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Analysis on Factors Related to Rabies Epidemic in China from 2007-2011*

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Abstract: To analyze features of the rabies epidemic in China between 2007 and 2011, identify factors influencing the epidemic and to provide a scientific basis for further control and prevention of rabies, Descriptive epidemiological methods and statistical analysis was used on data collected from the National Disease Reporting Information System between 2007 to 2011 and the National Active Surveillance System between 2007 and 2010. Our analysis shows that while the number of human rabies cases decreased year by year, the number of districts reporting cases did not show significant change. The situations in Guangdong, Guangxi, Guizhou and Hunan provinces clearly improved over the period but they remain provinces with high-incidence, and consequently influence the epidemic situation of surrounding provinces and possibly the whole country. Summer and autumn were high-incidence seasons. Farmers, students and pre-school children represent the high-risk populations, and rates of cases in farmers increased, those for students decreased, and pre-school children remained unchanged. Provinces with active surveillance programs reported a total of 2346 individual cases, of which 88.53% were associated with canines. Postexposure prophylaxis (PEP) of rabies cases was not significantly improved, whereas PEP in post-exposure population was good. In rural regions of China, canine density was reduced somewhat, and the immunization rate increased slightly. Finally we show that while the epidemic decreased 2007 to 2011 in China, cases continued to be diffused in certain regions. Lack of standardization of PEP on rabies cases was the main reason of morbidity. The high density and low immunization of dog in rural areas and the defective situation of PEP are still continuous occurrences in China and remain a cause for concern.

Key words: Rabies; Surveillance; Epidemic factor

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Rabies is a zoonoses infectious disease caused by the rabies virus and its mortality rate is nearly 100%. Each year, about 55000 people die of rabies worldwide, which is estimated to cause 1.74 million annual losses for a disability-adjusted lifetime [12]. Rabies is widely distributed throughout the world and China is one of countries that experience the most serious impact from the disease[13]. In 1980s, the epidemic situation of rabies in China reached a peak, in 1981, 7037 cases were reported but since then the number of cases decreased until 1996 when a minimum of 196 cases were recorded[20]. Since this time however, there has been a gradual reemergence of the disease, and cases once again increased on a yearly bases until 2007 when 3300 human rabies cases were recorded. Subsequently, the number of cases has slowly decreased; in 2011 there were 1918 cases, but the epidemic situation remains serious. To identify and understand the possible reasons behind the reduction of cases since 2007 and to endeavor to providing a scientific basis for further controlling the rabies epidemic in China, in this paper we carry out a retrospective epidemiological analysis of the rabies surveillance data of collected in recent years.

MATERIALS AND METHODS

Information sources

Data on epidemic situation of human rabies in China from 2007 to 2011 were collected as part of the "National Disease Reporting Information System" of the Chinese Center for Disease Control and Prevention. Individual case information, post-exposure prophylaxis (PEP) information of people who were bitten by dog or post-exposure population and animal surveillance information from 2007 to 2010 were from data collected by 15 rabies surveillance points in six provinces: Shandong, Guangxi, Anhui, Hunan, Jiangsu and Guizhou; Population statistics information from 2007 to 2010 was from the China Statistical Yearbook from 2008 to 2011.

Statistical analysis

Time distribution, spatial distribution and population distribution of the rabies epidemic were summarized to understand general characteristics of the rabies epidemic in recent years. Possible reasons for relief of the rabies epidemic situation at the national level and the major changes of the epidemic situation of specific regions were examined. In addition, a retrospective epidemiological analysis was carried out to investigate correlations of PEP and animal prophylaxis with the rabies epidemic data recorded at the active surveillance points. SAS9.0 was used for statistical analysis, and the $\chi 2$ test and T test were used as appropriate to identify significant changes in populations; Excel 2007 was also used for some statistical tasks and graphs; MapInfo7.0 was used for generation of maps.

RESULTS

Summary of Rabies Epidemic in China

For countrywide reported human rabies cases from 2007 to 2011, there were 3300, 2466, 2213, 2048 and 1918 cases, respectively. Annual reduction rate of reported cases from 2007 to 2011 were respectively 25.27%, 10.26%, 7.46% and 6.35%, and total number of disease cases reduced year by year. Over this five year period, there were a total of 11714 deaths, with a mortality rate of 98.07%, with the possible reason of case reporting not in time.

