Epidemiological trends and characteristics of Japanese encephalitis changed based on the vaccination program between 1960 and 2013 in Guangxi Zhuang Autonomous Region, southern China

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SUMMARY

Japanese encephalitis (JE) is one of the most severe kinds of viral encephalitis and is prevalent in Asia and the Western Pacific. In China, JE was first reported in the 1940s and became the main cause of viral encephalitis, including in the Guangxi Zhuang Autonomous Region. In 1951, JE was included in the Chinese mandatory disease reporting system. In the pre-vaccine era of the 1960s and 1970s, the incidence of JE continued to rise without any vaccine supply. Since JE vaccines became available in the late 1970s (MBD) and 1989 (LAV-SA-14-14-2), and as JE vaccine became freely available to patients beginning in 2008, the incidence of JE has declined significantly. Despite these gains, outbreaks continue to occur among children in rural and suburban areas. Strengthening vaccine delivery models and improving swine vaccine production are important in order to sustain continuous declines in the incidence of JE in Guangxi.

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1. Introduction

Japanese encephalitis (JE) is a serious threat to human lives and is caused by the Japanese encephalitis virus (JEV), which belongs to the Flaviviridae family. The first major epidemic of JE occurred in 1924 in Japan. Since then, JE has been found increasingly in most countries of Asia, especially in the south-east areas. Over three billion individuals have been found in JE epidemic/endemic countries. According to a report by the World Health Organization, the number of cases worldwide in 2007 was 9487, including 4330 cases in China, 4017 cases in India, and 435 cases in Nepal.

JEV generally affects young children (< 15 years old) and elderly people (> 65 years old), who have a weak immune system and hence are vulnerable. The fatality in JE cases ranges from 20% to 30%, with neurological and/or psychiatric sequelae observed in 30% to 50% of survivors. JE was first reported in the 1940s and became the main cause of viral encephalitis in China. Guangxi, which is in the south-east area of Asia, is a southern province of China. The geographic distribution of Culex gelidus Theobald, which is the vector of JEV and a mosquito native to Southeast Asia, has increased during recent decades, covering the whole of Southeast Asia, Australia, and several Pacific Islands.

2. Materials and methods

2.1. Data

The data for the period 1960 to 1998 were provided by the Department of Epidemic Information, Centre for Disease Control and Prevention of Guangxi Zhuang Autonomous Region. The data for the period 1999 to 2013 were extracted from the National Notifiable Disease Reporting System (NNDRS) of P. R. China. Statistics on the population were obtained from the Guangxi Statistical Almanac.

2.2. Methods

IBM SPSS Statistics for Windows, version 19.0 (IBM Corp., Armonk, NY, USA) was used for the data analysis. The administrative divisions of the Province, as suggested by the Provincial...
Government Administration of 2003, were used to assess geographical variations in the incidence of JE. Guangxi Province is divided into 14 regions.

3. Results

3.1. Epidemic situation and trends

Between 1960 and 2013, 65,520 cases were reported in Guangxi, including 11,879 deaths. The average incidence rate of JE over the 53 years was 3.39/100,000, the average mortality rate was 0.61/100,000, and the case fatality rate was 18.13%. The peak incidence (25.64/100,000) was reached in 1969. The lowest incidence of 0.03/100,000 was found in 2013. The incidence of JE in Guangxi increased continuously during the 1960s and 1970s, with an average incidence rate of 9.24/100,000 (the lowest rate was 1.69/100,000 and the highest was 21.82/100,000). The incidence decreased by degrees starting in the 1980s. In addition, the variability in the annual incidence rate ceased and regional outbreaks became more sporadic (Table 1, Figure 1).

3.2. Epidemic characteristics

3.2.1. Seasonal distribution

All of the cases in the 53 years from 1960 to 2013 were distributed across every month, with 95.83% of the cases concentrated in five consecutive months of each year: May, June, July, August, and September. July, accounting for 45.21% of the total number of cases during the years 1950–2013, was the month with the most serious epidemic (Figure 2).

3.2.2. Distribution of different geographic areas

All of the 14 cities in the province reported cases of JE in the 53 years from 1960 to 2013. Guilin City had the highest incidence rate of 5.40/100,000, followed by the cities of Fangchenggang, Beihai, Laibin, and Yulin with incidence rates of 4.12/100,000, 4.02/100,000, 3.88/100,000, and 3.81/100,000, respectively. In addition, with a proportion of 14.28% of the accumulated cases and a total incidence rate of 5.40/100,000, Guiyang City was considered to be the geographic area with the most serious JE epidemic situation.

