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Original Article

Current Development and Use of *Japanese Encephalitis* Vaccine

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Abstract

Although the number of JE cases has largely decreased since Taiwan started to fully implement JE vaccination program for young children in 1968, the people infected with JE virus has changed from young children population to young and mid-age adults. Since the population included in national vaccine policy currently is limited only to young children, the adults previously vaccinated with inactivated mouse brain-derived vaccine may have lost their protection levels against JE virus because the degradation of protective antibody and lack of opportunity for natural infection may lead to decrease of neutralizing antibody titers against JE virus. Although progress made in health care delivery has declined case fatality rate of JE, a patient may have been cured but continually suffer from severe and long-term mental and neurological sequels. In recent years, the cases infected with JE virus has shifted to young and mid-age population in Taiwan. Since JE has a bad prognosis, the acquisition of JE will have a big impact on patient himself, patient's family, and society, and become a huge burden on medical cost. Therefore, how to minimize the number of JE cases is one of the most important public health issues right now. A couple of new generation JE vaccines, including inactivated JE vaccine IC51 (IXIARO®/JESPECT®) and recombinant live attenuated JE vaccine ChimeriVax™-JE (IMOJEV®), have been licensed for routine use by countries in Europe, America, and Asia, and have been proved to have a good immune response in vaccinated adults, except having the advantages of that only small number of doses is required and having high safety record. Of the two new generation JE vaccines, IC51 could be given in two doses to adults who never received other JE vaccines or be given as a booster shot to adults who have been vaccinated three or more doses of inactivated mouse brain-derived vaccine, and ChimeriVax™-JE given in one dose could provide protection that lasts as long as ten years, based on statistical prediction. Therefore, to effectively minimize the number of cases infected with JE virus among adults in Taiwan, the use of new generation JE vaccine would be a practical way. However, the safety profile and economic benefits of the new vaccine should be evaluated more carefully, to provide as a reference for policy making decisions.

Keywords: Japanese encephalitis, inactivated mouse brain-derived vaccine

Introduction

In Asia, Japanese encephalitis (JE) virus is the leading cause of viral encephalitis and threatens health of three billion residents in the endemic areas and several million travelers each year. No effective antiviral drugs are currently available for therapy of JE except supportive treatment. Getting vaccinated is the best way to prevent infection with JE virus. In the article, we will review the current development and use of Japanese Encephalitis Vaccine.

First-generation Japanese encephalitis (JE) vaccine

A. Inactivated mouse brain-derived vaccine

Inactivated JE vaccine derived from JE virus infected mice brains was developed in Japan in 1930 and licensed for routine use in Japan in 1954. This inactivated vaccine was developed mostly using either inactivated Nakayama-NIH or Beijing-1(P1) virus strain [1-2,4,5] although it was made mainly from Nakayama-NIH strain in its initial stage. Except Japan, other countries in Southeast Asian regions, such as Taiwan, India, Korea, Thailand, Vietnam, Malaysia, and Sri Lanka, also produced the inactivated mouse brain-derived vaccine for use in her own country [1, 4].

Although the JE vaccine with Nakayama-NIH strain JE virus has good antigenicity, it was found later that the JE vaccine with Beijing-1(P1) strain even provided protection against a wider range of antigenic variants, produced sera with higher titers of virus neutralizing antibody, and was more potent to protect against other types of JE virus than with Nakayama-NIH strain [6]. Therefore, the Nakayama-NIH strain has been replaced by Beijing-1(P1) strain in the production of inactivated mouse brain-derived vaccine in Japan since 1989 [6]. However, JE-Vax® that has obtained licensure for routine use in Europe and the United States since 1993 was still prepared using the Nakayama-NIH strain, for people who will be traveling to JE endemic regions or soldiers who were serving in Southeast Asian regions to get vaccinated [1-2, 4].