Time distribution, spatial distribution and population

distribution of rabies cases from 2007 to 2011

Time distribution**:** monthly cases for each year are shown in Fig.1. Cases occurred throughout the whole year; the percentages of spring, summer, autumn and winter cases for the whole period were 21.17%, 30.00%, 29.01% and 19.82% respectively. Notably more cases occurred in the spring and summer months (41.11%); in contrast, there were fewest cases in February and March.

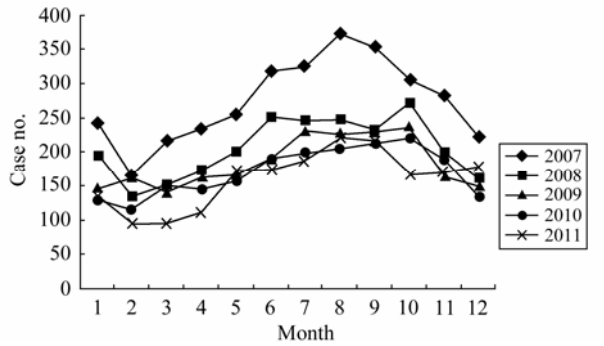

Fig. 1. Human rabies cases number by month in China, 2007-2011.

Regional distribution and characteristics of the epidemic: Nationally overall, the distribution of cases show no obvious change in the time period considered. In 2007, there were 984 counties and districts reporting an epidemic of rabies. In 2008, 2009, 2010 and 2011, the number of rabies-epidemic counties or districts were 858, 892, 817 and 862 respectively. However, the variation in number of cases for each county and district showed that the epidemic was consistently diffused between counties and districts in the same province and ultimately from high-incidence provinces to low-incidence provinces (Fig. 2). In some low-incidence provinces, the incidence of human rabies rose significantly. For example, the number of counties and districts reporting rabies cases in Shanxi increased from 2 in 2007 to 48 in 2011, and the number of counties and regions reporting rabies cases in Shaanxi increased from 1 in 2007 to 19 in 2011.

From 2007 to 2011, the five provinces with the highest number of rabies cases nationwide were Guangxi (1778 cases), Guangdong (1485 cases), Guizhou (1427 cases), Hunan (1075 cases) and Sichuan (803 cases), and the total cases in these five provinces accounted for 54.99% of all reported cases. In this five year period, with the exception of three provinces (Tibet, Qinghai and Heilongjiang) there were reported cases in every other province. For some

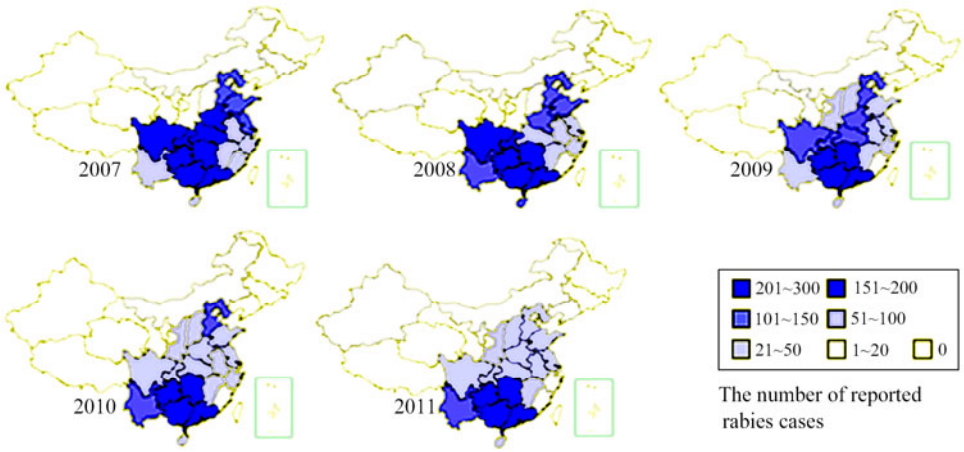

Fig. 2. The distribution of human rabies in China, 2007-2011.

