

## Changing Prevalence of Anti-Hepatitis A Virus in Adolescents in A Rural Township in Taiwan

Jing-Yi Chen<sup>1,2,5</sup>, MD; Jui-Chin Chiang<sup>1,2,6</sup>, MD; Sheng-Nan Lu<sup>2,3,4</sup>, MD, MPH, PhD; Shu-Fen Hung<sup>3,4</sup>; Jung-Ta Kao<sup>3,7</sup>, MD; Yi-Hao Yen<sup>3,4</sup>, MD; Jing-Houng Wang<sup>3,4</sup>, MD

**Background:** Hepatitis A virus (HAV) is transmitted through the oral-anal route. Areas of low prevalence of anti-HAV might have risks for a hepatitis A outbreak even under accidental infection as the source can spread easily. The prevalence of anti-HAV among children in Taipei is reported to be nearly 0%; however, the prevalence in rural areas remains undetermined. Our study aims to realize the prevalence change in a rural area.

**Methods:** We took blood samples for anti-HAV detection from the entire junior high school population in Taihsi Township of Yunlin County in Taiwan. Two cross-sectional studies were conducted in 1999 and 2006, with students born in the years 1984-1985 and 1993-1994 respectively.

**Results:** The prevalence of anti-HAV was 0.96% (2/209) among subjects born between 1984-1985, and 0.6% (1/168) in those born between 1993-1994. The HAV vaccine was not available for at the time of the earlier study, and it is suggested that this figure was caused by natural infection. The only anti-HAV-positive student in the later study had a history of HAV vaccination.

**Conclusions:** The prevalence of anti-HAV has decreased to a very low level in recent years and is almost 0% in the generation born after 1984 in rural areas. Therefore, the possibility of an HAV outbreak should be noted. Furthermore, it is also necessary to offer correct information and suggestions concerning hepatitis A for tourists traveling abroad and reentering Taiwan.

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**Key words:** hepatitis A virus, Taiwan, epidemiology

The prevalence of positive anti-hepatitis A virus (HAV) in adults was more than ninety percent in Taiwan in the 1970s.<sup>(1,2)</sup> In the Taipei metropolitan area, series studies show the prevalence has decreased markedly and has even dropped to 0%.<sup>(3-5)</sup> There have been similar downward trends in other areas of Taiwan,<sup>(5-7)</sup> but geographical differences

exist.<sup>(8-10)</sup> However, in maps showing the prevalence of anti-HAV, the World Health Organization (WHO) and the Centers for Diseases Control and Prevention (CDC) of the United States show that Taiwan is still a high prevalence area.<sup>(11,12)</sup>

To provide correct information to tourists, the prevalence of anti-HAV in Taiwan needs to be eluci-

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From the <sup>1</sup>Department of Family Medicine; <sup>2</sup>Department of Occupational Medicine; <sup>3</sup>Division of Hepatogastroenterology, Department of Internal Medicine, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan; <sup>4</sup>Graduate Institute of Clinical Medical Sciences, College of Medicine, Chang Gung University, Taoyuan, Taiwan; <sup>5</sup>Graduate Institute of Occupational Safety and Health, Kaohsiung Medical University College of Health Science, Kaohsiung, Taiwan; <sup>6</sup>Graduate Institute of Environmental and Occupational Health, Medical College, National Cheng Kung University, Tainan, Taiwan; <sup>7</sup>Division of Hepatogastroenterology, China Medical University Hospital, Taichung, Taiwan.

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Correspondence to: Dr. Jing-Houng Wang, Division of Hepatogastroenterology, Department of Internal Medicine, Chang Gung Memorial Hospital-Kaohsiung Medical Center, 123, Dapi Rd., Niasong Township, Kaohsiung County 833, Taiwan (R.O.C.)  
Tel.: 886-7-7317123 ext. 8301, Fax: 886-7-7322402; E-mail: jinghoung2001@yahoo.com.tw

dated. The lack of anti-HAV is related to progress in public health and the social economy. In the countryside, a higher prevalence has been noted,<sup>(8)</sup> particularly in rural townships.

When the prevalence of anti-HAV decreases, the risk of a hepatitis A outbreak increases. In 2008, the Centers for Disease Control, Taiwan (TCDC) reported for the first time that the number of cases of acute hepatitis A was higher than in previous years. More epidemiology information is essential before planning disease prevention.<sup>(13)</sup> The hepatitis A vaccine has been available in Taiwan since 1996. There has been no universal vaccination program except for some aboriginal townships with a high risk of hepatitis A outbreak.<sup>(4)</sup> The prevalence of anti-HAV is related to socioeconomic status.<sup>(14)</sup> Yunlin County is one of the poorest economic zones in Taiwan and is supposed to be one of the counties with the slowest decline in anti-HAV prevalence.<sup>(15)</sup> We conducted a series of studies on hepatitis B and C in Taihsi Township of Yunlin County in which junior school students born between 1984 and 1993 were enrolled.<sup>(16-18)</sup> This study used the same blood sampling for anti-HAV prevalence detection and aimed to offer epidemiological information about HAV infection in a rural township of Taiwan.

