage of anti-rabies immunoglobulin

Short incubation period – no enough time for vaccine to work

## 5, Government inaction – occurs mainly in rural areas



# Rabies control, prevention, and treatment

## Control the sources of infection:

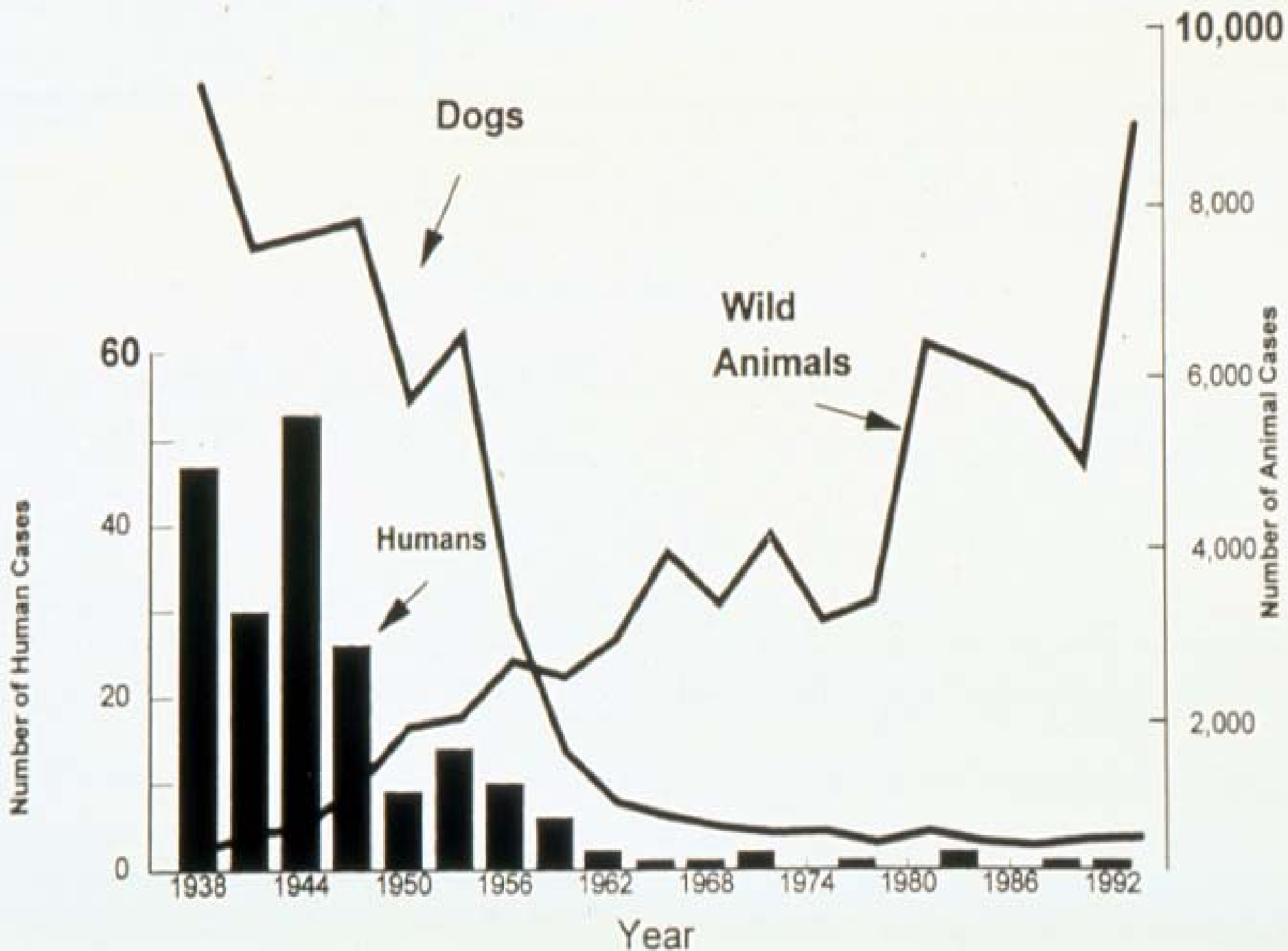
Animal control: removal of stray dogs and cats.

Vaccination of pet animals: compulsory vaccination of dogs, cats, and ferrets.

Vaccination of wildlife animals: immunization of wildlife animals in confined areas







# Major source of infection

**Dogs (97%), cats (3%), wolves (<0.01%)**

**Dogs are free-ranging animals in China. They move and wonder freely, but go home for meals.**

**Intimate interaction with humans, particularly children.**

**The numbers of dogs is estimated to be at least 100 million, in some areas, there are 1 dog per 3 people. Most of them are for family protection in suburban and rural areas. In the major cities, some dogs are considered pets.**

**Less than 3% of dogs are immunized with rabies vaccines mainly in the big cities.**

**Other reservoir hosts have not been thoroughly monitored.**









2004 12 16





2004 12 18

**No vaccination program for dogs (only in the major cities such as Beijing, Shanghai, and Guangzhou)**

**Animal rabies vaccines made domestically are live-attenuated rabies virus vaccines (ERA and LEP). It has been reported that ERA can revert to virulent phenotype. Thus usage of such type of vaccine may pose problems. 5-10 Chinese yuan/dose including injection**

**Inactivated RV vaccines are imported and thus expensive (Intvet, Merial, Ft. Dodge). About 50 Chinese yuan/dose including injection.**

**Veterinarian involvement is minimal**

**Neither surveillance nor reporting of animal rabies**





# Treatment of humans who might be exposed to rabies virus infection

WHO recommendation:

- Thorough cleaning of all wounds.
- Infiltrate all the wounds (if anatomically feasible) with Anti-Rabies immunoglobulins (RIG). Remaining half of the dose should be given i.m.
- Vaccinate on Days -0 3 7 14 and 28.  
90 (optional).