of these provinces, there were only isolated cases,indicating that the virus circulation has not yet been established in these regions. These include one case in Gansu in 2009; 1 and 2 cases in Xinjiang in 2008 and 2011 respectively; one case in Jilin in 2007; 2 cases in Liaoning in 2011; and 2 cases in Ningxia in 2011. For other 23 provinces and municipalities the changes are more marked, these are summarized in Fig. 3. The epidemic situation in rabies in Beijing, Tianjin, Shanghai and Inner Mongolia appears to be sporadic, but the number of cases in these regions was significantly less than other provinces or municipalities. For other provinces where rabies epidemic appeared to be well established at the beginning of the study (more than 100 cases recorded in 2007), the number of annual cases gradually decreased over the study period (Hebei, Jiangsu, Jiangxi, Shangdong, Henan, Hunan, Guangxi, Chongqing, Sichuan and Guizhou) although the magnitude of the decrease varied. The most notable reduction occurred in Sichuan with a 79.84% decrease in cases over the five year period. However, for Yunnan, Jiangsu, Shaanxi and Shanxi provinces, the number of cases appears to have increased over this period, particularly for Shaanxi and Shanxi, indicating the virus circulation began to establish itself in these regions over this period. In Shaanxi, before 2009, cases were sporadic but increased to 26 in 2009, 25 of which occurred in Hanzhong city; similarly Weinan city reported 5 cases in 2010 and 29 cases in 2011. For Shanxi province the number of cases rose continuously from 3 cases in 2007 to 88 cases in 2011. For Yunnan and Jiangsu provinces the pattern was less pronounced, but the number of cases has been gradually increasing.

Distribution of Occupations: Most cases from 2007 to 2011 were farmers, students and pre-school children. These three kinds of populations respectively accounted for 68.27% of cases (annual percentage over 5 years were respectively 66.27%, 68.13%, 69.32%, 69.14% and 69.76%), 12.47%(annual percentages 14.82%, 13.26%, 10.57%, 11.67% and 10.38%) and 6.32% (annual percentages 6.27%, 5.96%, 7.37%, 6.20% and 6.00%). Overall, these three populations together accounted for 87.10% of all cases (annual percentages 87.36%, 87.35%, 87.26%, 7.01%, and 86.13%). The percentage of farmer cases increased slowly, while the number of student cases reduced slowly, and the number of pre-school children cases was relatively unchanged over this period.

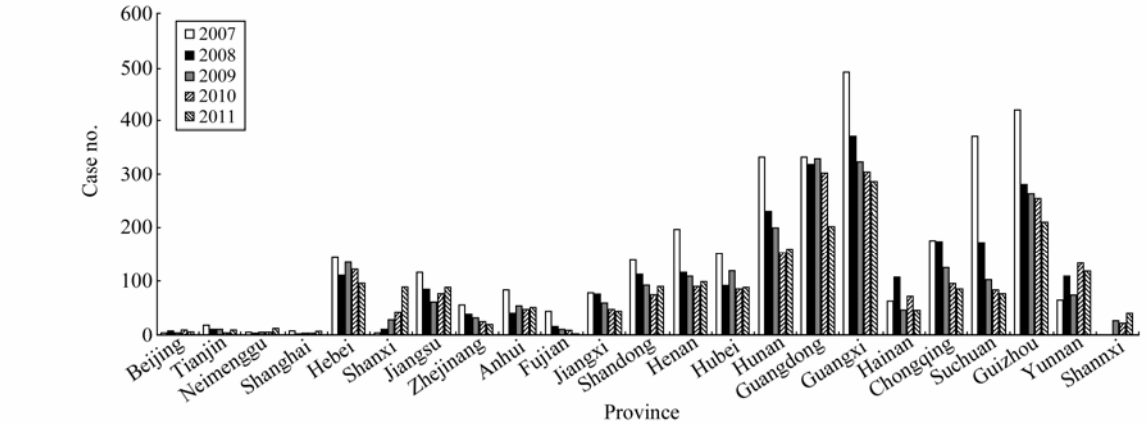

Fig. 3. Human rabies cases reported in 23 provinces in China, 2007-2011.

Gender and age distributions: The ratio of male cases to female cases was 2.32:1. Cases were primarily concentrated to ages 5-15 years and 35-70 years (Fig. 4 and 5). With the exception of the 45-50 year old male group which saw a gradual increase, the 45-50, 80-85,85- year old female groups, along with the 60-65,70-75, 80-85, 85- year old male group, remained relatively unstable, and Showed an overall increasing tendency. The number of cases in other age groups gradually decreased from 2007 to 2011. The largest decrease occurred 5-15 years old and 50-55 year old groups for both male and female, which had all previously been high-incidence groups.

