Rabies trend in China (1990-2007) and post-exposure prophylaxis in the Guangdong province

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Abstract

Background
Rabies is a major public-health problem in developing countries like China. Although the recent re-emergence of human rabies in China was noticed in several epidemiological studies, the reasons behind this phenomenon paralleling the findings of the previous reports were largely not attended. The purposes of this study were thus first to characterize the current trends of human rabies in China from 1990 to 2007, and then to define better recommendations for improving the post-exposure prophylaxis (PEP) schedules delivered to rabies patients.

Methods
The most updated epidemiological data for 22527 human rabies cases from January 1990 to July 2007, retrieved from the surveillance database of reportable diseases managed by the Ministry of Health of China, were analysed. To investigate the efficiency for the post-exposure treatment of rabies, 244 rabies patients with their detailed anti-rabies treatment of injuries or related incidents, were ascertained in Guangdong provincial jurisdiction. The risk factors predisposed to or regimens given to 80 patients who received any type of PEP were analysed to identify the reasons for the PEP failures.

Results
The results from analysis of the large number of human rabies cases showed that rabies in China was largely under control during the period 1990-1996. However, the number of reported rabies cases jumped since 2001 till a new peak (with incidence rate of 0.20 per 100000) reached in 2004, and stayed there afterwards. Then, we analysed the post-exposure prophylaxis (PEP) in 244 rabies cases collected in the
Guangdong province in 2003 and 2004, and found that 67.2% of the patients did not seek medical services or did not receive any PEP. Further analysis of PEP for the 80 rabies patients who received any type of PEP indicated that almost all the patients did not receive proper or timely treatment on the wounds or post-exposure vaccination or rabies immunoglobulins.

**Conclusions**
While the issue of under-reporting of rabies in previous years may well be a factor in the apparent upwards trend of human rabies in recent years, the analysis of PEP in the Guangdong province could provide evidence to suggest that the failure to receive PEP was a major cause of the number of human cases in China. Thus, the data underline the need for greatly improved availability and timely application of high quality anti-rabies biologicals, both vaccine and immunoglobulin, in the treatment of human bite victims. Control of dog rabies through pet vaccination schemes may also play a huge role in reducing the rate of human exposure. Changes in the current situation will also require education of the public, health care staff and veterinarians.

**Background**
Rabies is a viral disease that may affects the central nervous system of all species, but circulates in mammals only [1]. Rabies virus is mainly passed from animal to animal or animal to human through bites or scratches. And in addition the virus can also be transmitted by contamination of wounds. Under very exceptional circumstances, the virus can cross mucous membranes when the patient inhales aerosol [2, 3]. Rabies epizootics may be divided into two interrelated cycles, urban and sylvatic. The red fox (*Vulpes vulpes*) is one of major vectors of the disease and its reservoirs for sylvatic rabies in Eurasia and in parts of America, but it is not the most frequent risk for transmitting rabies virus directly to humans [3, 4]. The more serious rabies risk to
human is imposed by urban rabies. The domestic dog plays a principal role as a reservoir and transmitter of urban rabies to humans in China [5]. Humans are also at risk from affected domestic animals or pets such as cattle and cats at large, or wild animal such as raccoon dog in Eurasia and different terrestrial or flying mammals in the New world [4, 6, 7]. Moreover, direct human-to-human transmission has been observed [8]. There is no effective treatment after onset of the associated clinical symptoms. Therefore, the currently recommended intervention strategy is to remove and neutralize the infectious virus before it enters the nervous system [2].

According to the official World Health Organization (WHO) data [9-11], more than 2.5 billion people are at risk in over 100 countries reporting the disease. Rabies mortality ranks the tenth in all infectious diseases worldwide. There are still about 50000 to 60000 human deaths annually although effective vaccines for post-exposure treatment are available [12]. Developing countries account for almost all the reported human deaths, and most affected are the tropical countries or regions in Africa, Asia, South America and Oceania. During the period 1993–2002, the countries of the Americas reported a decrease of 82% in the number of human cases, with cases plummeting from 216 in 1993 (mortality rate: 0.03 per 100000 inhabitants) to 39 in 2002 (mortality rate: <0.01 per 100000 inhabitants) [13]. Rabies is considered a source of economic loss, above all, hampers the movement of animals between different countries or regions, which has serious implications for the “open market” since some countries are currently rabies free and wish to maintain their disease-free status [3].