In addition, Japan announced to stop using the inactivated mouse brain-derived vaccine in routine vaccination program and to cease production of this type of vaccine in 2005, including JE-Vax®, when a 15 years old juvenile was suspected of having symptoms of acute disseminated encephalomyelitis (ADEM) following administration of the vaccine [1, 5, 7]. As a result, the stockpiled vaccine of the same type in countries around the world was almost used up. The World Health Organization (WHO), in response to this event, indicated that no concrete evidences suggest that the use of inactivated mouse brain-derived vaccine will increase the risk of occurrence of ADEM, no cause-effect relationship between the vaccine and ADEM has been identified, and the probability that a person might suffer from ADEM was ranged between one in every fifty thousand or million people. However, the WHO

recommended that the inactivated mouse brain-derived vaccine should be gradually replaced by newly licensed vaccine under the condition of not changing current vaccine policy [8].

B. Inactivated tissue culture-derived vaccine

A new JE vaccine containing Beijing-3 (P3) vaccine strain grown in primary hamster kidney (PHK) cells was developed in China in 1968. The Beijing-3 (P3) strain became the major vaccine strain used in preparing vaccine for routine vaccination in China before 2000. An estimated more than seven million doses of the vaccine has been administered between 1968 and 2005 [1-3, 5]. However, since the safety of the vaccine made by PHK cells was not recognized by the WHO, the preparation of the vaccine during the subsequent period was using either Vero cells or PHK cells. A total of around three million doses of the vaccine were produced annually for using only in China. However, currently, these vaccines were gradually replaced by live attenuated vaccine [6].

In addition, Japan also actively contributed to the research and development of inactivated JE vaccine that was prepared by using Vero cells in place of mouse brain cells. The newly developed vaccine, BK-VJE®, was licensed by Japan government for routine use in 2009. Up to now, there are two manufacturers that are producing inactivated JE vaccine [22].

C. Live attenuated SA14-14-2 JE vaccine

China started conducting research and development of live attenuated JE vaccine prepared from SA14-14-2 vaccine strain grown in PHK cells in 1970's and gained the licensure for routine use in her country in 1988. The newly developed vaccine subsequently became the major vaccine and replaced the inactivated tissue culture-derived vaccine in the routine vaccination program. Currently, sixteen regions in China are using the live attenuated SA14-14-2 vaccine, eight regions using the inactivated tissue culture-derived vaccine, and three regions using both vaccines while other three regions do not implement routine vaccination program since they are not JE endemic areas [6, 9]. In addition, the live attenuated SA14-14-2 vaccine has gained licensure for routine use in Nepal, India, Sri Lanka, Thailand, and Korea [1, 2, 4-6, 9]. Based on the WHO statistics, the number of the live attenuated JE vaccine accounted for about half of total number of all types of vaccine used in 2005 [2, 4].

Second-generation JE vaccine or novel JE vaccine

In response to the possible adverse effects resulting from vaccination of inactivated mouse brain-derived vaccine and the problems of requiring multiple vaccine doses, the WHO chose the issue of research and development of novel JE vaccine as one of her priority missions [7]. At present, two novel JE vaccines have been licensed for routine use. They are inactivated tissue culture-derived JE vaccine, IC51 (IXIARO®/JESPECT®), and live attenuated JE vaccine, ChimeriVax™-JE (IMOJEV®), that is prepared by using the recombinant chimeric yellow fever-JE virus. Both vaccines have been proved to be safe and

effective, have rare side effects, and need less number of doses, and have gained licensure for routine use in many countries.