PEP situations of rabies death cases from 2007 to 2010

The active surveillance program reported 2346 rabies deaths from 2007 to 2010. Diagnosis of rabies cases complied with the national Diagnostic Criteria for Rabies (WS281-2008) [9], and a summary of PEP of all investigated human rabies cases is shown in Table 1. Over 50% cases were category III exposure, the wound treatment rates of received in medical institutions were low, and there was no difference between the various years ($\chi 2$ test $p>0.05$). For other prophylaxis procedures, there were significant differences between various years ($\chi 2$ test $p<0.05$); generally, the situations in 2007 and 2009 were better than those in 2008 and 2010. In 4 years, only 66 cases (2.81%) from 2346 rabies deaths completed the PEP rabies deaths, no timely and standard PEP was carried out.

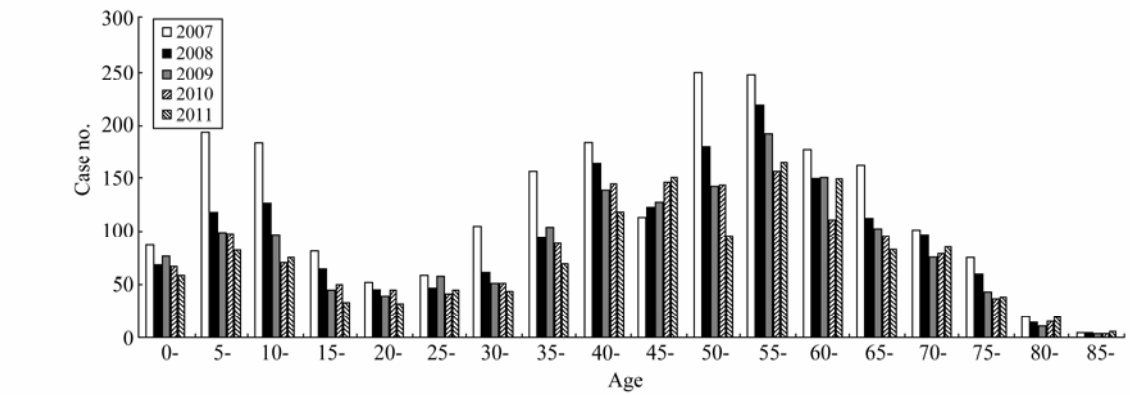

Fig. 4. Age distribution of male human rabies cases of in China, 2007-2011

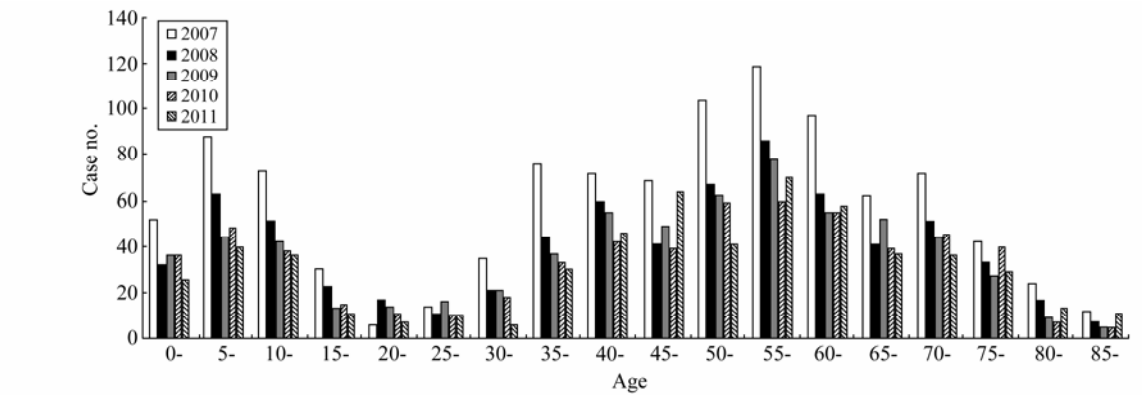

Fig. 5. Age distribution of female human rabies cases of in China, 2007-2011

Table 1. Post-exposure prophylaxis of human rabies cases in China, 2007-2010

Year	Case no.	Wound treatment (%)			Vaccination coverage (%)	Proportion of the category Ⅲ exposure(%)	Proportion using RIG or anti-serum (%)
		Self administered	Medical institutions	Total			
2007	678	20.80	13.00	33.80	12.54	49.14	5.92
2008	489	18.81	10.02	28.83	11.86	59.71	4.45
2009	539	28.08	12.57	40.65	15.20	50.14	6.29
2010	640	25.30	9.64	34.94	9.12	65.94	1.89
Total	2346	23.29	11.36	34.65	12.08	56.97	4.60
$\chi 2$		$\chi 2$=16.05	$\chi 2$=5.25	$\chi 2$=16.08	$\chi 2$=10.64	$\chi 2$=49.08	$\chi 2$=17.02
p		p<0.01	p>0.05	p<0.01	p<0.05	p<0.01	p<0.01

Note：RIG =Rabies immunoglobulin.

Incubation period of 72.21% cases was within half a year, and distributions of specific incubation time are shown in Table 2. After the incubation time, most cases presented typical rabies symptoms, such as anxiety, hydrophobia, anemophobia, salivation and dysphasia.

Situations of PEP in people who were bitten by dog from 2007 to 2010

The general situation of PEP of people after bitten by dog at surveillance points from 2007 to 2010 is shown in Table 3; the exposure was mainly category II or III. The rate of wounds treatment in medical institution of Guangxi was lowest and for whole-course vaccination rate of Shandong was lowest. Generally, injection rate of rabies immunoglobulin (RIG) or rabies anti-serum was not high, but on the whole, the rate of people who received PEP, vaccination and injection of RIG or rabies anti-serum for category III exposure were significantly higher than those for fatal rabies cases, suggesting that timely and standardization of PEP could greatly reduce incidence risk.

