Studies on Epidemics of Influenza —Relationship Between the Closure of Some or Whole Classes of the School and the time or Rate of Inoculation with Influenza Vaccine—

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Summary

A survey was conducted on the closure of some or whole classes of a grade in 66 primary and lower secondary schools operated by the Ward of Suginami, Tokyo, during the epidemic period of influenza-like disease in four years, 1979 to 1982. Therefore, the cumulative number of schools surveyed was 264 for the four years. In these schools was surveyed the relationship between the class closure in 1979~1983 and the time of inoculation of influenza vaccine or the rate of inoculation. The results obtained are summarized as follows.

1) In the 264 schools, the second inoculation of influenza vaccine was finished in 203 schools (76.8%) in November and in 61 schools (23.2%) in December. The closure of some or whole classes of a grade occurred in 125 schools (61.6%) of the former 203 schools and in 20 schools (32.7%) of the latter 61 schools. Accordingly, it took place significantly more frequently ($p<0.001$) in the former than in the latter.

2) Of the 264 schools, 145 schools (54.9%) experienced class closure (group C), but the other 119 schools (45.1%) did not (group N). The average rates of the first and the second inoculation were 86.7% and 77.3%, respectively, in group C and 88.0 and 78.9%, respectively, in group N. Therefore, the average rate of the second inoculation was significantly lower ($p<0.01$) than that of the first inoculation in both groups.

3) The interval between the two inoculations was 8~14 days in 136 schools (51.5%) and 15~21 days in 90 schools (34.1%) of the 264 schools.

From the results mentioned above it was concluded to be necessary for the further enhancement of the immune effect of the existing HA vaccine to make the interval between the first and the second inoculation 4 weeks, to perform the second inoculation about one month prior to the beginning of an epidemic period (from the end of January to that of February), and to increase the rate of the second inoculation.

Introduction

There has been a rapid decrease in incidence of many acute infectious diseases. A large number of patients, however, have been suffering from influenza almost every year. The reasons for such high incidence are that the etiological virus attacks the respiratory system, showing a very high transmissibility, that antigen variation takes place continuously or discontinuosly, and that the land is too densely populated.

In Japan, a large group of schools, especially primary and lower secondary schools, is considered to contributed much to the enhancement of epidemic of influenza[1]. Therefore, a collective vaccination program has been performed in this group.

In general, signs predicting an epidemic of influenza are noticed in Japan about the middle of October or a

little later every year. One of them is an outbreak of "collective common cold" which causes the closure of some or whole classes of a primary, lower secondary, or other school. Another is the isolation of influenza virus from children of such school affected with "the common-cold-like disease complex" to confirm the incidence of influenza.

Such being the case, the existing vaccination program is started with the first inoculation nearly at the beginning of October every year. The second inoculation is carried out 1~4 weeks later. Therfore, the program is finished mostly in the group of schools in November.

The efficacy of the program has frequently been discussed from a clinical or serological point of view. It cannot be denied that the existing program is not always free from a doubt about its efficacy.

The present survey was conducted to examine the relationship between the period of a vaccination program against influenza or the interval between the two inoculations and the closure of some or whole classes of a school in the primary and lower secondary schools operated by a local government in Tokyo.

Materials and Methods

Materials were collected from 66 schools located in Suginami Ward, Tokyo, and operated by the Ward Offce. These schools consisted of 43 primary and 23 lower secondary schoools. Information was provided by the Health Department of the Ward Office on the vaccination programs in four years, 1979~1982, and the closure of some or whole classes of a school in these schools over the epidemic of influenza-like disease in 1979~1983.

In the survey, the relationship between the period or interval of inoculation with influenza vaccine and the closure of some or whole classes of a school was examined in the 66 schools by the month of inoculation or the interval between the two inoculation. When necessary, the chi-square and t-tests were carried out to detect a statistically significant difference.

In the statistical analysis the data obtained from the 66 schools for 4 years were regarded as those obtained from 264 schools for a year. Hereinafter, the closure of whole classes indicates not that of a school but that of only one grade of the school.

Results

1. Vaccination program and rate of inoculation.

Table 1 presents the date of inoculation in the 264 schools over a period of 1979 to 1982. The first inoculation was preformed in 17 schools (6.4%) in October, in 246 schools (93.2%) in November, and in only one school (0.4%) in December. In other words, it was carried out in most schools in November. Besides, it was conducted in 168 schools (63.6%) of the 264 between 1st and 15th, inclusive, of November. Accordingly, it was performed in 185 schools (about 70%), including the 17 schools where it was performed in October, by November 15.

The second inoculation was finished in 203 schools (76.8%) of the 264 by the end of November and in the other 61 schools (23.2%) in December. It was completed in 184 schools (90.6%) of the 203, or in 69.7% of the 264 schools, between 16th and 30th, inclusive, of November.