The 14 cities were sorted in descending order of JE incidence rate for six different time-periods and the top five were ranked. In the 1960s, the cities of Guiyang, Beihai, Fangchenggang, Chongzuo, and Yulin led the way with incidence rates of 19.60/100,000, 16.43/100,000, 14.01/100,000, 10.17/100,000, and 9.56/100,000, respectively. In the 1970s, the top five were Fangchenggang, Laibin, Guilin, Guigang, and Beihai with rates of 11.98/100,000, 11.33/100,000, 11.25/100,000, 10.89/100,000, and 10.31/100,000, respectively. In the 1980s, the order was Yulin, Fangchenggang, Laibin, and Hechi and their incidence rates were 3.36/100,000, 3.28/100,000, 2.69/100,000, 2.01/100,000, and 1.75/100,000, respectively. In the 1990s, Hezhou City, with an incidence rate of 2.49/100,000, became the most seriously affected area, followed by the cities of Hechi, Qinzhou, Yulin, and Baish had incidence rates of 2.28/100,000, 1.87/100,000, 1.74/100,000, and 1.66/100,000, respectively. The highest incidence rate of 1.19/100,000 was found for Hechi City in the 2000s and the other cities in the top five were Baish (1.10/100,000), Hezhou (0.74/100,000), Guiyang (0.50/100,000), and Chongzuo (0.42/100,000). Finally, from 2010 to 2013, the order was Hechi (0.34/100,000), Yulin (0.17/100,000), Guiyang (0.16/100,000), Laibin (0.14/100,000), and Wuzhou (0.09/100,000).

3.2.3. Distribution of different population subgroups

Population distribution data were extracted from the NDNRs, which provided the data since 2004. There were 1288 JE cases reported between 2004 and 2013 in Guangxi, including 764 males and 524 females (sex ratio 1.44:1.98). Sixty percent of the JE cases were younger than 15 years old. Across all categories of profession, housebound preschool children comprised the main JE population (68.48%), followed by students (22.75%) and kindergarten children (6.60%).

4. Discussion

4.1. Trends and characteristics of JE in Guangxi

Two epidemiological patterns of JE are recognized: epidemic and endemic.8,9 Epidemic patterns are observed mainly in northern areas, including P.R. China, Korea, and Vietnam.3 The JE case reporting system has been mandated by law since 1951 in P.R. China.10 Accumulated JE cases and average incidence rates for Guangxi changed with a similar trend, increasing in the 1960s, reaching a peak in the 1970s, and decreasing dramatically from the 1980s. However, its ranking increased. The JE incidence rate of Guangxi ranked between 9th and 14th between 1990 and 2002 in China, and rose to 5th in 2005.
JE cases were reported intensively from May to September in Guangxi, but the seasonal distribution across the whole country is from June to October. The incidence reached a peak in July, which is comparatively earlier than in the north of China.5,10-12 Between 1950 and 2013, few regional outbreaks were reported and most of the cases were sporadic. Concentrations of cases in geographical areas were associated with different decades, and most of them were south of the Tropic of Cancer and located in eastern coastal areas. The main JE population was children aged 0–14 years in rural and suburban areas, especially housebound preschool children. The reasons for this tendency and these characteristics have already been mentioned.

4.2. Application of JE vaccine

Without the promotion of JE vaccine, the number of JE cases and the incidence rate increased continuously during the 1960s and 1970s in Guangxi. The use of the MBD JE vaccine began in the late 1970s, and LAV-SA-14-14-2 was introduced in 1989. However, few individuals received the vaccine because of its high price. Since 2008, JE immunization has been included in the national immunization program, with LAV-SA-14-14-2 being used in 28 Chinese provinces, including Guangxi.12 Nevertheless, adult JE cases and outbreaks have been reported.13 JE vaccine has been provided free-of-charge to children aged 0–14 years, and the number of cases and incidence rate were found to have decreased dramatically from 2008 to 2013 (average 74 cases per year; average incidence rate 0.16/100 000). However, according to Pearson correlation analysis, the increased coverage with JE vaccine did not reduce the incidence of JE ($r = 0.595$, $p = 0.25$) (Table 2). Some research has indicated that approximately 55 000 (75%) JE cases occur in areas with well-established or developing JE vaccination programs, while about 12 900 (19%) cases occur in areas with minimal or no JE vaccination programs.14 It appears that the linear relationship between coverage with the JE vaccine and incidence is not consistent and the actual situation is more that JE vaccine should be taken according to JE monitoring data.