Surveillance of rabies host animals from 2007 to 2010

From 2007 to 2010, 88.53% of identified cases were exposure to canines, followed by cats (5.20%); the majority of incidents were bites. Other reported cases included rats, horses, squirrels, pigs, bats, monkeys and raccoons. Canine density and canine immunization rate were estimated in two ways. In the first method information was retrieved from local farming and public security departments (Ecological investigation); in the second method information was collected by performing household surveys at a local level, i.e. one village or town was considered a unit(Household investigation) [5]. From 2007 to 2010, the goal was to collect 60 estimated (15 surveillance points over 4 years), of which 51 were completed; of these, 33 estimates used the public records and 18 were based on household surveys. The results are shown in table 4. It was found that estimates of canine density obtained by the ecological investigation method were consistently less than that obtained by the household surveys, whereas estimates of canine immunization rate was consistently greater when estimated from public records. Due to the limited investigation range, an estimate of these quantities at a national level was not possible. Several years of continuous survey showed that canine density and immunization rate in our investigation were in variable trends: from 2008 to 2010, canine density obtained by

Table 2. Estimated incubation period of rabies cases reported in China, 2007-2010

Incubation period	2007	2008	2009	2010	Total (case no.)	Proportion (%)	Accumulative Proportion(%)
⩽15 days	45	31	37	38	151	6.44	6.44
15~30 days	107	62	88	69	326	13.90	20.34
31~60 days	159	118	103	143	523	22.29	42.63
61~180 days	200	146	178	170	694	29.58	72.21
0.5 year~1 year	65	44	46	52	207	8.82	81.03
>1 year	102	88	87	168	445	18.97	100

Table 3. Post-exposure prophylaxis for people bitten by dog in clinics of national surveillance sites in China, 2007-2010

Province	Post-exposure population	[c]Sex ratio	Proportion of exposure category (%)			Treatment in medical institution (%)	Vaccination (%)	Wholecourse vaccination rate(%)	[a]Injection RIG or anti-serum (%)	[b]Injection RIG or anti-serum/no of category Ⅲ exposure(%)
			Ⅰ	Ⅱ	Ⅲ					
Hunan	273970	1.57	24.78	45.73	29.49	92.97	99.84	99.50	21.00	71.23
Guizhou	26392	1.38	3.73	41.44	54.83	84.30	99.69	87.45	12.15	22.15
Guangxi	96382	1.25	7.37	71.68	20.89	58.00	99.90	99.81	9.95	47.66
Anhui	43894	1.42	4.07	47.19	48.67	78.84	99.66	98.86	17.72	36.41
Jiangsu	160432	1.18	27.9	40.71	31.37	82.84	94.08	93.41	7.69	24.50
Shandong	338348	-	0.05	55.04	44.94	86.17	94.30	58.11	3.63	8.08
Total	939418	1.38	13.05	50.84	36.11	84.43	96.42	82.13	10.94	30.30