Table 2 shows the occurrence of the closure of some or whole classes of one grade during the four epidemics of influenza over a period of 1979 to 1983, as classified by the rate of vaccination. (In the present survey, when some or whole classes of the same grade were closed twice or more in the same school during one and the same epidemic, it was recorded that only one class closure had taken place in the school during the epidemic.)

The 264 schools were divided into two groups, A and B, of 145 and 119 schools, respectively. Group A experienced class closure, but group B did not. The rate of the first inoculation exceeded 80% in 130 schools (89.7%) of group A and in 112 schools (94.1%) of group B. The rate of the second inoculation exceeded 80%

Table 1 Annual distribution of the day inoculation with vaccine

Date	Yeat	1979	1980	1981	1982	Total	1979	1980	1981	1982	Total
10.	22				1	1					
	23										
	24		2			2					
	25										
	26			1	2	3					
	27		1			1					
	28										
	29			1	2	3					
	30	1	1	1		3		The second inoculation			
	31	2	2			4					
11.	1	1			2	3					
	2	1		3	6	10					
	3										
	4		3	3	6	12					
	5	4	1	4	2	11				1	1
	6	5	8	5		18					
	7	2	7			9					
	8	10			5	15					
	9	8		5	7	20				1	1
	10		5	6		11		1	1		2
	11		11	1		12				1	1
	12	2	2	4	5	13	2		2	2	6
	13	9	6	5		20		2	1		3
	14	3	3			6		2			2
	15	4			4	8				3	3
	16	3		2	6	11	1		1	2	4
	17		5	6		11		1	1	2	4
	18		2	1	5	8		3	1	1	5
	19	3	2	7	2	14	5	1	3	3	12
	20	3	1	2		6	6	4	5		15
	21	2	1			3		5			5
	22	1		1	1	3	2			4	6
	23										
	24			1	1	2			8	2	10
	25			2	4	6	1	11	6	8	26
	26	1		2	3	6	5	5	5	4	19
	27	1	2	1		4	5	9	7		21
	28		1			1	5	8			13
	29				1	1	8			7	15
	30			1	1	2	8		13	8	29
12.	1							2			2
	2			1		1		2	1	4	7
	3						3		1	3	7
	4						4	1	1		6
	5							2			2
	6						3				3
	7						3		1	2	6
	8							1	3	1	5
	9		The first inoculation					2	2	4	8
	10						1	1	2	2	6
	11						4	1			5
	12							2			2
	13										
	14										
	15										
	16								1	1	2

Table 2 On the rate of preventive inoculation

Classification / Rate[1]	Closed schools[2]		Non closed schools[3]		Total	
	First[4]	Second[5]	First	Second	First	Second
~59.9		2				2
60.0~64.9		1		1		2
65.0~69.9		14		5		19
70.0~74.9	1	36		26	1	62
75.0~79.9	14	37	7	35	21	72
80.0~84.9	27	42	19	31	46	73
85.0~89.9	65	12	49	16	114	28
90.0~94.9	36	1	41	5	77	6
95.0~	2		3		5	
Under 79.9	15 (10.3)	90 (62.1)	7 (5.9)	67 (56.3)	22 (8.3)	157 (59.5)

1) Rate of inoculation, 2) 145 schools, 3) 119 schools
4) The first inoculation, 5) The second inoculation

in 55 schools (37.9%) of group A and in 52 schools (43.7%) of group B.

In other words, the rate of the first and the second inoculation exceeded 80% in 242 schools (91.7%) and in 107 schools (40.5%), respectively, of the 264 schools. In groups A and B, the average rate of the first inoculation was 86.7 and 88.0%, respectively, and that of the second inoculation 77.3 and 78.9%, rsspectively. When examined statistically by the t-test, the rate of the second inoculation was significantly lower ($p<0.001$) than that of the first inoculation in both groups.

2. Occurrence of class closure by the month of vaccination.

Table 3 presents the occurrence of class closure classified by the month when the second inoculation was performed. Of the 203 schools where the second inoculation was finished in November (the November subgroup), 125 schools (61.6%) experienced class closure. Of the 61 schools where the second inoculation was finished in December (the December subgroup), 20 schools (32.8%) experienced class closure. Then the chi-square test was conducted to examine the difference in occurrence of class closure among the months when the second inoculation was finished from a statistical point view. As a result, the November subgroup experienced class closure significantly more frequently ($p<0.001$) than the December group.

