

. . . . * . † . ‡
, †, + ,

= Abstract =

**Persistency of Neutralizing Antibody to Inactivated Mouse
Brain Derived Nakayama Japanese Encephalitis Vaccine and
Current Observations of Booster Vaccination and Adverse Events**

Young Mo Sohn, M.D., Ji Ho Park, M.D., Jin Soo Lee, M.D.
Hye Ok Roh, M.D., Moran Ki, M.D.^{*}, Bo Yul Choi, M.D.[†]
and Young Ho Kim[‡]

*Department of Pediatrics, College of Medicine, Yonsei University, Seoul,
Department of Preventive Medicine^{*}, College of Medicine, Eulji University, Daejeon,
Department of Preventive Medicine[†], College of Medicine, Hanyang University, Seoul,
Mapo Public Health Center[‡], Seoul, Korea*

Purpose : We need to reconsider booster vaccination schedule of Japanese encephalitis vaccination. To do that we evaluate the long-term immunogenicity and the incidence of adverse events with inactivated mouse brain derived Nakayama Japanese encephalitis vaccine.

Methods : We tested neutralizing antibody for 311 elementary school students by plaque reduction neutralizing test(PRNT) at USAMC-AFRIMS(United States Armed Forces Research Institute of Medical Science/Department of Virology). We evaluated vaccine related adverse events by spontaneous reporting prospectively among 15,487 vaccinees who were vaccinated at public health center and 2,277 elementary school students who were immunized previously by a questionnaire and school health record.

Results : According to the time interval from the last booster injection of 311 children, PRNT antibody titers gradually decreased as the interval increased; 239 mIU/mL, 188 mIU/mL, 134 mIU/mL, 49 mIU/mL each at 6, 18, 30, 42 months after the last booster injection. The seropositivity rates were 98%, 99%, 95.6%, 71.4% each at 6, 18, 30, 42 months after the last booster injection. There were 21(0.13%) cases with systemic reactions among 15,487 vaccinees who had visited the hospital by prospective passive reporting system at public health center. According to the questionnaires and school health records in elementary school students, local induration and pain were 17.4% and 14.8%, respectively. Systemic reactions including fever, vomiting, rash were reported in few cases.

1998

Tel : (02)3497-3350 Fax : (02)3461-9473 E-mail : youngmo@yumc.yonsei.ac.kr

Conclusion : Biannual booster vaccination that has been recommended so far should not be necessary. Surveillance for adverse events with inactivated mouse brain derived Nakayama vaccine should be strengthened to better assess the number of cases and reactions associated with immunization.

Key Words : JEV, Vaccination, Neutralizing antibody, Persistency

(JE) 1. 가
 35,000 1996 8 2,277
 10,000 1, 2) -70
 가 311 가
 , (Plaque
 가 reduction neutralizing antibody test, PRNT) United
 가 States Armed Forces Research Institute of Medical
 가 Science, Department of Virology, Bangkok(USAMC-
 AFRIMS) 50%
 1 : 10 .
 가 2. 가
 가 가 가 8 (, , ,
 가 , , , ,) 1 6
 가 1 2,277
 3 6 .
 90 , 15 27 , 18 24 , ()
 가 12 가
 , 14 15 2 6 , 3 .
 7 1 가 .
 가 1995 5 6
 15,487 .
 Nakayama ,
 가 , 1996 5 6
 8 .

2. 가

1) 2,277

1. 가

가 가 311

가 가 4 47.5% 1,906

. 가 6 93.5%

1, 18 2, 30 3, 42 가 ($P<0.05$)(Table 2).

4 155, 가 가

104, 45, 7 . 1 95 96

98.1%(152/155), 2 99.0%(103/104), 3 95.6 75.6%

%(43/45), 4 71.4%(5/7) 가 ($r=0.268$)(Table 3).

(Table 1).

2) 2,277

Geometric Mean Titer(GMT) 1 239 가 1,176 48.5%, 가 1,101

mIU/mL, 2 188 mIU/mL, 3 134 mIU/mL, 46.4% 가 ($P>$

4 49 mIU/mL 4 가가 0.05)(Table 4).