Note：[a]The rate of RIG or anti-serum=the number of people who have RIG or anti-serum for their PEP/ the number of people who come to PEP clinics; [b]The rate of injection RIG or anti-serum=the number people of who have injection RIG or anti-serum /the number people who had category III exposure. [c]Sex ratio male:female

Table 4. The surveillance of host animal in monitor point in China, 2007-2010(median)

Year	2007		2008		2009		2010	
Method of (investigation)	Ecological	Visiting	Ecological	Visiting	Ecological	Visiting	Ecological	Visiting
Density of dog (1 dog/100persons)	4.08	10.23	3.80	21.78	5.66	16.32	6.22	12.25
Vaccination coverage in dogs (%)	43.00	9.58	65.44	20.39	79.51	18.03	44.60	32.93

Note: Cities of Fuyang, Mengcheng and Lujiang in Anhui province and Yulin in Guangxi province used household surveys of rural residents in 2007; Linquan, Yingshang, Mengcheng and Lujiang in Anhui province and Sheyang in Jiangsu province used household surveys of rural residents in 2008 and 2009; Mengcheng, Fuyang, and Lujiang in Anhui province and Yancheng in Jiangsu province and Dushan, Yixing in Guizhou province used household surveys of rural residents in 2010. All other surveillance data was obtained using the public records.

the household investigation method reduced year by year, and canine immunization rate was in an overall increasing trend.

Social factors

Economic situation and medical treatment: Number of rabies cases and distribution were significantly associated with social factors. According to an estimation by the WHO, over 99% of human rabies cases occur in developing countries, and rural areas were more affected than cities. Similarly, overall reduction of epidemic situations in China in recent years was closely related to social economic

improvement. From 2007 to 2010, average per capita annual net incomes of towns and rural residents respectively increased by 2041.60 Yuan and 592.87 Yuan ($t=9.58$, $p<0.01$) and average per capita annual medical care expenditures of towns and rural residents respectively increased by 57.56 Yuan and 38.23 Yuan ($t=11.50$, $p<0.01$). It was found that the bearing capacity for disease burden of towns was far higher than that of rural areas and it requires further investigation to determine whether this is directly associated with cost of rabies PEP treatment in rural populations. Annual governmental health expenditure and the accounted ratio increased year by year. Also, rural health facilities were constantly enhanced with a consequent improvement in health care. These findings are summarized in Table 5.

High-incidence rabies regions such as Guangdong and Hunan have included rabies PEP expenditures into the new rural cooperative medical reimbursement coverage, including vaccine cost and the whole PEP treatment. This has greatly improved the PEP situations of peasants and thus increased treatment rate of PEP. The state is trying to further expand the scope of medical insurance for rabies PEP treatment to cover the entire rabies epidemic region.

Development of rabies vaccine for human use in China: The quality of rabies vaccine for human use has been increasing on a yearly basis. In 2001, it was forbidden to use concentrated rabies vaccines in China, but it was permitted to use refined purified vaccine [8]. From August 1, 2005, a trial rabies vaccine was approved for human use with the goal of supervising and improving rabies vaccine quality in China. This is reflected in a comparison of relative efficacy of the treatments available in 2005 and 2010. The protein content in the 2010 vaccine was reduced from 120 μg/dose to 80 μg/dose, DNA residual content was no more than 100 pg/dose, bacterial endotoxin was reduced to 1/4 of the 2005 standard content and preservative thiomersal content reduced from 100 μg/mL to 50 μg/mL [6]. All of these improvements have helped to reduce side effects of vaccination and increase patient tolerance.