Table 4 indicates the number of classes closed as classified by the month when the second inoculation was finished. Of a total of 5,331 classes, 4,108 classes (77.1%) belonged to the November subgroup. Of them,

Table 3 Relationship between the month of inoculation with vaccine and the occurrence of temporary closing of classwork in some schools

Classification / Month	Temporary closing of classwork in some schools		Total
	yes	no	
November	125 (61.6)	78 (38.4)	203
December	20 (32.8)	41 (67.2)	61
Total	145	119	264
Chi-square test	$\chi^2=15.93$, n = 1, $p<0.001$		

Table 4 Relationship between the month of inoculation with vaccine and the number of classes involved in temporary closing of classwork in some or all the classe in schools

Classification / Month	Temporary closing of classwork in some schools		Total
	yes	no	
November	645 (15.7)	3462 (84.3)	4108
December	49 (4.0)	1174 (96.0)	1223
Total	694	4637	5331
Chi-square test	$\chi^2=113.80$, n = 1, $p<0.001$		

Table 5 Occurrence of closure of some or whole classes of the school as analyzed by the interval between the first and the second inoculation

Classification / Interval (day)	November inoculated group				December inoculated group				Total			
	No. of schools	No. of classes	Temporary closed[1]	Rate of closed	No. of schools	No. of classes	Temporary closed[1]	Rate of closed	No. of schools	No. of classes	Temporary closed[1]	Rate of closed
～ 7	12	245	44	18.0	4	79	8	10.1	16	324	52	16.0
8～14	116	2291	381	16.6[2]	20	385	36	9.4[2]	136	2676	417	15.6
15～21	65	1361	195	14.3[3]	25	503	5	0.9[3]	90	1864	200	10.7
22～28	10	211	25	11.8[4]	12	256	0	0.0[4]	22	467	25	5.3
29～												
Total	203	4108	645	15.7[5]	61	1223	49	4.0[5]	264	5331	694	13.0

1) : No. of Temporary closing of classwork in some schools, 2), 3), 4), 5) : $p < 0.001$

645 classes (15.7%) experienced closure. Of the 5,331 calsses, 1,223 classes (22.9%) belonged to the December subgroup. Of them, only 49 classes (4.0%) experineced closure. The chi-square test revealed that the rate of class closure was significantly higher ($p<0.001$) in the November subgroup than in the December subgroup, as shown in Table 4.

3. Occurrence of class closure by the interval between the two inoculations.

Table 5 exhibits the relationship between the occurrence of class closure and the interval between the first and the second inoculation. In the 203 schools of the November subgroup, a predominant interval was 8~14 days found in 116 schools (57.1%) and followed by an interval of 15~21 days noticed in 65 schools (32.0%). In the 61 schools of the December subgroup, a predominant interval was 15~21 days found in 25 schools (41.0%) and followed by an interval of 8~14 days noticed in 20 schools (32.8%).

In the 264 schools, a predominant interval was 8~14 days found in 136 schools (51.5%) and followed by an interval of 15~21 days noticed in 90 schools (34.1%). Therefore, an interval of 8~21 days was seen in 226 schools (85.6%).

Then, the rate of class closure, as classified by the interval between the two inoculations, was compared between the November and the December subgroup. There was no difference in this rate at the interval of 7 days between the two subgroups. At intervals of 8~14 days, 15~21 days, and 22~28 days the rate was significantly lower ($p<0.001$; the chi-square value being 13.3, 68.2, and 32.0, respectively) in the December subgroup than in the November subgroup.

Discussion

It is generally known that antigen variation takes place in influenza virus unlike any other virus, whenerver an epidemic of influenza is repeated[2]. This phenomenon is especially remarkable in the virus of type A. There are two patterns in the antigen variation in the virus of this type. One pattern is an antigenic shift appearing periodically with a cycle lasting for about 10 years. The other is an antigenic drift appearing in the same subtype of the virus in each epidemic. The appearance of a strain produced by the antigenic shift indicates the sudden apparition of a new virus in the human world which is not related at all with any conventional virus strain isolated from any previous epidemic of influenza. This phenomenon has been met with several times. That is, a new etiological virus appeared in the 1957 epidemic of Asian influenza[1], the 1968 epidemic of Hongkong influenza[3][4], the epidemic of Italian influenza over a period of 1947 to 1956, and the epidemic of Russian influenza[5], which was the successor to Italian influenza, in 1977 and later.

The virus appearing as a variant in these epidemics entered the human world generally as a new-type virus. It has been recognized as such, since it has always been accompanied with a pandemic of influenza.

Even in the case of antigenic drift (which is found also in the virus of B type[6]), when the drift is too severe, it is seldom that any effect can be expected from influenza vaccine prepared from a strain isolated from any previous epidemic.

In an epidemic of influenza caused by the virus of A or B type, the effect of vaccine has been suspected and a social problem raised actually when the antigen variation was severe in the virus. Then it is necessary to consider what step should be taken in order to enhance the effect of influenza vaccine for such epidemic.

On the other hand, if the technical level of production of various vaccines, especially influenza vaccine, is as high in Japan as in any other advanced country, consideration will have to be given to a more effective and efficient use of the existing vaccines which are regarded as the bast ones.