## METHODS

The study was conducted in Taihsi Township of Yunlin County, located in central Taiwan. In 2006, we took blood samples for anti-HAV detection (anti-HAV Ab for AxSYM, Abbott, IL, U.S.A.) from the entire junior high school student population in Taihsi Township. There were 169 students in the first year of junior high school and a total 168 (99.4%) students were enrolled under their parents' informed consent. These students were born between July, 1993 and November, 1994. We also recorded the history of HAV vaccination among those subjects who were positive for anti-HAV.

We also took blood samples which had been collected in 1999 and stored at  $-70^{\circ}\text{C}$  for anti-HAV detection from the same junior high school. There were 216 students in the third year of junior high school and a total 209 (96.8%) students were enrolled. These students were born between July, 1984 and June, 1985. Because this part of our study was conducted using stored blood samples, investi-

gation of the history of HAV vaccination was not performed. Hepatitis A vaccine has been available in Taiwan since 1996. Before blood sampling in 1999, the opportunity for HAV vaccination for adolescents in rural townships was quite small.

The study protocol was approved by the Institutional Review Board of Chang Gung Memorial Hospital, Kaohsiung, Taiwan.

Two cross-sectional studies were conducted in 1999 and 2006, and our research described the positive rate with percentages for descriptive statistics.

## RESULTS

In our study in 2006, the prevalence of anti-HAV was 0.6% (1/168) in the subjects born from 1993-1994. The only student who was positive for anti-HAV had a history of HAV vaccination. In the study of stored blood from the earlier generation in 1999, the prevalence of anti-HAV was 0.96% (2/209) among subjects born from 1984-1985. Although the HAV vaccination history was not recorded, the opportunity for HAV vaccination was considered low.

## DISCUSSION

There is only one junior high school in our study area and our conjecture was that all students of school age should study there. The response rates of these two generations were 99.4% and 96.8% respectively; it was considered a population study. Although not many subjects were examined, it is representative because there was no sampling bias.

In Taiwan, there have been many investigations of the prevalence of hepatitis A in different areas, ages, and generations. In an investigation of 946 restaurant workers in the Taipei metropolitan area,<sup>(19)</sup> in the generation who were born before 1948, and around 1955 to 1964, the prevalence of anti-HAV was up to 98% and 92%. A study in southern Taiwan showed the prevalence of anti-HAV in those born before 1964 was close to 100%.<sup>(14)</sup> According to these studies, the prevalence rate of anti-HAV in the generation born before 1964 is close to 100% throughout Taiwan.

In a series of cross-sectional surveys in pupils 12 years old in the Taipei metropolitan area, who were born in 1963, 1972 and 1977, the prevalence of

anti-HAV was 50%, 10% and 5% respectively.<sup>(3,5,20)</sup> These studies revealed that the prevalence of anti-HAV has decreased to a very low level within 14 years and is almost zero percent in areas with good living conditions such as Taipei. In fact, in the third investigation of this series, the prevalence was zero percent in pupils born after 1979. In an investigation from Tainan, the prevalence of anti-HAV in students born in 1976 was 6%, and in students born in 1983 was 0%.<sup>(14)</sup> The study result in Tainan had a trend similar to Taipei, but it took Tainan 4-5 years longer than Taipei to approach 0% prevalence. Our study revealed that the prevalence of anti-HAV in the generation born in 1984 was 0.6% in Taiwan townships with relatively poor economic conditions, and this had decreased to 0% in the generation born in 1993. The downward trend was the same as with metropolitan areas but was delayed. Our investigation enrolled two populations with a birth gap of nine years. It might be representative for Taihsi Township in Yunlin County, but whether it is the same as other areas is uncertain. It may be impossible to know exactly which year the prevalence of anti-HAV decreased to 0%. However, this minor shortcoming will not influence the spirit in which the result of this study should be expressed.

Our study showed the prevalence of anti-HAV in remote areas remains at 0.6% and it is presumed to have decreased to a very low level and become almost 0% in the generation born between 1983 and 1993 in Taiwan. Previous studies also show low prevalence in young subjects in other countries and reveal that this susceptible group is at risk for pandemic eruption.<sup>(21-23)</sup> An outbreak with relatively mild symptoms in children and more serious symptoms in adolescents has been reported.<sup>(24)</sup> In Taiwan, the prevalence of chronic hepatitis B and C is high and is often accompanied by liver cirrhosis. If superinfection with hepatitis A virus occurs, this may lead to fulminant hepatitis.<sup>(25,26)</sup> There have been some outbreak events in recent years which were mainly diet-related, such as in Lin-Kou township in Taipei County in 1982,<sup>(27)</sup> the aboriginal townships of Ilan County in 1991,<sup>(28)</sup> Su-Chi village in Ilan County in 1994,<sup>(29)</sup> Sanmin township in Kaohsiung County in 1993,<sup>(30)</sup> and Taipei City in 2007.<sup>(31)</sup> Although this research only represents the prevalence in a rural township, it should serve as an alert.

