Reviewer's report

Title: Epidemiological investigations of human rabies in China

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Reviewer: Millicent Eidson

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Minor Essential Revisions: This is an excellent article that will help elucidate ways to prevent rabies cases worldwide. I have one question:

1) In most of the article, the term ‘cities’ is used for the lettered subdivisions of the provincial map. However, the term ‘county’ is used in the middle of page 12. Because the article discusses the preponderance of peasants being infected, and rural areas, perhaps the word ‘county’ should be substituted more widely in the manuscript when referring the lettered subdivisions of the map?

2) The following suggestions for the text should be considered to make the wording clearer for the readers. The specific wording I have suggested is not required, but the authors should consider language such as this or other language to clarify the wording. Suggested rewordings are as follows:

p. 3 bottom, For humans after rabies exposure, the rate of prophylaxis . . .

p. 4 top, Our study shows that the number of human rabies deaths increased rapidly and the prevalence area began to expand in western and . . .

p. 4 top, Thus, the public education of rabies should be strengthened. The management and vaccination of dogs, and the government financial support for PEP, may also . . .

p. 4 middle, In the 1980s, . . .

p. 4 middle, . . . and factors related to the local prevention and control of rabies.

p. 4 bottom, . . . were collected from the annual reports of the Chinese . . .

p. 5, top, . . . by the number of vaccinated dogs/the number of all dogs . . .

p. 5, middle, After the wound has been thoroughly cleansed, rabies vaccine is administered for Category II and III contacts, and rabies immune globulin (RIG) is administered for Category III contacts. There are two types of RIG used in China, equine RIG (purified . . .

The dose of equine RIG is 40 international units . . . for Rabies Postexposure Prophylaxis of Humans based on the WHO criteria above.

p. 5 bottom, . . . were collected by the local CDC . . .

p. 6 top, . . . the traditional standard in rabies diagnosis, was used . . .

p. 6 middle, . . . three selected provinces. The status of . . .

a logistic regression model was used to analyze . . .
The fewest cases per 100,000. The cases were more than twice as frequent as female cases. Nearly 1/3 of the cases were under 15 years old. In all the patients, peasants (rural agricultural workers) represented 61.9%. Of 846 cases was reported compared to 2002, which had a 71.0% increase. In 2005, the increase of 5,841 cases over the 10 years from 1996, an average increase of 35.4% per year. Initially and until now, most . . .

Dog brains were tested for rabies virus antigen by DFA in 15 of the X cities in the three provinces. The infection rate of rabies is 8.2% of dogs tested. All 15 cities showed an infection rate of 1.0-18.9% in the 11-year period. The infection rate was significantly different among . . .

Of these, 1,157 dogs were male with 20 rabies positives (1.7%) and 761 were female with 23 rabies positives (3.0%). There was no significant difference between the genders on rabies positivity . . . was collected in 10 of the 15 cities with dog rabies testing data. The highest rabies vaccination rate was in GG (93.0%), and the lowest rate was in LZ (10.0%).

Of these, 1,157 dogs were male with 20 rabies positives (1.7%) and 761 were female with 23 rabies positives (3.0%). There was no significant difference between the genders on rabies positivity . . .

We collected detailed information on 711 of the 7,046 human rabies cases (X%) from the local CDC. . . . were female. The youngest . . . 2.81% had been vaccinated, and all the cats were unvaccinated. . . . 6.3% of the patients . . . 15.1% had exposures to the head . . .

Occupation, species of attacking animal, animal vaccination status, . . .

To clarify these results, we further analyzed the factors . . . The rate of wound handling (P<0.001) and vaccination . . . especially in 2001 and 2003, with a small drop in 2005. . . . were not vaccinated because they could not afford . . .

Although the atypical pneumonia pandemic in 2003 in China caught the attention of the world, in the same time period the number . . . Perhaps the huge number of resources directed to atypical pneumonia influenced . . .
p. 12 top, ... incidence decreasing in 2005 may be due to rabies control being emphasized and strengthened by local governments in ...