4.3. Geographical and climatic features and industrial structure of Guangxi

According to the latest report of the Intergovernmental Panel on Climate Change (IPCC), the average warming of the global mean surface temperature was $0.85\degree C$ (range 0.65–1.06\degree C) over the period from 1880 to 2012.15 With the warming of the global surface, the greatest health risks will occur in populations that are most affected by climate-sensitive diseases, such as vector-borne diseases, and in those left behind by economic growth.16 JE is one of the vector-borne diseases and leads to major outbreaks in tropical regions of Asia, along with China, Japan, Korea, and countries of Southeast Asia.17

Guangxi is a coastal province situated in the south of P.R. China and has a subtropical monsoon climate, with an annual mean temperature of 16.0–23.0\degree C. Most rain falls between April and September and the annual average precipitation is 1070 mm. These features provide suitable conditions for mosquitoes, including Culex tritaeniorhynchus, to survive and breed. Another factor is pig farming in Guangxi. As an underdeveloped area, agriculture involving pig and poultry rearing is the principal industry in Guangxi. In 2013, 34 567 000 live pigs were sold and the number retained was 24 715 000. Many rural families have a few free-range pigs and pigs are the hosts that spread JE between mosquitoes, pigs, and humans. In addition, large-scale commercial poultry farming and family poultry rearing are common in Guangxi, and young poultry may be amplifying hosts of importance in disease-endemic regions.18 The pathogen JEV, the transmitter C. tritaeniorhynchus, the host pigs, and poultry represent acute risks for JEV infection in humans, and they are all found in Guangxi. In addition, bats play a role in the natural cycle of JEV.19

4.4. Constituent ratios of susceptible population

The constituent ratio of children aged 0–14 years (the susceptible JE population) has decreased each decade: 31.6% during the 1990s, 26.19% during the 2000s, and 21.71% between 2010 and 2013. The average JE incidence rates in these three decades were 1.34/100 000, 0.47/100 000, and 0.10/100 000, respectively. Analyzing the constituent ratio and JE incidence rate in the same decades via linear-by-linear association shows their linear relationship to be significant (Chi-square = 2691.44, $p = 0.00$). This suggests that populations under the age of 15 years are at higher risk of infection with JEV. Some animal experiments have indicated the importance of age of infection on the magnitude of viremia for JEV.18

4.5. Proposals on JE prevention based on epidemic features

JEV is the leading cause of vaccine-preventable encephalitis in Asia and the Western Pacific. There is no specific treatment for JE, although ajwain oil has been found to have potential in vitro antiviral activity against JEV.20 Avoiding being infected with JEV is significant for decreasing JE, because there is no specific drug or treatment that can cure the disease.

On July 19, 2013, the Advisory Committee on Immunization Practices (ACIP) voted to extend the existing recommendations for the use of inactivated Vero cell culture-derived JE vaccine (Ixiaro; Intercell Biomedical, Nanning, Guangxi, China) to include children aged 2 months to 16 years.21 By age subgroup, the constituent ratio of JE cases younger than 10 years was 91.53% between 2010 and 2013. Due to the climate in Guangxi, JE vaccine should be administered during the period from March to April to the population aged 2 months to 10 years old.

The eradication of mosquitoes would be another effective measure. Monitoring the changes in climate and mosquito density, and predicting JE tendency using the Gray model, would be useful.

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Table 2

Japanese encephalitis incidence and vaccine distribution by year, 2000–2013; Guangxi, China

<table>
<thead>
<tr>
<th>Year</th>
<th>Consumption of JE vaccine ($\times10000$)</th>
<th>Incidence of JE ($100000$)</th>
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<tbody>
<tr>
<td>2000</td>
<td>242.50</td>
<td>0.03</td>
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<tr>
<td>2001</td>
<td>75.00</td>
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</tr>
<tr>
<td>2002</td>
<td>342.51</td>
<td>0.05</td>
</tr>
<tr>
<td>2003</td>
<td>175.09</td>
<td>0.05</td>
</tr>
<tr>
<td>2004</td>
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<td>0.04</td>
</tr>
<tr>
<td>2005</td>
<td>332.54</td>
<td>0.05</td>
</tr>
<tr>
<td>2006</td>
<td>261.03</td>
<td>0.01</td>
</tr>
<tr>
<td>2007</td>
<td>57.95</td>
<td>0.04</td>
</tr>
<tr>
<td>2008</td>
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<tr>
<td>2009</td>
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<td>2010</td>
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<td>2011</td>
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<tr>
<td>2013</td>
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<td>0.01</td>
</tr>
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</table>

JE, Japanese encephalitis.

* Pearson analysis: $r = 0.595$, $p = 0.025$. 
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**Conflict of interest:** No conflict of interest to declare.

**References**