DISCUSSION

From 1997 to 2007, the rabies epidemic in China followed a rapidly-increasing trend, but since 2007, the number of cases has decreased slightly. Although the epidemic remains serious in rural areas of south China, in recent years, cases of in the majority of

Table 5. Economic and health care changes in China, 2007-2010

	Annual net incomes (yuan/person)		Annual medical care expenditures (yuan/person)		Govemmental health expenditure		Health facilities in rural (no.)			
Year	Urban	Rural	Urban	Rural	Health expenditure (yuan)	Proportion of expenditure (%)	Clinic in rural (no.)	Coverage of the medical care	number of technical people per One thousand	*People join medical care(billion)
2007	14908.6	4140.4	699.1	209.6	2581.6	22.3	613855	2451	2.7	0.73
2008	17067.8	4760.6	786.2	245.3	3593.9	24.7	613143	2729	2.8	0.82
2009	18858.1	5153.2	856.4	287.5	4816.3	27.5	632770	2716	2.9	0.83
2010	21033.4	5919	871.8	324.3			648424	2678	3.0	0.84

*No. of people join in the new rural cooperative medical care(billion).

high-incidence provinces have been greatly reduced. In this study we have examined surveillance data collected between 2007 and 2011 to identify factors that have contributed to the increase and decrease of cases in specific regions of the country.

Our results indicate that the number of cases peak each year between July and October. Considering the latency of most cases is in the six months, this would suggest that the primary exposure time occurred in spring and summer seasons. In these two seasons, animals and people have more outdoor activities and consequently have more contact opportunities. If this is the case, then it is important for people to remain aware of heightened risk to control contacts with animals in these high-incidence seasons. This is further supported by our finding that the male morbidity rate is far higher than the female morbidity rate, which is associated with cultural factors in rural areas that lead to males having more outdoor activities and subsequently greater contact with host animals. Our investigation of the distribution of cases by occupation and ages, revealed three high-incidence populations: farmers, students and pre-school children. Within these groups, the percentage of peasant cases increased somewhat over the surveillance period in contrast to the number of cases in students. The decrease in cases amongst students may well be a consequence of efforts to increase awareness of risk from rabies and may reflect both enhanced attention by parents and greater availability and accessibility of education resources for students.

Dogs remain the main host animal of rabies in China, followed by cat; in addition, there are significant portion of cases that can be associated with other wild host animals. However, dogs are not considered to be economically important animals in China, so dog rabies surveillance hasn't been carried out and current surveillance data may not truly reflect the current situation; a more comprehensive surveillance program may provide a more accurate picture. According to current statistics, it is estimated that currently there are ~130,000,000 canines in China, and more than half of these are in rural regions [2]. Peasants breed canines mainly for protecting the house, and the majority of these reproduce randomly in a scattered manner, which facilitates the spread of rabies and greatly increases chance of exposure for peasants; it is not surprisingly therefore that rural cases are always the most common. However, canine immunization rate have increased somewhat in recent years due to efforts of government to introduce canine immunization programs. Also, various places have carried out the culling of stray canines. Following the introduction of such an immunization program Guangxi carried out random sampling inspections of homebred canines and found that the rabies positive rate was somewhat reduced[23]. Zhang Fei *et al.*[18] investigated canine immunization coverage rate in partial regions and found that canine immunization rates in China have increased year by year [22] and the results of household surveys estimates that from 2008 canine density reduced, while canine immunization rate increased, both of these appear to be important factors for achieving the observed reduction of rabies cases in China. However, current canine immunization rates in China remain far below the 70%-80% of immunization rate considered necessary for establishing an inter-canine immune barrier according to WHO recommendations[13]. Therefore, China has still needs to strengthen communications and

cooperation between various departments, increase investment and promote the attention of government at all levels to the importance of canine immununization programs.

In recent years two publications titled “Rabies PEP Guidelines (2007)” and “Rabies PEP Work Specification (2009)” were issued according to the definition of the WHO standard for enhancing and specifying the rabies PEP, and various regions also embarked on specific training for outpatient treatment to provide better rabies PEP. However, despite these efforts, prophylaxis of individual cases was not significantly improved. The reasons behind this may because changes in the epidemic in different provinces of China were not the same, and influencing factors were consequently different, therefore it was impossible to find a general set of guidelines from the data. Nevertheless, PEP of postexposure population appeared to be quite effective and wound treatment after postexposure, vaccine injection and application RIG or anti-serum were far higher than those received in fatal cases. Although 56.97% fatal cases from 2007 to 2010 were degree III exposure, only 11.36% of the patients went to medical institutions to get PEP, suggesting that untimely PEP in medical institutions was an important reason for the ultimate onset of full blown rabies symptoms. Out of all the surveillance points in this study, the whole-course vaccination rate, and application rate of RIG or anti-serum of Linyi city in Shandong province were notably lower throughout the study, which was possibly a reflection of poor economic conditions and lack of awareness of the risks associated with rabies.