Rabies is a major public-health problem in most of the parts of the developing world [9, 14-16]. Prophylactic measures taken in the past, like destroying foxes and reducing dog population, did not prevent the spread of the rabies, although recently
developed genetically modified rabies virus vaccines provide an effective way for prevention of rabies virus infection in dogs, foxes and raccoons [17-19]. During the recent years, most of the research on the control of rabies has concentrated on the development of post-exposure prophylaxis (PEP) of rabies [3]. The use of human rabies immunoglobulins (HRIG) and of equine rabies immunoglobulin (ERIG) has saved the lives of countless patients who would have died if treated with vaccine alone. However, both products are often in short supply worldwide and virtually unaffordable in developing countries [20]. Therefore, the high demand for PEP in Africa and Asia exerts a substantial economic burden, not only as a result of the high costs of human vaccine and RIG products, but also because of considerable indirect (patient) costs associated with travel and income loss for PEP [21]. Additional economic losses relate to livestock deaths, which, although poorly quantified, may be significant, with an estimated annual incidence of 5 deaths per 100000 cattle, costing $12.3 millions annually in Africa and Asia. The total (direct and indirect) cost of PEP accounts for 5.8% of annual per capital gross national income in Africa ($40 per treatment) and 3.9% ($49 per treatment) in Asia [22].

In China, over a 55-year period, between 1950 and 2004, 108412 human rabies cases were reported with three major epidemics occurring during this period [23, 24]. The first epidemic outbreak occurred in the mid-1950s when cases rose to a peak of about 2000 annually. After a decline in the 1960s, the number of cases again started to increase in the early 1970s reaching a peak in 1982, and then remained at levels of 5000–6000 cases per year until the end of the decade [25]. Therefore, one of the purposes of this study was to conduct a comprehensive analysis of the country rabies situation using all the official data to characterize the current epidemiological trends of rabies in China from 1990 to 2007. In order to define better recommendations for
improving the PEP schedules delivered to patients, we also analysed the reasons for
the post-exposure treatment failures (or absence of PEP), based on the medical
records of anti-rabies treatment of injuries or related incidents for 244 rabies patients,
ascertained in Guangdong province of China in the years of 2003 and 2004.

**Methods**

**Data collection**

The epidemiological data for 22527 human rabies cases from January 1990 to July
2007 were obtained from the surveillance database of reportable diseases managed by
the Ministry of Health of China. The rabies diagnosis in humans reported to the
national surveillance data bank was based on the clinical criteria set by the Ministry of
Health of China including history of animal bite(s), intense anxiety, nervousness,
paralysis in the area of the bite, hydrophobia, and final death. The history of animal
bite was confirmed by subsequent case epidemiological surveys from various
provincial Centres for Disease Control and Prevention (CDC) offices. To investigate
the efficiency for the post-exposure treatment of rabies, 244 rabies patients with their
detailed medical records of anti-rabies treatment of injuries or related incidents,
enrolled at Guangdong province in the years of 2003 and 2004, were ascertained from
all the reported rabies cases (441 patients) during the periods. Clinical evaluations
were obtained from all the participants (or their relatives) according to the protocols
approved by the collectors’ institution review boards of the ethics committees.

**Schedule table**

The patient’s record form adopted for anti-rabies treatment was a standard form
designed by the Ministry of Health of China. At the CDC offices, the form was
completed by the staff who were responsible for clinical evaluation and treatment. The patients or their responsible parties supplied the information entered into the forms. The variables taken into account for an affected patient were: (a) the patient’s demographic profile: place of residence, age and sex; (b) exposure characteristics: date of event, type of exposure (scratch, lick, indirect contact or bite), site of lesion, number of lesions (single or multiple), type of lesion (superficial or deep); (c) treatment: time lag between exposure and onset of treatment (delay in days), procedure adopted (wound care and medication), type and route of drugs (rabies vaccine, animal antiserum and/or immunoglobin), number of doses prescribed, number of doses administered, type of professionals who assessed the patient and prescribed or delivered the treatment.

