Original Article

SHIFT IN THE BCG VACCINATION AGE REGARDING THE 2013 REVISION OF THE JAPANESE VACCINATION SCHEDULE

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Abstract [Objectives] In Japan, infants ranging from 3 to 4 months of age were excluded from the standard vaccination period for Bacillus Calmette-Guérin in 2013. The aim of this study was to evaluate the contribution of immunization methods and the means of communication employed by municipalities to inform the parents of infants about this revision on the shift in the immunization age. [Methods] In 35 municipalities, I assessed the monthly proportion of infants vaccinated between 3 and 4 months of age relative to all infants in 2013, in reference to the immunization method (group or individual immunization) and the application of two-way communication (TWC) between the municipalities and parents. The types of communication that were defined as TWC were as follows: home guidance and face-to-face explanation at the health examination for the infants. [Results] In most municipalities, the proportion of infants vaccinated between 3 and 4 months of age relative to all infants gradually decreased after following revision of the vaccination period. No significant differences were observed in these proportions between the municipalities with group immunization and those with individual immunization; however, the variability of these proportions among the municipalities with group immunization increased with duration. In the municipalities with individual immunization schedules, the application of TWC to parents promoted the decrease of infants vaccinated between 3 and 4 months of age, as compared to that seen in the other municipalities. [Conclusions] The municipalities with group immunization were characterized by variation in the shift of the immunization age. TWC with parents accelerated this shift in the municipalities with individual immunization.

Key words : Bacillus Calmette-Guérin, BCG, Vaccination, National immunization program, Group immunization, Individual immunization, Communication

Introduction

The Japanese national immunization program (JNIP) includes Bacillus Calmette-Guérin (BCG) vaccination as a regular vaccine, as the overall incidence of tuberculosis is higher than that observed in other developed countries[1)2)]. Although BCG vaccination decreased the tuberculosis incidence among Japanese infants, this vaccination in early infants rarely causes severe complications, such as osteomyelitis[3)]. The JNIP has been regarded as delayed in comparison to similar programs in Western countries, which has limited the available combination vaccine delivered in early childhood[4)]. Finally, *Haemophilus influenzae* type b vaccine and pneumococcal conjugate vaccine were approved as separate regular vaccines in April 2013[5)]. Due to this history, some Japanese parents tend to hesitate to receive simultaneous vaccination[6)], and their infants thus have to be vaccinated at short intervals. As a result of this situation, the revision of Order for Enforcement of the Preventive Vaccination Law and the related Notice from Director-General were established in 2013 (revision 2013), which refers to the routine BCG vaccination schedule, as follows: the limit of months for regular vaccinations was expanded from 6 months to 1 year of age and the number of months of standard vaccination was revised to between 5 and 8 months (formerly, between 3 and 6 months)[5)7)].

In the JNIP, all municipalities implement an immunization plan for regular vaccines and individually determine whether they should provide group and/or individual immunization[8)9)]. The municipalities have the responsibility to provide adequate information about the immunization plan for citizens[9)]. As individual immunization provides parents with a higher degree of freedom to decide the day of immunization in comparison to group immunization, the related information has a greater

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impact on the decision of parents in the municipalities with individual immunization.

As changes in human behavior and decision-making are susceptible to increased knowledge as well as related information, the behavior of citizens can occasionally be modified by local government information[10)11)]. Communication is a factor determining the impact of local government information on the public awareness. Previous reports on the effectiveness of communication of municipalities to citizens showed that face-to-face contact, namely two-way communication (TWC), enhances the understanding of the contents among residents[12)13)].

Taken together, the focus of this study was to evaluate the contribution of the immunization method and the TWC of municipalities when they informed parents of the 2013 revision on the shift in the month in which infants were vaccinated.