There is difficulty in epidemiology research on

HAV vaccination, because anti-HAV is the only marker of hepatitis A. It can be assumed from the positive reaction that the protective antibody is present, but the pathways from a natural infection course and from vaccination cannot be distinguished. If there is a universal program of HAV vaccine, a questionnaire is needed to determine the vaccination history to clarify the prevalence of HAV infection using the anti-HAV marker. In our research, only 0.6% of participants had received HAV vaccination in 2006. In the study of stored blood from earlier generations in 1999, the prevalence of anti-HAV was 0.96% (2/209). Although the HAV vaccination history was not recorded, the opportunity for HAV vaccination of adolescents in rural townships was considered low in the 3 years after the vaccine was first offered, and it is suggested that a natural infection course was responsible for these 2 positive anti-HAV cases. Whether positive anti-HAV is naturally acquired or results from vaccination does not detract from the merits of this investigation. The important point is that the prevalence is low and comparable to that in metropolitan areas.

Based on the low prevalence of anti-HAV in Taiwan, there are three points that should be considered. First, the prevalence of anti-HAV decrease may be associated with improvements in public health. On the other hand, the risk of hepatitis A outbreak has increased. It is not clear if universal HAV vaccination was conducted, but it is suggested that vaccination in high-risk groups be introduced without compulsion.<sup>(32)</sup> Early monitoring of cases of acute hepatitis A for to prevent pandemics is important. Second, due to the progression of global transportation networks, the idea of infectious disease prevention is important. When travellers arrive in an epidemic area, proper vaccination programs should be offered for prevention. Third, maps reporting of the prevalence of anti-HAV by the WHO and the CDC of the United States show that Taiwan is still a high prevalence area. Both research evidence and publicity efforts by the Taiwan government are needed to clarify this misunderstanding.

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## 某鄉間國中生之 A 型肝炎抗體陽性率的演變

陳靜宜<sup>1,2,5</sup> 江瑞錦<sup>1,2,6</sup> 盧勝男<sup>2,3,4</sup> 洪淑芬<sup>3</sup> 高榮達<sup>3,7</sup> 顏毅豪<sup>3,4</sup> 王景弘<sup>3,4</sup>

**背景：** A 型肝炎 (A 肝) 是人與人之間經由糞口途徑傳染的疾病，在抗體盛行率低的地區可能因偶然有感染源傳入而引起暴發流行。在台北都會區小孩的 A 肝抗體 (Anti-HAV) 盛行率下降至幾近於零。然而在經濟條件較不理想的鄉間，Anti-HAV 陽性率為何，有待進一步的釐清。因此本篇研究的目的即在探究鄉間地區 Anti-HAV 陽性率的演變。

**方法：** 分別在 1999 及 2006 年收集雲林縣合西鄉唯一一所國中學生的血清檢體，檢測其 A 肝抗體 (Anti-HAV Ab for Axsym, Abbott, IL, U.S.A.) 來做分析，而這兩群學生分別出生於 1984 至 1985 及 1993 至 1994。

**結果：** 1999 年檢測 1984~1985 年出生之學生，發現其 Anti-HAV 陽性率為 0.96% (2/209)，雖無法得知陽性者的 A 肝疫苗接種史，但推論曾接種疫苗的機會不高。2006 年調查，1993~1994 年出生的學生其 Anti-HAV 的陽性率為 0.6% (1/168)，且此唯一的陽性個案曾經接種過 A 肝疫苗。

**結論：** 本研究顯示在此經濟條件不理想的鄉間，Anti-HAV 陽性率在年輕世代已經降到很低的程度，甚至在 1984 年以後出生的世代已經近乎於零。對於 Anti-HAV 抗體盛行率低的地區避免爆發流行應該是重要的課題。再者，對於擬出境旅遊的國人及入境的旅遊者對我國 A 肝的流行狀態有正確的資訊及建議，也是有必要的。  
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**關鍵詞：** A 型肝炎，台灣，流行病學

長庚醫療財團法人高雄長庚紀念醫院 <sup>1</sup>家庭醫學科，<sup>2</sup>職業醫學科，<sup>3</sup>內科部 胃腸肝膽科系；長庚大學 醫學院 <sup>4</sup>臨床醫學研究所；<sup>5</sup>高雄醫學大學 職業安全衛生研究所；<sup>6</sup>成功大學 環境與職業研究所；<sup>7</sup>中國醫藥大學 胃腸肝膽科

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通訊作者：王景弘醫師，長庚醫療財團法人高雄長庚紀念醫院 內科部 胃腸肝膽科系。高雄縣833鳥松鄉大埤路123號。

Tel.: (07)7317123轉8301; Fax: (07)7322402; E-mail: jinghoung2001@yahoo.com.tw