1 3 가

가 (ANOVA, $P<0.01$). 3) 가

94 가

Table 1. Neutralizing Antibody Seropositive Rate Among the Vaccinees who had been Immunized with Booster Injection

Group	Time interval from the last booster injection	Seropositive rate		PRNT Ab titer	
		(No. of positive cases/ No. of cases)	95% CI	(mIU/mL) (GMT)*	95% CI
1	6 month	98.1(152/155)	94.5 99.6	239	197 291
2	18 month	99.0(103/104)	94.8 99.9	188	144 245
3	30 month	95.6(43/45)	84.9 99.5	134	90 198
4	42 month	71.4(5/7)	29.0 96.3	49	9 284

* $P<0.01$

Table 2. Immunization Rate According to a School Health Records and a Questionnaire

	Health records		Questionnaire	
	No. of subjects	Immunization rate(%)	No. of subjects	Immunization rate(%)
City	1313	61.8	1,170	93.8
County	964	27.9	736	92.9
Total	2277	47.5	1,906	93.5

$P=0.038$

Table 3. Immunization Rate According to School Health Records and Questionnaires at 1995 and 1996

Confirmed by health record	No. of subjects	Confirmed by questionnaire			
		Not V* at 95, 96	V* at 95 only	V* at 96 only	V* both at 95 & 96
Not V* at 95, 96	589	14.3%	33.3%	14.4%	38.0%
V* at 95 only	647	9.6%	30.3%	9.0%	51.2%
V* at 96 only	462	9.5%	12.3%	23.2%	55.0%
V* both at 95 & 96	45	4.4%	11.1%	8.9%	75.6%

*V. : vaccinated

Table 4. Immunization Rate According to Sex in Preschool Children

	No. of subjects	Immunization rate(%)
Male	1,176	48.5
Female	1,101	46.4
Total	2,277	100.0

P>0.05

(P=0.711)(Table 5).

가

가

(P<0.05)(Table 6). 가

가 (P=0.256)
(Table 7).

4)

가 60.1% 가

가 25.1%, 가 14.1%
(P<0.01)(Table 8).

3.

1995 5 6
15,487

21

가

Table 9 . 21 (0.13%)

Table 5. Immunization Rate According to Year of School Entrance

Year	No. of subjects	Immunization rate
1996	331	26.6
1995	330	54.5
1994	325	29.5
1993	424	53.5
1992	418	52.2
1991	449	46.1
Total	2,277	47.5

P=0.711

Table 6. Booster Immunization Rate According to Year of School Entrance

Year	No. of subjects	Immunization rate according to a number of booster injection(%)					
		One	Two	Three	Four	Five	Six
96	235	98.3					
95	254	89.4	9.1				
94	306	40.5	58.2	1.3			
93	414	5.6	28.5	65.2	0.2		
92	402	3.2	10.7	33.1	48.8	4.2	
91	437	1.6	2.5	14.0	41.9	38.9	1.1
Total	2,048	30.5	18.2	22.9	18.6	9.1	0.2

P<0.05

0.02%

0.03%

57%

1

3

. 1996

(syncopal attack)

Table 7. Immunization Rate According to Year of School Entrance and Year of the Last Booster Vaccine Injection

Year of school entrance	Immunization rate at each year of school entrance(%)	Immunization rate at each year of the last booster vaccine injection(%)						
		1996	1995	1994	1993	1992	1991	1990
96	91.2	68.3	52.6	54.4	41.7	36.6	27.2	21.8
95	95.3	59.8	58.5	49.1	44.8	32.7	26.4	20.9
94	93.2	76.5	55.4	52.9	45.5	36.0	30.2	27.4
93	94.1	56.7	59.2	50.0	50.7	38.7	31.8	28.8
92	93.3	70.0	64.8	64.1	57.2	52.6	43.5	38.0
91	93.8	55.3	65.9	63.3	59.7	52.3	50.6	41.2
Total	93.5	62.6	59.9	56.1	50.8	42.4	36.0	30.6

P<0.05

Table 8. Place where the Subjects were Vaccinated at 1996

Place of immunization	No. of subjects	%
Clinic, Hospital	208	14.1
Public health center	370	25.1
School	885	60.1
Others	9	0.7
Total	1,472	100.0

P<0.01

17.4%, 14.8%, 4.3% (Table 10).

1967 , 1/3 가 1983 (Nakayama) 가 3, 4) 가 1 5 1985 1 4 1994 10 18 5).

, 1994 가 가 , 6 90 3 가 2 15 27 2 2 가 , 18 3 1 가 2000 3 2 가 Nakayama 가 data가 5 가 가 가 Hemagglutinin Inhibition(HI) 가 (plaque reduction neutralizing test, PRNT) . HI

Table 9. Adverse Events after Inactivated JE Vaccine from May to June in 1995 at Public Health Center