Data analysis

Distribution and the cumulative number of rabies cases over all provincial administrative regions of China for the period 1990-2007 were investigated. The data were then subjected to statistical analysis, and frequencies were calculated for the categorical variables. Two epidemiological indices, incidence rate and mortality rate, were computed to characterize the infectious disease in China. Incidence rate was the number of new cases of rabies diagnosed or reported during a defined period of time (e.g. a year), divided by the number of persons in a stated population in which the cases occurred, expressed as cases per 100000 per annum in this study. Mortality rate was calculated by dividing the number of rabies deaths occurring in the population during the stated period of time (e.g. a year), by the number of persons at risk of dying during the period. The rabies-specific mortality rate covered deaths due to the only disease and was reported on the basis of 100000 persons in this study. To analyse the
risk factors predisposed to or regimens given to 244 patients for identifying the
reasons for the PEP failures or absence of PEP, McNemar test, as implemented in a
public server [26], was used to test two studied proportions due to the different
exposures or factors obtained from the 244 patients. This test took into account the
correlation between two sets of the same patients, occurring because the patients
received alternative exposure 1 only, alternative exposure 2 only, or neither exposure.

Results

Epidemiological characteristics
The annual incidence rate for rabies was summarized in Figure 1. The results from
analysis of a total of 22527 human rabies cases from January 1990 to July 2007
showed that rabies in China was largely under control during the period 1990-1996,
when nation-wide rabies vaccination campaigns were conducted. The data collected
showed that after a decrease in human rabies cases during the period, the incidence
started to rise and a total of 3279 cases were reported in 2006.

(Figure 1 about here)

In 1996, the reported cases dropped to the lowest frequency (159 cases), in a sharp
contrast to the figure for the year of 1990, having 3520 cases reported nationwide.
The 1996 yearly incidence rate of rabies in China was 0.013 per 100000 inhabitants.
During 1996-1999, the yearly incidence rate of rabies, though slightly increasing,
were relatively stable, but later the figures jumped dramatically. In 2005, 2571 cases
of rabies were documented. Since the new century, the incidence rates of human
rabies increased from 0.0889 per 100000 inhabitants in 2002 (1159 cases) to 0.1511
(2037 cases) in 2003; then, this incremental trend continued into 2004 (2651 cases),
2005 (2571 cases) and 2006 (3279 cases). The data for 2007 remained to be
completed, and between January and July of this year, there were 1740 human rabies cases reported, increased by 28.98% by comparing the same period in the previous year 2006 (1349 cases).

Human rabies, however, are not evenly distributed in the vast country. Figure 2 shows the geographic distributions in two recent years (Figure 2A for the year of 2003, and Figure 2B for the year of 2005). The highest prevalence in both years was registered in the south-western and southern territories of China. Hundreds of rabies cases were identified in the regions including Guizhou, Guangxi, Hunan and Guangdong provinces. In the year of 2003, there was no case reported in the North, the Northeast, and the West of China. However, in the year of 2005, human rabies expanded to much wider regions, even the far west region (Xinjiang provincial jurisdiction) (Figure 2B). In both years, there was no case reported in Inner Mongolia, Heilongjiang, Qinghai, Ningxia, Tibet, Gansu and Liaoning provinces. In almost all provinces of China, the mortality rate (data not shown) was identical or similar to the incidence rate as once clinical signs of rabies appeared, the disease was essentially 100% fatal.

(Figure 2 about here)

We had particular interests in four neighbouring, most populated provinces (Guangdong, Guangxi, Hubei and Hunan) in southern/central China, because the incidence rates were relatively higher, and the corresponding CDCs had more clinical details for the human rabies patients. A comparison between the provinces, shown in Figure 3, demonstrated that Hubei had on average the highest number of rabies cases in 1990-1995 (e.g. 311 cases in 1990), then, the number of cases dropped or maintained until 2000, but from 2001 it jumped again. The same or similar temporal trend of rabies was also observed in other three provinces, which may well capture the
unique epidemiological profiles to the tropical or subtropical southern regions in the recent years. These data indicate that human rabies, largely free in the last years of the last century in China, started to emerge to trigger a warning sign for control and prevention.