A. Inactivated tissue culture-derived JE vaccine IC51 (IXIARO®/JESPECT®)

IC51 (IXIARO®/JESPECT®) is an inactivated tissue culture-derived vaccine developed from Vero cells, consisting of SA14-14-2 strain, which has obtained licensure for use in the United States, Canada, Australia, and Europe in 2009 [2]. For global marketing, the agents engaged in selling vaccine are the India Vaccine Research Institute in India and Pakistan areas, the Commonwealth Serum Laboratories, Australia (CSL) in Australia and New Zealand areas, and Novartis International AG in other areas. However, the United States military can purchase the vaccine through in house charge privilege. The vaccine has been approved to be used for immunization of adults older than 17 years, which two doses administered 28 days apart is recommended. No gelatin and thiomersal has been added in the vaccine manufacturing process and even no mouse protein might probably exist in the vaccine is perhaps the reasons why the vaccine has less side effects than others. However, we still need to continually observe the occurrence of some rarely seen side effects and at the same time to think about the issues of the duration of protection following immunization of the vaccine [7].

B. Live attenuated JE vaccine ChimeriVax™-JE (IMOJEV®)

To develop live attenuated JE vaccine, a ChimeriVax™-JE virus is prepared by using yellow fever (YF) 17D virus as a vector and replacing the premembrane (prM) and envelope (E) genes of yellow fever 17 D viruses with the corresponding genes of the SA14-14-2 strains of JE virus. Laboratory testings have demonstrated that the recombinant viruses are less neurovirulent than yellow fever 17 D virus in mice and non-human primate [2]. Live attenuated JE vaccine is prepared through serial passages of the ChimeriVax™-JE virus in Vero cells. Although the vaccine itself contains live viruses, the viruses are unable to replicate within the body of mosquitoes *Culex Tritaeniorhynchus, Aedes albopictus*, and *Aedes aegypti* when they are ingested by the mosquitoes [11]. Another similar study conducted by Australia in different species of mosquito, *Culex annulirostris*, *Culex gelidus*, and *Aedes vigilax*, also found the same results [12]. These studies indicate that we do not need to fear that spread of the virus through live attenuated ChimeriVax™-JE vaccine can occur. The vaccine has already been approved for routine use in Australia and Thailand [1, 2, 5]. Table 1 presents information on various JE vaccines.

Immunization policy and use of JE vaccine in selected countries

The JE immunization programs conducted for children in Asian countries, such as Japan, Korea, Taiwan and China, Thailand, Sri Lanka, and Nepal have obviously decreased the number of JE cases in their countries [1, 9]. Among these countries, Japan, Korea, and Taiwan have the most significant reduction in the number of JE cases, and China and Thailand also presents an obvious decreasing trend in the annual number of confirmed cases.

Table 1. List of different types of JE vaccines

	Types of vaccine	Culture media for vaccine virus	Strains of virus in vaccine	Vaccine manufacturers	No. of doses for primary series	Countries having approved the vaccine for routine use	Remarks
First-generation JE vaccine	Inactivated vaccine	Mouse brain	Nakayama or Beijing-1(P1)	Japan, Thailand, India, South Korea, Taiwan, Vietnam, Malaysia, and Sri Lanka	3	JE-VAX® (Nakayama): the U. S., Australia, and Europe	Japan has ceased the production of JE-VAX® in 2005. Whether having inventory in the market is unknown.
		Vero cell	Beijing-1(P1)	Japan	2	BK-VJE®(2009) and ENCEVAC® (2011):Japan	
		primary hamster kidney cell or Vero cell	Beijing-3(P3)	China	3	China	
	Live attenuated vaccine	primary hamster kidney cell	SA14-14-2	China (1988)	1	Nepal, India, Sri Lanka, and South Korea	
Second-generation JE vaccine (novel JE vaccine)	Inactivated vaccine	Vero cell	SA14-14-2	Manufactured by Intercell Biomedical, UK, and marketed by Novartis in the U.S.	2	IXIARO® /JESPECT®(2009): the U.S., Europe, Canada, Switzerland, Hong Kong, and Australia	Approved for use in adults over 17 years of age
	Live attenuated vaccine		Recombinant virus by replacing the prM and E genes of YF 17 D viruses with the corresponding genes of the SA14-14-2 strains	Sanofi Pasteur, France	1	ChimeriVax™ -JE (IMOJEV®)(2010): Australia and Thailand	Approved for use in people older than 12 months of age

However, the vaccine policy and immunization schedule for JE vaccine, and the component of JE vaccine used for immunization program are not completely identical among these countries.