Subjects and Methods

Subjects

I conducted a cross-sectional survey in municipalities in Aichi Prefecture, Japan. Aichi is a typical modern Japanese prefecture. The number of live births in 2012 was 48,303. The number of infants who received the BCG vaccination in the prefecture between April 2013 and March 2014 was 40,153, which amounts to 4.58% of the infants that were vaccinated in Japan. In May 2014, I asked all 53 municipalities to provide details on the number of infants who were vaccinated at each month of age in 2013; 45 municipalities responded (response rate, 84.9%). Three municipalities responded that they were unable to count the number of infants who were vaccinated at each month of age. The distribution of the BCG immunization method among the responding municipalities was 23 (59.0%) group immunizations, 13 (33.3%) individual immunizations and three (7.7%) combinations of both. The exclusion criterion was set as the number of infants vaccinated BCG per year of <30 ($n=4$) and the combinations of both immunization methods ($n=3$), and 35 municipalities (66.0% of all municipalities in the prefecture) were assessed in this assessment. According to the protocol implemented in the revision 2013, infants 3 and 4 months of age were excluded from the standard period for BCG vaccination on and after April 2013. Therefore, the proportion of infants vaccinated between 3 and 4 months relative to all infants was considered as an indicator of the shift in the BCG vaccination age regarding the revision 2013, abbreviated as "INDEX" in this paper. The influence of this revision was assessed based on two parameters: i) the monthly data of the INDEX in 2013, ii) the proportion of months in which the INDEX was 0% to all months after implementation of the revision 2013.

Two-way communication

I also asked the municipalities, using a self-administered questionnaire with multiple-choice items, about how they communicated with the parents to inform them of the 2013 revision. In all municipalities, the parents received home guidance about childcare until 2 months of age as a public health service. TWC was defined as face-to-face communication between the receiver of the information (parents) and the sender (municipality) regarding the substance of the information. The types of communication that were categorized as TWC were as follows: home guidance (23 municipalities) and face-to-face explanation at the health examination for the infants (17 municipalities). The remaining types of communication (one-way communication), were as follows: mail (21 municipalities), public magazine (7 municipalities), and website (6 municipalities). A total of 17 (77.3%) municipalities in which group immunization was performed used TWC, whereas 8 (61.5%) municipalities that provided individual immunization used TWC.

The association between the application of TWC and the municipality scale was assessed in the municipalities. As the number of infants who were intended to receive the BCG immunization in 2013 was nearly equal to the number of live births, the number of live births in the municipality in 2012 was used as the indicator for the municipality scale.

Statistical analysis

The assessments were evaluated from the standpoint of the immunization method (group vs. individual) and the application of TWC (applied vs. not applied) in the municipalities. Continuous data were analyzed using Mann-Whitney's U test. The coefficient of variance (CV) was used as the indicator for the variability among the municipalities with each immunization methods. The bootstrap method is used to obtain confidence intervals (CIs) for the CV[14)]. When the CIs of two coefficients do not overlap with each other, the difference between these coefficients is statistically significant at a given level. The bootstrap method involves repeated random sampling with replacement from the data at hand: in this study, this process is repeated 2,000 times and the normal approximation method is used to produce the 95% CI using R, a statistical program[15)]. The data were analyzed using PASW Statistics Ver.18, expect for the bootstrap method, and a P value of <0.05 was considered to be significant.

Ethics

The purpose and design of the research, level of data protection and voluntary nature of participation were clearly stipulated in the opening statement of the questionnaire for municipalities. It was also explicitly written that the submission of a response would be considered as providing consent to participate in the research. This study was approved by the institutional ethics committee.

Results

A total of 25,629 infants were vaccinated in the municipalities that were assessed in 2013. Following the implementation of the 2013 revision, i.e. from April onward, 17,949 infants

were vaccinated; of whom 2,357 (13.1%) were vaccinated at between 3 and 4 months of age.

Before the implementation of the 2013 revision, the INDEX for group immunization was higher than that in municipalities with individual immunization. The CV was constant in the municipalities with each immunization methods (Table 1).

Following the implementation of the 2013 revision, no significant differences were observed in the INDEX between the municipalities with group immunization and those with individual immunization, however, a greater number of months for which the INDEX reached 0% was observed in the municipalities with group immunization than in those with individual immunization on and after May (Figure A and B). The maximum INDEX in the municipalities with group immunization remained stable after the implementation of the revision 2013, whereas that in the municipalities with individual immunization gradually decreased. Two municipalities with group immunization continued to show an INDEX of ≧60% through 2013. The CV for group immunization significantly increased with duration, whereas that noted in the municipalities with individual immunization was fairly constant over time (Table 1).