## Problems with post-exposure treatment consisting of wound cleaning, vaccination, and anti-rabies immunoglobulin

In a survey of 178 human patients, we found that

118 (66%) did not receive any wound treatment

129 (72%) did not receive any vaccine

Among the rest of the victims (49), 2, 4, 9, 15, and 19 patients received 1, 2, 3, 4, and 5 or more doses, respectively

Only 2 out of the 178 victims received anti-rabies immunoglobulin



**The fact that so many people did not receive vaccination is not simply that there are no vaccine available.**

**There are at least 16 registered rabies virus vaccines on the Chinese market including the Sanofi-Aventis (Vero) and Chiron (CEF) vaccines (Novartis?).**

**Nervous tissue vaccines are no longer made or marketed in China.**

**Currently the capacity for rabies virus vaccine production is about 12 million doses in China (compared with less than 2 million doses in the 1980s). There may need about 15 million doses.**

**Vaccines are still cost prohibitory for many, particularly in the rural areas. Domestically produced vaccines are about 100 Chinese yuan and imported are 300 to 600 Yuan. Although China has changed a lot economically in the past 25 years, there are still many poor areas in the countryside.**

# **Some patients still die after vaccination because:**

**The quality, transportation, storage, management, and usage of vaccines have a lot of problems.**

**Although all the vaccines are licensed by SFDA, but each batch was not monitored. As competition increased, quality decreased.**

**Some patients may get the first dose in the hospital, the rest doses were given to the patients to bring home for local doctors for injection. They may or may not have a refrigerator for storage.**

**Vaccines are distributed through local CDCs, normal hospitals may not have access to vaccines.**

**Very few people use anti-rabies immunoglobulin because of its shortage and cost.**

**There are two manufacturers who makes HRIG and the cost is still too high (200 yuan/dose)**

**The incubation period is short (<15 days) and there might be no enough time for vaccine to work.**



# Incubation period in relation to site of bite in Anlong, Guizhou

Incubation period	Head, neck and face		Upper limbs		Lower limbs		Mixed		Total	
	No	%	No	%	No	%	No	%	No	%
≤15	3	33.3	2	22.2	1	11.1	3	33.3	9	22.5
16-30	1	7.7	9	72.7			3	23.0	13	32.5
31-60			8				3		11	
61-90	1	20.0	2	40.0	1	20.0	1	20.0	5	12.5
≥91			1	50.0	1	50.0			2	5.0
Sub-total	5		22		3		10		40	
Percent	12.5		55.0		7.50		25.0			

Zhang, ... Fu, Virologica Sinica 2006.





# Government attention and actions

**Rabies occurs sporadically, mostly in rural areas, there is not enough attention from the central and regional governments.**

**There is no communication nor cohesive planning for rabies control between relevant departments, for example, Departments of Health and Agriculture. No body is responsible.**

**In the local level, there is very little interaction between medical doctors and veterinarians.**

**There is no standard diagnostic laboratory for rabies (animals and humans alike) in any level of government.**

**Rabies is not reportable disease in animals and there is no requirement for immunization of dogs and cats.**



## Summary

**Human rabies is still a serious public health problem in China.**

**Dogs remain the most important reservoir.**

**The rate of dog vaccination (3%) is too low to have a significant effect.**

**Quality, usage, availability of RV vaccines have problems**



## **Summary (Cont.)**

**Incubation period is short in some cases which makes post-exposure treatment difficult.**

**Post-exposure treatment is not carried out properly (no vaccination, incomplete vaccination, no antibody)**

**There is no surveillance and laboratory diagnosis for animal rabies.**

**There is no major plan for control of rabies.**





## **Governmental:**

Central Government began to pay more attention to rabies because recent publicity. There are more bulletin boards advising people to seek treatment and there are more facilities for post-exposure treatment in different levels of health departments (CDC).

There are more research activities in rabies epidemiology and control in governmental research facilities and universities. China CDC is actively involved in training local CDC personnel for rabies diagnosis and establishing surveillance .

Government has increased monitoring of vaccine quality (batch controlling).





# Major development in dog vaccination and vaccine R/D

- 1, Dog vaccination is now required in major cities.
- 2, There are more interest in developing inactivated rabies virus vaccines for pet animals. At least 5 companies are interested in developing such vaccines.
- 3, The Ministry of Science and Technology is making 5 million yuan grants for such vaccine development in the next few years.



## **People:**

More people are educated and aware of dog bites and rabies immunization. People are better off economically and can afford post-exposure treatment. More people use legal weapon to fight with companies to improve qualities of biological products.

## **Market Driven:**

There are more human vaccines available and there are more facilities to manufacture human anti-rabies immunoglobulin. The production of horse anti-rabies immunoglobulin is decreasing. Clinical trials are underway for testing human monoclonal antibodies in post-exposure settings.



# Acknowledgements



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Guizhou CDC

**Renjie Jiang**  
Director, Yancheng CDC  
Jiangsu