Case	Name	Age	Sex	Date of vaccination	Onset of symptom	Symptom	Treatment
1	SSY	10	M	5/16	5/17	Fever(38.7)	Hospital visit
2	JEH	6	F	5/16	5/17	Fever(38.7)	Hospital visit
3	KSB	12	F	5/17	5/18	Syncope 3 min. after the injection	Resuscitation, recover
4	SHJ	15	F	5/17	5/18	Vomiting	Medication
5	SMS	7	M	5/17	5/19	Fever, Swelling on injection site	Medication
6	NYH	8	F	5/17	5/19	Fever	Hospital visit
7	SDK	4	M	5/17	5/19	Fever, Vomiting	Hospital visit
8	SSJ	13	F	5/18	5/19	Fever(39.0)	Hospital visit
9	SSC	9	F	5/18	5/19	Fever(38.5)	Hospital visit
10	LJY	5	M	5/18	5/19	Fever(38.5)	Hospital visit
11	LKJ	7	M	5/22	5/23	Fever(38.5)	Hospital visit
12	LJH	5	F	5/23	5/24	Fever(38.5)	Hospital visit
13	AJH	7	M	5/24	5/25	Swelling on injection site, Urticaria	Medication
14	CHC	9	M	5/24	5/25	Swelling on injection site, Urticaria	Medication
15	LMH	14	F	5/24	5/27	Fever, Sore throat, Cough	Hospital visit
16	LJY	5	F	5/29	5/29	Fever	Hospital visit
17	HKJ	15	M	6/9	6/10	Swelling on injection site, Urticaria	Hospital visit
18	ANM	8	M	6/13	6/13	Vomiting	Medication
19	MJY	10	F	6/15	6/16	Swelling on injection site	Medication
20	KYS	9	M	6/19	6/20	Vomiting, Diarrhea	Hospital visit
21	LAR	9	F	6/21	6/22	Fever, Swelling on injection site	Hospital visit

Table 10. Adverse Events after Inactivated JE Vaccine from May to June in 1996 at Primary School Children Survey

Adverse events	%
Local erythema, induration	17.4
Injection site pain	14.8
Fever	4.3
Dizziness, headache	1.8
Hospital visit	0.8
Abdominal pain, vomiting	0.6
Skin rash	0.3

50%가

90%

.

94 100%

3

33 77%

6 9)

가

1 2

2

50%

12

1

3

(cut-off value)

1: 10

가

가

3

, 가 ,

^{10 12)} Advisory Committee of

가

Immunization Practice(ACIP) 0, 7, 30

¹³⁾ 0, 7, 14

37 3

가 가

가가

¹⁰⁾ 가

¹¹⁾

1994 4 5

가

5 가

가

가 30

95.6%(95% CI 84.9 99.5%)

가

가 134

가

2

42

71.4%

가

가

1994

가

가

가

3

가

1 2

2

5

(

가

가 1:10

) 가

가

85

95

10

가

8

가

12

3 가

(60)

가

900

가가

1 가

1

4

6

가

1

90%

2 3

가

가

¹⁴⁾

가

1994

¹⁵⁾

가

10

가

1

가

(

HI

가

3

1.7 /)

94 (5 8)

93

(1

(5 8)

94

10

가 5 10)

가

70%

가

1994

HI (>10⁻¹)

GMT

18.8(93

), 17.7(94

)

가

1995

1996

가

가 1:20

가

1

1

boosting

¹⁶⁾

39

가
 : 15,487
 2,277
 311
 United States Armed
 Forces Research Institute of Medical Science/Depart-
 ment of Virology, Bangkok(USAMC-AFRIMS)
 50% 1 : 10
 : 2,277
 47.5%
 93.5% 가
 48.5%, 46.4%
 가 가
 가 가
 가 가
 95 96
 75.6% 가
 가 60.1% 가
 가 25.1%, 14.1%
 . 1995 5 6
 15,487
 0.13%
 57% 1
 3
 0.02%
 0.03%
 . 1996
 17.4%,
 14.8%, 4.3%
 311
 6
 (1)가 155 , 18 (2
) 104 , 30 (3) 45 , 42
 (4)가 7
 1 98.1%(152/ 155), 2 99.0%(103/

104), 3 95.6%(43/45), 4 71.4%(5/7)
 :
 가
 1) Monath TP. Japanese encephalitis - a plaque of
 the orient. N Engl J Med 1988;319:641-3.
 2) 86 1986;1:
 40-1.
 3) , , .
 1967:55-2.
 4) , . HI
 1979;22:113-9.
 5) 4 .
 1997;93-102.
 6) , , .
 HI
 1980;10:65-9.
 7) , , .
 1983;20:119-23.
 8) , .
 , 1984 1985.
 1986;15:1-9.
 9) , , . 1987
 HI
 1989;19:41-7.
 10) Poland JD, Cropp CB, Craven RB, Monath TP.
 Evaluation of the potency and safety of inacti-
 vated Japanese encephalitis vaccine in U.S. in-
 habitants. J Infect Dis 1990;161:878-82.
 11) Gambel JM, DeFraités R, Hoke C, Brown A,
 Karabatsos N, Tsai T, et al. Japanese encephal-
 itis vaccine : Persistence of antibody up to 3
 years after a three-dose primary series. J Infect
 Dis 1995;171:1074.
 12) Sanchez JL, Hoke CH, McCowan J, DeFraités
 RF, Takafuji ET, Diniega BM, et al. Further