Then the authors examined the chronological relationship between the degree of production of hemagglutination-inhibiting (HI) antibody in blood after inoculation with the existing vaccine and the outbreak of influenza-like disease in Japan.

The second inoculation against influenza was finished in November in 203 schools (about 77%) of the 264 schools, or the cumulative number for the 66 schools for 4 years.

Studies were made on the relationship between the time of inoculation with vaccine and the time of the highest incidence of influenza-like disease in Japan for the past 7 years[7]. As a results, it was pointed out as follows.

When observation was made on the degree of production of HI antibody in blood after inoculation with the existing vaccine, the production reached a peak about a month after the second inoculation. It was continued later, although it showed a gradual decrease. Therefore, the low incidence in November and December reflected the effect of inoculation with vaccine. A peak of incidence appeared over a period from the end of January to that of February. It was interpreted that most of HI antibodies produced after inoculation might have been reduced in ability to be below the level of prevention of infection[8]. Moreover, the higher the rate of inoculation, the more remarkable the effect of the collective inoculation program[9]. It has been considered that the effect of this program can be expected only when the rate of inoculation exceeds 80%. In the present survey the rate of the second inoculation was 79.9% or less in 157 schools (59.5%) of the 264 schools examined. Therefore, the collective immune ability was low in those schools, on which no distinct effect of vaccination could be expected.

The 264 schools were divided into two subgroups, a November and a December, on the basis of the month when the second inoculation was finished. As a result, the frequency of occurrence of class closure was significantly higher in the November subgroup than in the December subgroup. Even when the 5,331 classes of the 264 schools were divided into the same subgroups as these, the November subgroup also showed a higher frequency of occurrence of class closure than the December subgroup.

In general, the interval between the two inoculations of influenza vaccination program is 1~4 weeks. Judging from th condition of production and manitenance of HI antibody, the inoculations should be performed at an interval of 4 weeks, since they can develop a higher level of immunity than when they are done at an interval of 1 or 2 weeks. In the present survey, the interval was 2 weeks or less in 57.6% (and 3 weeks or less in 91.7%) of the 264 schools examined. Therefore, it is clear that no sufficient effect could be expected from the vaccination program in most of these schools.

From the results mentioned above, discussion is mode on a procedure to be taken for the enhancement of the immue effect of an influenza vaccination program.

One suggested procedure is to carry out a third inoculation in January as an addition to the existing two-inoculation program. The third inoculation, however, is expected to bring about difficulties in the supply of vaccine and the administration of a vacination program. Then, a second procedure is suggested as follows. It is to prepare a vaccine which will contain a larger amount of virus than the existing commercial HA vaccine, since this vaccine exerts much less side effects than the previously used vaccine[10]. It will not be so difficult to

enhance the immune effect of vaccine by raising the degree of production of HI antibody in blood as a result of increase in the amount of virus contained in the vaccine. A third procedure suggested is to modify the existing influenza vaccination program to some extent on the basis of the results of the present survey. It may be suggested to postpone the time of the second inoculation from the middle of December to the beginning of January and to perform this inoculation 4 weeks after the first inoculation. As a fourth practicable procedure, it is suggested to raise the rate of inoculation, so that the effect of the program may be enhanced. To do this, the guidance of the administrative authorities is strongly desired.

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インフルエンザの流行に関する研究
—ワクチンの接種時期や接種率と学級閉鎖や休校との関係について—

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東京都杉並区の公立の小・中学校66校を対象に1979～1982年の4年間に延べ264校のワクチン接種時期や接種率と1979～1983年の間の同区内のインフルエンザ様疾患流行時の学級閉鎖や休校などとの関係について調査し，次のような成績が得られた．

1. 264校の第2日目のワクチン接種完了を月別にみると11月接種完了群が203校の76.8%，12月接種完了群が61校の23.2%を各々示し，また，両群の学級閉鎖または休校の有無をみると，前者の125校の61.6%に対し，後者では20校の32.7%を示し，前者の方が有意（$p<0.001$）にその割合の多いことが認められた．

2. 264校中閉鎖群は145校の54.9%に対し，非閉鎖群は119校の45.1%であった．両群の第1回目，第2回目の平均ワクチン接種率は各々前者は86.7%，77.3%，後者は88.0%，78.9%を示し，両群共に第2回目の接種率の方が有意（<0.01）に低いことが認められた．

3. 264校を接種間隔別にみると8～14日間隔が最も多く136校の51.5%，次いで15～21日間隔で90校の34.1%であった．

以上の事実からみて，現行のHAワクチン接種による免疫効果を，さらに増強するためにはワクチン接種間隔を4週間とし，しかも，現行の第2回目の接種時期を約1カ月ぐらい主たる流行期（1月下旬～2月下旬）に近づけること，また，第2回目の接種率を高めることなどがその目的を満たす上で重要なことであると考える．

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