This indicates that the attention and participation of the government may improve control of infectious diseases.

p. 12 middle, ... as the economic condition is improving in China ...

Many areas that had no previous human rabies reports have reported outbreaks of rabies since 1996, such as AL county ...

p. 12 bottom, ... occurred in the rural areas of the counties.

... and to a low vaccination rate in dogs ...

Affected populations are primarily peasants, students and unattended children, probably due to increased chance of dog contact, lack of prevention awareness, and reduced capability of defending against dog attack.

p. 13 top, However, dog rabies surveillance often hasn’t been carried out because the dog isn’t an important economic animal in China. Insufficient data was obtained to fully address the relationship ...

In our research, the rabies infection rate (8.2%) in dogs was higher than in other investigations ...

The vaccination rate was lower in most areas, and the attacked animal primarily was the dog. The rise of ... in these areas, although this association was not statistically significant in our research.

p. 13 middle, In 2006, the estimated number of dogs in Chinese homes was over 75,000,000. Among those, over 11,000,000 dogs are raised by urban families ...

... the vaccination rate of dogs ...

[delete, becaused modified and moved above to earlier para.: So the correlation between the DFA positive rate of rabies and the rate of vaccination in dogs in the investigated areas showed non significant relationship.]

As suggested in previous studies, low dog vaccination rates is one of the ...

The vaccination coverage in dogs needs tremendous improvement.

p. 13 bottom, In China, there are no official administrative rules ...

p. 14 top, ... concerning the animals attacking humans. In some areas, the dog would be killed after attacking humans, with few receiving observation and rabies detection. The status of animals after attacking humans was not always obtained.

p. 14 middle, In our study the rate of PEP in patients with rabies exposure in the three provinces is extremely low. Among the investigated ...

One of the reasons for the low rate of rabies PEP might be related to the low level ...

... and the rates of wound treatment and vaccination administration ...

p. 14 bottom, This illustrates that with serious exposures at sites close to the head, face and neck, the patients were more likely to seek medical assistance. Those patients with a lower category of exposure or exposure sites on the limbs
more often handle the wound by themselves without wound treatment and vaccination, which is often inappropriate. Thus, education on rabies and its prevention is necessary and important in endemic areas . . .

p. 15 top, . . . economic development . . .

. . . total of the cost for PEP/person . . .

Thus, the lower cost intradermal regimens are being considered in China. p. 15 middle, In addition, some cases receiving PEP still died of rabies. Almost none of them received adequate PEP. For example, many Category II exposure cases only washed the wound without visiting medical doctors. Some category III exposure cases were vaccinated but received no RIG, and some of the patients died quickly . . . [Can the number of cases be added here instead of ‘many’ and ‘some’?]

. . . resulted in these patients dying of rabies. Knowledge of rabies prevention . . .

In summary, comprehensive steps including . . . proper rabies exposure PEP, and increasing the knowledge of rabies prevention, as well as government financial support for PEP, are necessary for . . .

p. 15 bottom, Our study shows that human rabies numbers have increased rapidly . . .

Thus, the public education of rabies should be strengthened. The management and vaccination of dogs and the government financial . . .

p. 16 top, . . . may also play a huge role in reducing the rate of human rabies deaths.

3) Suggested changes for Figure titles:

Figure 1 – Location of Guangxi, Hunan and Guizhou provinces within China. Data on human cases and dogs was included for highlighted counties.

Figure 2 – Number of human cases and incidence rate between 1996 and 2006 in China

Figure 3 – Changes in the number of cases of human rabies . . .

4) Suggested changes for Table titles and column/row headings:

Table 1 – The demographic characteristics of all the human rabies cases in China (n=14,065) and in the three affected provinces (Guangxi, Hunan and Guizhou, n=7,046) from 1996 to 2006

Table 2 – The infection rate and vaccination rate in dogs and incidence of human rabies in 15 investigated counties

Change 4th column title: Incidence of human cases (1/100,000)

Table 3, Change ‘Exposure degree’ to ‘Category of Exposure’ to match the terminology in the text.

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.