(Figure 3 about here)

Post-exposure treatment (PEP)
According to the current WHO guidelines, we divided rabies post-exposures into three categories (see Additional file 1 for detail). Exposure category I described the lightest degree of exposure to infects, without any skin injury, while category III described the most serious situations where single or multiple transdermal bites or scratches occurred that needs immediate wound treatment and receiving anti-rabies vaccines.

(Additional file 1 about here)

China banned nervous tissue vaccines (NTV) in 1981, and then different provinces adopted slightly different options for rabies vaccine products. For example, Guangdong provincial CDC recommended using the following products: purified Vero cell rabies vaccines (PVRV, Aventis Pasteur, Lyon, France), purified chick embryo cell vaccines (PCEV, ChengDa Biologicals, Shenyang, China), and hamster kidney cell vaccines (PHKCV, Lanzhou Institute of Biological Products, Lanzhou, China). Nevertheless, there was substantial amount of vaccine products produced by small companies or institutes in China, thus lacking suitable quality and efficacy control. These low-quality vaccine products not only increased the difficulties in controlling and preventing rabies, but also complicated the public health programmes in other Asian countries who imported these products. The standard post-exposure vaccination schedule was the ‘Essen’ 5-dose intramuscular regimen on days of 0, 3, 7,
14 and 28. However, five pre-exposure or post-exposure schedules were currently used in China (see Additional file 2 for detail).

(Additional file 2 about here)

**Analysis of post-exposure treatment failures**

We analysed the post-exposure prophylaxis (PEP) in the rabies cases in Guangdong province. This could be a suggestion that lack of adequate PEP is one of the major problems in the current situation in China, since Guangdong is one of the provinces with a higher incidence rate and one with the best information available. There were 197 and 244 human rabies cases reported respectively in the years of 2003 and 2004. However, only 244 cases (130 cases in 2003 and 114 cases in 2004) had sufficient information (demographic and clinical data) suitable for analysis of post-exposure treatment failures or absence of PEP. To look at the information for the virus transmitters, we found that most of the 244 human rabies cases were infected by dogs (209 cases, 85.7%), followed by cats (9 cases, 3.7%) and rats (6 cases, 2.5%). In detail, these dogs consisted of the ones owned by the patients themselves (101/209, 48.3%), dogs belonging to neighbourhhood (38/209, 18.2%), stray dogs (38/209, 18.2%), and others (32/109, 15.3%). McNemar Test revealed that dog’s virus transmission was highly significant (P < 0.01) than other animals. The frequency of incidents was higher for male patients and most patients were under 20 years old. Direct or indirect contacts accounted for 96.47% of the types of exposures and remaining 3.53% were via unknown means. Per the degrees of exposure described, categories I-III accounted for 33.6%, 38.9% and 22.5% of the patients, and the remaining 5% were not classified due to the incomplete data. The time lags between the incidents and the presentation of patients for anti-rabies assessment ranged from 0 to 3 days in most cases. According to the available data on the lesion sites for 109
patients in 2004, most often affected were arms (31 of 109, 28.4%), legs (31 of 109, 28.4%) or fingers (24 of 109, 22.0%) (see Additional file 3 for a graphical illustration). Single injuries (82/109, 75.2%) were more frequent than multiple ones (18/109, 16.5%) (McNemar Test, P < 0.01).