Following the implementation of the revision 2013, in the municipalities with group immunization, there were no significant differences in the INDEX between the "applied" and "not applied" municipalities for TWC. The proportion of months in which the INDEX was 0% in the "applied" municipalities for TWC to parents was comparable to that noted in the "not applied" municipalities (median [25%ile value, 75%ile value]; applied, 50.0 [14.3, 77.8]; not applied, 88.9 [18.8, 100]; $P=0.405$). In contrast to these results, among the municipalities with individual immunization, the application of TWC to parents showed a tendency to decrease the INDEX, as compared to that seen in the "not applied" municipalities (Fig. C), and a significant difference was observed in September ($P=0.016$) and October ($P=0.039$). The proportion of months in which the INDEX was 0% in the municipalities applying TWC to parents was higher than that seen in the "not applied" municipalities (44.4 [22.2, 79.5] vs. 0 [0, 27.8], $P=0.044$). There were no significant differences in the INDEX for the combined use of TWC with one-way communication in comparison to the application of TWC alone, irrespective of the immunization methods (data not shown).

In the municipalities with group immunization, the number of live births in the municipalities that applied TWC to parents was comparable to that noted in the "not applied" municipalities (Table 2). Among the municipalities with individual immunization, the number of live births in the municipalities that applied TWC to parents was significantly less than that seen in the "not applied" municipalities.

Discussion

In the Japanese setting, each municipality has the authority to decide the means of communication when informing residents of the immunization schedule as well as its method of immunization. In the present study, I assessed the shift in the immunization age of BCG after the implementation of the revision 2013.

The INDEX in the municipalities with the group immunization appeared to change diametrically after the implementation of the revision 2013. It is conceivable that these opposing changes were apparently dependent on the months of age for immunization determined by the municipalities. As the municipalities with the group immunization informed the parents of concrete indications including the date of immunization, most parents have their infants undergo vaccination at the designated month of age. Although the "standard" BCG vaccination schedule was partly changed in the 2013 revision, municipalities have the power to decide the vaccination schedule with regard to achieving effective tuberculosis control. Among the assessed municipalities, two municipalities continued to provide group vaccinations for infants of 3 months of age: one municipality continued to

Table 1 Immunization method and the variability of the proportion of infants vaccinated between 3 and 4 months relative to all infants in 2013

Immunization	Jan	Feb	Mar	Apr	May	Jun
Group (n=22)	11.3±2.5 [7.0−16.7]	17.5±4.2 [10.1−26.5]	12.3±2.2 [8.6−17.0]	42.6±7.6 [28.7−58.7]	123±31 [57−179]	182±36 [111−252]
Individual (n=13)	34.9±10.0 [16.9−56.0]	35.7±11.7 [14.5−60.4]	39.7±13.2 [15.8−67.4]	79.9±22.1 [36.1−123]	95.0±20.4 [55.9−135]	138±28 [87−198]

July	Aug	Sep	Oct	Nov	Dec
206±51 [101−299]	201±43 [120−287]	207±46 [118−296]	228±51 [132−331]	215±57 [95−318]	223±56 [105−324]
132±27 [90−195]	120±29 [62−175]	114±29 [58−170]	127±40 [45−201]	111±23 [68−157]	133±30 [78−196]

The data are presented as the coefficient of variance±standard error [95% confidence interval].
The standard error and 95% confidence interval were obtained by the bootstrap method.
The perpendicular dashed line indicates the implementation of the revision.