The quality of rabies vaccines manufactured in China has been improving and the associated side effects have also been greatly reduced. Recent reports on the effectiveness of domestic vaccines [3,15,16] showed that they exhibited good immunogenicity, intradermal and intramuscular injections had a low incidence of adverse reactions, and side effects were mild. In 2009 a quality control issue resulted in the release of a substandard of a rabies vaccine for human use in Foshan city. While the Health Ministry dealt with the event rapidly and effectively, giving PEP for all the exposed person in the affected area, this highlighted the need for regulation and supervision of vaccine production at the national level. Therefore, the state is creating supervision methods to integrate risk management technology into the whole process of medicine quality management to better ensure rabies vaccine quality.

China is a large country and the efficient distribution and application of rabies vaccines for human use remains a challenge. Every year, the number of people receiving rabies vaccination reaches about 10~12 million, and direct expenditures on PEP is estimated to be about 2~ 3 billion Yuan[8]. In particular, immunoglobulin costs represent a significant portion of the annual budget (on average treatment for each person costs ~1000 Yuan) [7]. An additional problem is that a percentage of the populations still believe animals do not carry rabies, do not present a risk and, given the cost of rabies PEP, fail to seek treatment after being bitten or scratched by an animal.

Compared with rabies vaccines for human use, an additional and important consideration for controlling rabies in China (especially rural regions with serious rabies outbreaks) is to accelerate the research and development of efficient, safe and convenient rabies

vaccines for animal use. Many researchers have investigated the phenomenon of domesticated animals with rabies virus positive in southern region of China [1,20,21] and have determined this is a major reason why rabies in southern regions remains a serious problem. Thus, it would seems feasible to block the spread of the rabies virus from host animals by promote adaption of human rabies vaccines for use in animals. Successful foreign efforts at controlling human rabies cases showed that in order to control rabies it was necessary control the spread of rabies between host animals [10]. China has already achieved a preliminary success in the development of novel animal rabies vaccines [11,17], and it is expected to apply these results to a larger scale of canine study in the near future.

Although China has implemented some effective measures for controlling rabies in many ways, many problems still remain. It can be seen from the regional map of epidemic distributions that rabies in China has continued to diffuse. Provinces and municipalities that were previously without rabies have begun to record small numbers of incidences which are becoming progressively severe year by year. A number of molecular epidemiological studies have demonstrated the diffusion occurs from high-incidence to low-incidence regions. Xiong Chenglong *et al.*[14] showed that several strains of viruses in Henan were evolutionarily very close to isolates from Guizhou and Hunan and Meng Shengli *et al.*[4] showed that multiple isolated strains in Yunnan and Guangxi had close homology, and also found that strains in Mongolia raccoons and the isolated strains in adjacent Jilin province had 100% nuclear protein gene homology in the nucleotide sequence. In addition, epidemiological analysis by Zhang Hailin *et al*.[19] showed that rabies virus strains isolated from human in Baoshan city in Yunnan province were from overseas. All of these findings highlight the need to strengthen canine management and strengthen interprovincial quarantine work and animal trade with neighboring countries. In addition, although the economic level and health care investment of in China has increased year by year, the health care system still needs to be adjusted to increase reimbursement of rabies PEP. For rural regions in particular, increasing subsidies for rabies medication would significantly increase the rate of rabies PEP and further reduce the number of cases of human rabies.

In summary, enhancing canine immunization rate and rabies PEP of human cases is critical for controlling the current rabies epidemic in China. Since 2007, the situation has been improved somewhat, but it is still necessary to further implement rabies control measures via targeted prevention according to specific conditions in each region. Additionally, communication between different departments and interdisciplinary experts needs to be improved, investment increased and a public prevention program to implement the comprehensive measures of “Management, immune, elimination and awareness” is needed for timely elimination of human rabies in China.

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