(Additional file 3 about here)

Among the 244 cases with informative medical records, 67.2% (164/244) did not seek any medical service and the remaining 32.8% (80/244) received PEP. Table 1 shows the analysis of post-exposure treatment failures per the risk factors predisposed to or regimens given to the 80 patients who received any type of PEP. Among the 80 patients, 62.5% (50/80) only had their wounds washed with water by themselves, 37.5% (30/80) patients went to hospitals or local CDCs to have proper treatment on their wounds (washed with soap water or clean water for at least 15 min, and then embrocated with 2-3% tincture of iodine or 75% alcohol). Forty-five percent (36/80) patients did not receive any rabies vaccine or passive immunization and 47.5% (38/80) patients received 1-4 shots of rabies vaccine, but none of passive immunization. Of the 80 cases who received PEP, 7.5% (6/80) patients received a full regime. The six patients had a category III exposure(s), of which five had a bite on head and neck and one case had multiple bites. They all received the following treatment within 24 hours after the bites: wounds were washed with soap water or clean water for at least 15 min; then embrocated with 2-3% tincture of iodine or 75% alcohol; next, animal antiserum (40 IU/kg) or human immunoglobulin (20 IU/kg) was injected onto the surroundings of the wounds; one full ampoule of rabies vaccine was administered IM on days 0, 3, 7, 14 and 28. Five cases received PCEV or PHKCV made in China, and one received PVRV imported from France. Nevertheless, all the six patients finally died from the rabies infection. After careful scrutiny of the six cases, reduced
quality of the vaccine due to improper storage done by the patients themselves after the first shot and lower doses might contribute to the failures, while the lesion site (on the head and neck or multiple bites) may well be a factor causing the failures in the six cases. In short, according to the current WHO guidelines, none of 244 cases reported received both adequate and sufficient post-exposure treatment.

(Table 1 about here)

Discussion
In China, human rabies was largely under control between the period of 1990-1996, via nation-wide rabies vaccination programmes. Since the vast majority of cases were due to canine rabies in the early time, an extensive dog vaccination programme was initiated in 1987 [27]. From 1990 to 1996, canine rabies decreased by 95.5%, while the GDP (gross domestic product) increased considerably in the same period. During the period 1996-1999, the yearly trend for human rabies was relatively stable, and then the number of human rabies cases jumped dramatically since the new millennium. Overall, our data implicate that human rabies, largely free in the last years of the last century in China, started to jump high enough to trigger a warning sign for control and prevention.

However, the data ascertained at various CDCs may not well capture the real epidemiological scenarios for human rabies in China. For example, since the SARS epidemic of 2003, the Chinese government has set up a systematic and nationwide surveillance network for zoonotic diseases. Increased surveillance together with increased dog or other pets populations may be the principal factors explaining the increasing number of cases of human rabies reported in China in the recent years [27]. The same issues for obtaining unbiased estimates for the epidemiological indices of
rabies (incidence or mortality rates) were noticed by Torrencea et al. [28] in the similar studies, and by Brazuna et al. [29] in studying Brazilians. It should be noted that this ascertainment bias is not unique to the data ascertained at various CDCs, instead common to many medical experiments (e.g. hospital-based) where random sampling is not a feasible (often less efficient) strategy for data collection. Yet, there is a list of factors influencing precise and accurate estimation of human rabies parameters. To list a few, they are: (1) many people, especially in remote areas, did not have an easy access to public health service; (2) there was a dearth of knowledge about rabies in general public and among health workers; (3) there was insufficient diagnostic capability and facility in the country so that some case reports may not be able to be sent to the surveillance database at the Ministry of Health of China. Despite these limitations, the results clearly demonstrated that rabies constituted a real public problem in China and its control should be a top priority.