In most of the Asian countries, the JE vaccines are prepared from Nakayama-NIH strain of JE virus, usually licensed for young children aged 12-36 months, and administered in a two-dose primary series separated by one to four weeks. Then, a booster shot will be given one year after receipt of the final dose of primary series and another booster every 1-3 years

after receipt of the last booster. The age group for routine immunization, vaccination schedule, and number of booster doses of JE vaccine in selected countries are described as follows Table 2.

A. Inactivated mouse brain-derived vaccine

The Nakayama-NIH strain has been replaced by Beijing-1(P1) strain for production of inactivated mouse brain-derived JE vaccine in Japan since 1989. Since the JE vaccine prepared from Beijing-1 strain provides protection against a wider range of antigenic variants and has higher vaccine effectiveness, the dose volume for routine vaccination of the vaccine prepared from Beijing-1 strain is only half of that of the vaccine from Nakayama-NIH strain. The vaccine is mainly offered to those of young children around 3 years of age, is given as a two-dose primary series (with 1 to 4 weeks apart). A booster shot is administred 6-12 months after receipt of the final dose of primary series and another booster shot at the age of 9-10 years, with a total of four doses [9]. When Japan government resumed the implementation of vaccination program in 2009, the inactivated Vero cell culture-derived vaccine instead of inactivated mouse brain-derived vaccine was provided for routine vaccination, with a total of four doses as before.

Table 2. Summary on JE vaccination program in selected countries

Countries	Types of vaccines/vaccine strain	Age to get first shot	Total No. of shots	Vaccination schedule
Japan	Inactivated Vero cell culture-derived vaccine/Beijing-1(P1) strain	Around 3 years of age	4	Two-dose primary series given at around age 3 Two booster shots given 6-12 months after the final dose of primary series and at age 9-10, respectively
South Korea	Inactivated mouse brain-derived vaccine/Nakayama-NIH strain	1 year of age	5	Three-dose primary series given at age 1 Two booster shots given at age 6 and 12, respectively
Taiwan	Inactivated mouse brain-derived vaccine/Nakayama-NIH strain	15-27 months of age	4	Three-dose primary series given at 15-27 months with an interval of two weeks and one year between previous dose Booster shot given between at real age 5 and before entry into elementary school
Thailand	Inactivated mouse brain-derived vaccine/Beijing-1(P1) strain	18-24 months of age	3	Two-dose primary series given at age 18-24 months, one month apart Booster shot given 1 year after the final dose of primary series (or between age 2.5 and 3)
China	Inactivated Vero cell or PHK cell culture-drived vaccine/Beijing-3 strain	1 year of age	5	Three-dose primary series given at an interval of two weeks and one year between previous dose Two booster shots given at age 6 and 10, respectively
China	Live attenuated PHK cell culture-derived vaccine/SA14-14-2 strain	8 months of age	3	First dose given at age 8 months Two booster shots given at an interval of two and seven years between previous dose
Europe, U.S., Canada, Switzerland, Hong Kong, and Australia	Inactivated Vero cell culture-derived vaccine/SA14-14-2 strain (IXIARO®)	17 years of age and older	2	To be administered 28 days apart
Australia, Thailand	Live attenuated Vero cell culture-derived vaccine/ Chimeri YF/JE SA14-14-2strain (IMOJEV®)	12 months of age and older	1	

In South Korea, the JE vaccine was prepared from Nakayama-NIH strain of JE virus and was given to young children aged 3 years for routine vaccination that started in 1983. It was recommended that a total of 14 doses should be administered before the age of 15. Because society was questioning that the increase in reported adverse events following vaccination might be caused by the overuse of the vaccine, the coverage for JE vaccination was constantly decreasing. Therefore, the Korea governments revised their vaccine policy by reducing the total number of doses from 14 to 8 in 1994, and revised again by reducing from 8 to 5, including a 3-dose primary series administered at 1 year of age and two booster shots given at the age of 6 and 12, respectively [9, 13].