Our data also indicate that most incidents occurred in the south-western and southern territories of China, and most frequent in the rich-populated areas. For example, in 2005, rabies was routinely identified in Guizhou (481 cases), Guangxi (480 cases), Hunan (379 cases) and Guangdong (306 cases) provinces. The four rabies-endemic provinces lacked strictly enforced measures to eliminate dog rabies or the ample supply of modern cell culture rabies vaccines for humans. It was also interesting to note that most of patients were teenagers in the range of 0-20 years old and the major victims of rabies were the children of less than 16 years old, perhaps owing to being bitten by dogs more often than adults. When attacked by dogs, the lesions were often on the child's head and neck, thus, not surprisingly, this lesion site was associated with the highest risk for developing rabies [21, 30, 31].
In our study of the 244 human rabies cases in Guangdong province, 67.2% of the patients did not seek medical services or did not receive any PEP. The time lag between the incidents and the presentation of patients for anti-rabies assessment ranged from 0 to 3 days in most cases. Up to 62.5% of the patients did not receive proper treatment on the wounds, 92.5% did not receive adequate post-exposure vaccination and 91.25% did not receive any anti-rabies immunoglobulin. These results suggest that the population investigated may not be well aware of the risks for rabies transmission, as previously revealed [23]. This fact could be a significant issue for public health based on the large number of failures for human post-exposure prophylaxis (PEP) occurred in Chinese cases recently. During the study, we found that the education/information for rabies can only seen from the public boards at municipal or district CDCs in Guangdong province. We did not see such public boards or web pages at police departments (stations), community hospitals or offices, villages and so on. In December, 2007, we conducted a survey among 270 students of preventive medicine at our institute. We observed that the students had basic knowledge about rabies, but had some misunderstandings. Among the students, 92.2% could answer PEP regimes correctly. However, only 47.4% knew “washing the wounds can remove the virus residue on the lesions, and the correct rate for grades 2-5 students was 42.6%, 32.0%, 60.0% and 70.4%, respectively. Only 58.9% of the students knew that the pre-exposure administration regime for rabies vaccine. However, 71.5% of the students knew the post-exposure administration regime for rabies vaccine and 57.8% knew the immunization sites for rabies vaccine.
In the rabies-infested developing countries, modern cell culture vaccines are too
costly to afford in the poorly developed remote regions, where dangerous neural
tissue derived vaccines are still used [32-34]. Over the last 4 years in China, of more
than 2000 people yearly who died of rabies, only about one-third of people did
receive rabies vaccination. This figure was even lower (7.5%) in Guangdong province
estimated by this study. In most cases of vaccine failures, patients came down with
the disease before the full PEP regimen was completed [24]. In addition, there was a
critical shortage of human and purified equine rabies immunoglobulin in these
regions, which was the essential biological in the treatment of severe exposures.
Although the costs of modern vaccines are decreasing, the current price of a full-dose
intramuscular vaccine treatment is somewhat beyond what an average family in
developing countries can afford [35, 36]. For example, average annual income per
capita in Guangdong province is 3000 US dollars. The rabies vaccine costs 12.5-45.0
US dollars, taking up 0.42%-1.51% of average annual income per capita. This figure
would be much higher if considering the fact that about 60%-70% cases were from
poor rural areas or habos. Furthermore, the supplies of modern and safe vaccines for
many provinces are grossly inadequate, whereas the demand for affordable and safe
human post-exposure treatment is increasing in these provincial regions [23, 24].
Consequently, anti-rabies vaccines and human immunoglobulin are only available,
and provide feasible solutions for efficiently controlling rabies in majority of
municipalities of China or other developing countries [16, 37-39].

Finally, for the control and elimination of rabies transmitted by dog is very important
mass vaccination dog campaign. China did not implement enforced immunization for
dogs. Rabies vaccine was provided at the cost of the owners, and the cost was
expensive, from tens to hundreds of Chinese dollars. Dogs were registered at local police departments, while animal rabies vaccine was administrated by veterinarians, thus lacking good communications and effective strategies for dog rabies control. It appears that increase in canine rabies, increase in dog population, and decrease in vaccine coverage of dogs may also contribute to the apparent upwards trend of human rabies in recent years in China. Based on Chinese CDC’s surveillance of dog rabies in some typical affected areas, the positive rate was 3.9% (4/102, Guangxi province) in 1999, 9.1% (76/838, provinces Hunan, Henan, Guangxi, Guizhou and Jiangsu) in 2004, and 5.9% (5/85, Guizhou province) in 2005. This pattern is fairly consistent with human rabies. Nevertheless, the actions of control done by the Latin American countries might provide promising ways for China to develop a more effective programme for controlling human rabies transmitted by dogs. With the support from the Pan American Health Organization, several measures such as decentralization of health units with PEP available, dog vaccination coverage and dog rabies surveillance had been successful in achieving the goal to eliminate human rabies transmitted by dogs [40].

Conclusions
This large-scale epidemiological study demonstrated that human rabies was largely under control in China between the years of 1990 and 1996, via the national rabies vaccination programmes. However, the number of reported rabies cases started to grow since then. From 2001 this figure jumped again till a new peak reached in 2004, and stayed there afterwards. Based on the investigation of 244 human rabies cases collected in Guangdong province in the years of 2003 and 2004, 67.2% of the patients did not seek medical services or did not receive any PEP. Further analysis of the post-
exposure treatment failures for 80 rabies patients who received any type of PEP indicated that majority of patients, if not all, did not receive proper and timely treatments on the wounds or post-exposure vaccination. The study implicated that (1) human rabies, largely free in the last years of the last century in China, started to emerge to trigger a warning sign for control and prevention; (2) the need for improving the current rabies control programme in order to reduce non-compliance rates and to decrease the occurrence of flaws in the surveillance programme and in the provision of health care. Given the findings of the study, we view the implementation of the following measures as appropriate [9-12, 41, 42]: (a) continuing supervision of the current human rabies control programme, in order to reduce both non-compliance rates and the occurrence of flaws in health care provision; (b) improving interaction of professionals from the divisions of the municipal health care network and teams of national programmes; (c) increasing rabies awareness among China health authorities and policymakers; improving training of general practitioners and health care workers; educating school children and the general public that are crucial for effective rabies control and (d) urban planning and development should take ecosystem preservation into account, in an attempt to balance the interaction between humans and animals.

**Competing interests**
The author(s) declare that they have no competing interests.

**Authors' contributions**
JHL, HS and SQR conceived and designed this study, and drafted the manuscript. HS and SQR collected the data, and performed the statistical analysis. All the other authors (ZMG, YTH, YGL and DMZ) significantly contributed to this work by
providing assistance and helps for data collection, data manipulation and analysis. All authors read and approved the final manuscript.

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Figures

Figure 1 - The temporal trends of human rabies in China, from 1990 to 2006

Figure 2 - Geographic distribution of human rabies in China over the years of 2003 (A) and 2005 (B)
Shown are incidence rates per million people with the scale: blank = none, blue = 0~0.2, green = 0.2~0.4, and red= >0.4.

Figure 3 - A comparison of rabies incidences between four southern provinces (Guangdong, Guangxi, Hubei and Hunan) of China
Note that the data for 1997-1999 for Guangdong were not available.

Tables

Table 1 - Analysis of post-exposure treatment failures per the risk factors predisposed to or regimens given to 80 patients who received any type of PEP, collected in Guangdong province

Additional files

Additional file 1 – Table S1 - Degree of exposure and treatment schedules for human rabies, adopted from the criteria set by the Ministry of Health of China, 2006

Additional file 2 – Table S2 - Pre-exposure and post-exposure schedules for rabies, currently used in China

Additional file 3 – Figure S1 - Spatial distributions of rabies classified by the sites of lesion
Table 1 - Analysis of post-exposure treatment failures per the risk factors predisposed to or regimens given to 80 patients who received any type of PEP, collected in Guangdong province

<table>
<thead>
<tr>
<th>Factor</th>
<th>Known cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>multiple wounds and/or bite on head and neck</td>
<td>55 (68.8%)</td>
</tr>
<tr>
<td>insufficient wound treatment</td>
<td>50 (62.5%)</td>
</tr>
<tr>
<td>delay ≥2 days</td>
<td>34 (42.5%)</td>
</tr>
<tr>
<td>no RIG given</td>
<td>73 (91.3%)</td>
</tr>
<tr>
<td>no rabies vaccines given</td>
<td>74 (92.5%)</td>
</tr>
</tbody>
</table>
Figure 1

Incidence rate (per 100,000)

Year
Additional files provided with this submission:

Additional file 1: additional file 1.doc, 31K
http://www.biomedcentral.com/imedia/1788242339193390/supp1.doc
Additional file 2: additional file 2.doc, 26K
http://www.biomedcentral.com/imedia/6006164971933906/supp2.doc
Additional file 3: additional file 3.ppt, 37K
http://www.biomedcentral.com/imedia/1388212975193391/supp3.ppt