The JE vaccine is also prepared with Nakayama-NIH strain in Taiwan, which is mainly licensed for use in young children at 15-27 months of age. The vaccination schedule includes a 3-dose primary series and a booster shot, with a total of 4 doses. The first two doses, two weeks apart, is given to children at the age of 15-27 months, the third dose is administered one year after the receipt of the last dose, and the last dose, booster shot, is given before entering elementary school [14]. Starting in 2013, the governments required that children should receive booster shot during the time when they are at the real age of 5 and before they are entering elementary school. In Thailand, the primary two doses of JE vaccine given one month apart is administered to young children aged 18-24 months and a booster shot given one year after the last primary dose (or at the age of 2.5-3), with a total of three doses. The Nakayama-NIH strain used for production of JE vaccine was replaced by Beijing-1(P1) strain in 1989.

B. Inactivated tissue culture-derived vaccine

An inactivated tissue culture-derived JE vaccine is prepared using Beijing-3 strain in China and is approved for immunization of baby at one year of age with two primary doses, two weeks apart, and the third dose one year after receipt of second dose, an then two booster shots given at the age of six and ten, respectively, with a total of five doses.

C. Live attenuated SA14-14-2 vaccine

The live attenuated JE vaccine made from the SA14-14-2 strain is approved for routine vaccination in China, which the first dose is administered to baby at the age of eight months and two booster shots are given two and seven years after receipt of previous dose, respectively, with a total of three doses. Currently, the live attenuated SA14-14-2 vaccine has become the major type of vaccine used for routine vaccination in children [9]. Moreover, the vaccine has been licensed for routine use in Nepal, India, Sri Lanka, and South Korea, and is the one with the largest number of doses being used currently.

D. Novel JE vaccine

The IXIARO® is currently approved for use in adults over the age of 17, with a total of two doses, 28 days apart. The IMOJEV®, another novel vaccine, is a type of live attenuated vaccine approved for use in young children aged more than 12 months and adults, and requires only a one-dose primary dose. The novel JE vaccine has now been approved by the

U.S., Australia, and Europan countries for use in laboratory workers, or people travelling to and soldiers serving in JE endemic areas.

Vaccine effectiveness and side effect

A. Inactivated mouse brain-derived vaccine

A large-scale evaluation of inactivated mouse brain-derived JE vaccine conducted by Thailand in 1980 shows that the vaccine effectiveness after two doses reached as high as 91% among children [19]. In Taiwan, similar evaluation conducted in 1999 shows that the effectiveness of JE vaccine was 85% among Japanese encephalitis confirmed cases receiving two or more doses, and, in another study, the effectiveness after three doses was 95.54% [23].

Based on previous reports, 20% of the people receiving inactivated mouse brain-derived vaccine had side effects, including redness, swelling, and pain, at the injection sites, and 10% presented general side effects of moderate intensity, such as fever, chills, headache, rash, and muscle pain [8, 15]. Severe adverse events and occasionally hospitalized cases associated with vaccine have constantly been reported since 1989 [1]. The adverse effects commonly seen include urticaria and angioedema, with an incidence of 1-17 cases per ten thousand people [2, 7]. In addition, statistics obtained from 99,000 JE vaccine reipients in Germany, Sweden, United Kingdom, Australia, Canada, and the U.S. found that 0.7-104 persons per ten thousand recipients presented allergic reaction [5]. It is generally thought that the adverse effects might result from reactions to the gelatin, thimerosal, and mouse serum proteins contained in the vaccine, but the real reasons are still unclear. In the United States, incidence rate of adverse effects associated with JE vaccine was 24 persons per hundred thousand people during 1999-2009, 35% of them with allergic reactions and 1% with neurological symptoms [15]. In Germany, the incidence rate of adverse effects was 1-17 persons per ten thousand people during 1983-1995 [16].

Since the case definition and investigation methods applied to the evaluation of vaccine-associated allergic reactions were different, the findings among different countries were not fully consistent. Generally, the incidence rate of severe adverse effects caused by vaccine was roughly 10 to 260 persons per hundred thousand population among these countries, the incidence rate of moderate to severe neurological diseases, such as encephalitis, epilepsy, gait disturbances, and Parkinson's disease, was 0.1-2 cases per hundred thousand population [8]. Besides, cases with symptoms of temporary ADEM following JE vaccination were also reported among children in Japan and Korea [8, 13].

B. Inactivated tissue culture-derived vaccine

Some studies indicate that the efficacy of PHK cell culture-derived JE vaccine produced by China at an earlier stage was ranged from 76% to 95%, around 4% of the recipients had local adverse effects, 1% presented moderate general symptoms, and the probability of occurring allergic reactions like urticaria was 1/15,000 [1, 5]. The vaccine is currently approved only for use in China.

C. Live attenuated SA14-14-2 vaccine

The evaluation of live attenuated SA14-14-2 vaccine conducted in Sichuan, China in 1993 demonstered that the vaccine offered 80% effectiveness after one shot and 97.5% after receipt of one booster shot given at an interval of one year since previous shot [9]. A large scale evaluation indicates that the vaccine effectiveness was ranged between 88% and 96%, but the incidence rate of adverse events was very low, in the range 0.2% to 6% [1, 9]. Furthermore, an evaluation performed one and five years after receipt of one dose in Nepal shows that the vaccine effectiveness was 98.5% one year after the shot and maintained its high effectiveness, 96%, five years after the shot [17]. To evaluate vaccine safety, a randomized, case-control study was conducted among 26,239 children in Chengdu, China in 1995. The study found that the incidence rate of adverse effects is not significantly different between cases and controls. This supports that the live attenuated SA14-14-2 vaccine actually has a better safety profile than others [10].

D. Novel JE vaccine

a. IC51 (IXIARO®/JESPECT®)

An international, multi-center, randomized, bouble-blind, case-control study implemented during 2005-2006 revealed that the safety of IXIARO® was comparable to that of controlled injection. Moreover, a multi-national, randomized, case-control study conducted in the U.S., Germany, and Australia in 2006 indicates that, 56 days after getting vaccinated, either in seroconversion rates (98% vs. 95%), antibody titers, or safety, IXIARO® is better than JE-Vax®[1, 8, 10]. In addition, a study conducted to compare the safety of IXIARO®, JE-Vax® and controlled injections also found that IXIARO® has a higher safety profile than JE-Vax®[18]. A small-scale study implemented among the U.S. soldiers in 2012 demonstrated that the neutralizing antibody titers measured in soldiers who were given one dose of IXIARO® following the vaccination of three or more doses of inactivated mouse brain-derived vaccine were obviously higher than those in soldiers who were never vaccinated with inactivated mouse brain-derived vaccine but received only two doses of IXIARO®. These findings support that IXIARO® has good immunization effectiveness when it is given as a booster shot for adults, especially for those who ever received three or more inactivated mouse brain-derived vaccine. However, researchers also recommended that further studies regarding immunization effectiveness in different population and long-term effectiveness of the vaccine should be conducted [20,25].

b. Live attenuated ChimeriVax™-JE(IMOJEV®)

A randomized, double-blind, case-conrol study was undertaken in Australia and the U.S. during 2005-2006 by dividing the subjects into two major groups including four subgroups (IMOJEV® vs. JE-Vax® and IMOJEV® vs. placebo) to compare the efficacy of IMOJEV®, JE-Vax®, and placebo injection. The study found that one dose of IMOJEV® has better results than three doses of JE-Vax® either in seroconversion rate (99.1% vs.95.1%) or

occurrence of adverse effects [5]. During 2003-2008, Australia conducted a randomized, bouble-blind, crossover design study in adult subjects, which found that the seroconversion rate measured at 28 days and six months after the study subjects were given one dose of IMOJEV® was 99% and 97%, respectively [5]. In 2009, a cross-nation study was carried out in the U.S., Thailand, and Philippines to evaluate the vaccine effectiveness in subjects, including 1,400 children and 2,400 adults, receiving one dose of IMOJEV®. As a result, a vaccine effectiveness of 94% and 99% was observed at 14 days and one month after vaccination, respectively [1-2]. To evaluate long-term effectiveness, a follow-up study of adult population was conducted in Australia in 2012. The study shows that the vaccine still provided protection against JE virus even five years after receipt of one dose of the vaccine. The estimates obtained using the statistical model indicate that the protection can last as long as ten years [21]. Although no problems related to vaccine safety have been identified currently, we could not exclude the possibility of occurring severe adverse effects.

Conclusions

Taiwan started to fully implement JE vaccination program for young children in 1968 and has been using the Nakayama-NIH vaccine strain to produce inactivated mouse brain-derived vaccine since then. In the last ten years, the annual number of confirmed JE cases ranged between 20 and 30 in Taiwan. More than 76% of them are young and mid-age adults aged more than 30 years. The people infected with JE virus changed from young children population to young and mid-age adult, i.e., economically productive population. Although progress made in health care delivery has declined case fatality rate of JE, severe sequelae, such as permanent neurological symptoms or psychiatric anomaly, are still a huge burden of JE in terms of patient's health, patient's family, and social economy. These are issues that we ought to face them seriously. Since no effective antiviral drug are available for treatment of JE virus infections, getting vaccinated has become the only way that can effectively prevent infction of JE virus. Moreover, except having the advantages of that only small number of doses is required and having high safety record, the new generation JE vaccine has broken through the limitations that most of the JE vaccine is licensed for only use in young children and teenagers, and has been approved for adults and even population in all age groups. For example, studies conducted either in the U.S. or Europe demonstrated that IXIARO® given in two doses in adult could induce a good immune response. Furthermore, one dose of IXIARO® given to people who received three or more doses of inactivated mouse brain-derived vaccine produce a higher level of neutralizing antibody titers than two doses of IXIARO® administered to people who never getting vaccinated with inactivated mouse brain-derived vaccine. Prediction made by statistical model shows that only one dose of live attenuated IMOJEV® could provide protection that lasts as long as ten years or longer and have greater safety profile and effectiveness than inactivated mouse brain-derived vaccine. Therefore, new generation JE vaccine would be a good choice to protect against JE virus infection.

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Outbreak Investigation Express

Varicella Outbreak in a Child Day Care Center, Hsinchu County, January 2013

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Abstract

Five varicella cases, including four children and one teacher (age range: 1 year 5 months – 29 years) in a child day care center in Hsinchu county were reported within a month during 2012 – 2013. The overall attack rate was 6%. After investigating the incubation period, communicable period, and possible exposure period of the cases, varicella outbreak was confirmed. Case 1 (index case, primary case of varicella infection) probably transmitted varicella to case 2 (secondary infection) and case 3, 4, and 5 became infected from case 2 (tertiary infections). We conducted contact investigation of the contacts in the child day care center, including the children and staff, and assessed staff pregnancy status, chickenpox infection history and immunization record. Environmental investigation showed that the probable site of disease transmission was the pick-up area on the first floor. Our control measures included case isolation and follow-up, contact tracing and education for the children and staff in the center, and investigation and contact tracing of the contacts in families and the clinic. For varicella outbreak investigations, we recommend that public health authorities and associated organizations should monitor high-risk contacts closely, especially pregnant women, and consider using post-exposure prophylaxis. Knowledge on varicella infections and immunity should also be strengthened for staff in child day care centers and high-risk populations to prevent future varicella outbreaks.

Key words: Varicella (Chickenpox), Child day care center, outbreak

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