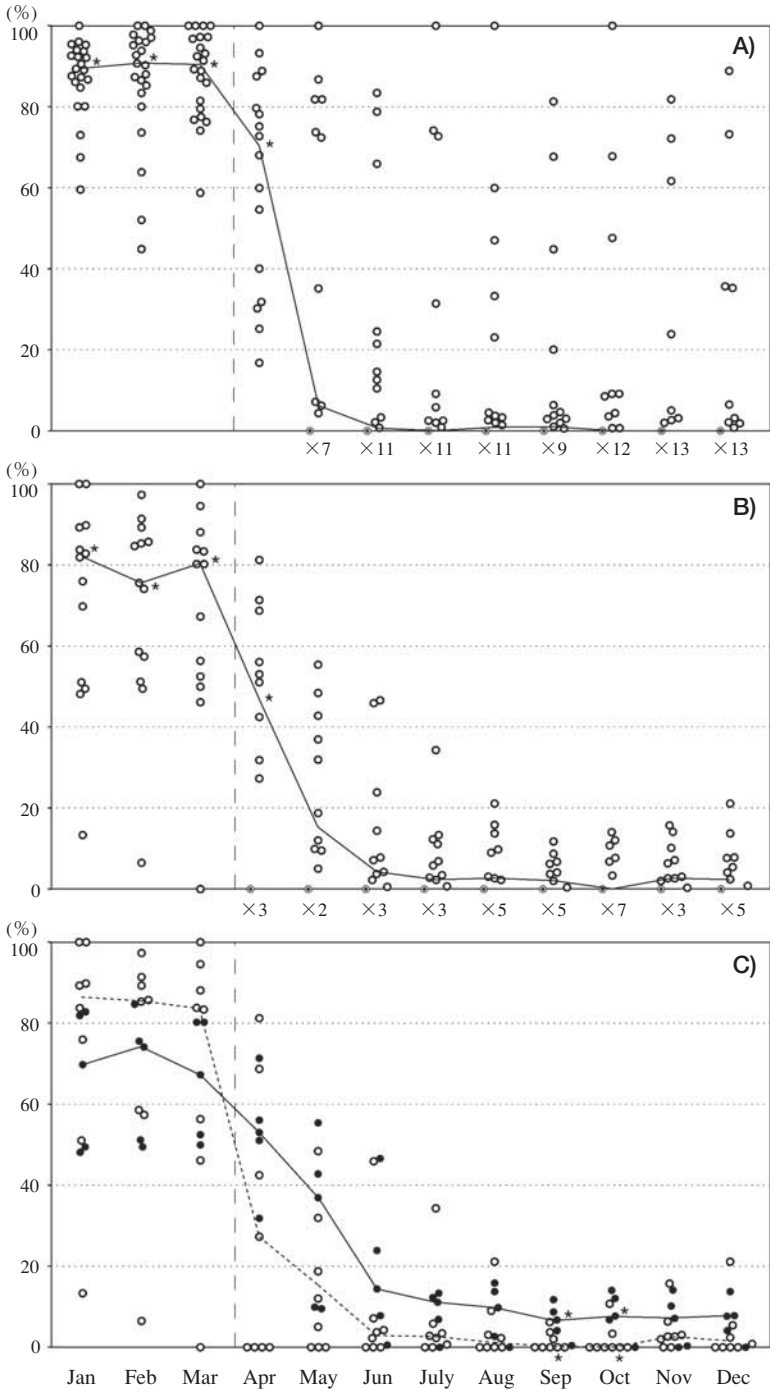

Fig. The proportion of infants vaccinated BCG between 3 and 4 months age in the municipalities: A, the municipalities with group immunization; B, the municipalities with individual immunization; C, the municipalities with individual immunization. The data calculated from January to December in 2013 are shown. The perpendicular dashed line indicates the implementation of the revision. Each circle represents a municipality, respectively. The double circle at the bottom line represents the existence of multiple data: the number appended in the bottom right represents the number of multiple datasets. The line represents the median value in each month. A P value of <0.05 was considered to be significant (Mann-Whitney U test).

In Figure A, the median values with asterisk show significant differences at each month in the municipalities with group immunization, as shown in Figure B.

In Figure B, the median values with asterisk show significant differences at each month in the municipalities with individual immunization, as shown in Figure A.

In Figure C, the type of the circle represents whether the municipalities applied two-way communication (TWC) to the parents: open circle, applied; closed circle, not applied. The definitions of communication included in TWC are shown in the Subjects and Methods section. The line represents the median value in each month (dashed line, applied; solid line, not applied). The median values with asterisk show significant differences at each month in the municipalities with or without the application of TWC.

Table 2 Application of two-way communication and the municipality size

	TWC		*P**
	Applicable	Not-applicable	
Total (n=35)	540 [388, 769]	1051 [381, 2458]	0.053
Group immunization (n=22)	553 [316, 783]	402 [228, 1172]	0.906
Individual immunization (n=13)	522 [429, 745]	2029 [1051, 3924]	0.008

The data are presented as the median number of live births [25%ile value, 75%ile value].
The number of live births was used as the index of the municipality size in the assessment of TWC with parents.
**P* -values were calculated using the Mann-Whitney test.
Abbreviations used: TWC, two-way communication

provide group immunization at the time of a health examination at 3 months of age as they intended to maintain an efficient health service in a depopulated area. The other municipality provided group immunization for infants of 3 months of age due to the higher incidence of tuberculosis in the area. Therefore, it was considered that these two municipalities decided the vaccination schedule based on the situation in each area.

Individual immunization provides parents with a higher degree of freedom to decide the age of immunization as compared to group immunization. Previous reports have shown that parents rarely reach a decision on their own as to whether their infants should be vaccinated[16)-18)]. Therefore, the decision of parents in the municipalities with individual immunization is more susceptible to variation in the quality and/or efficiency of the related information. This study showed an earlier decrease in the INDEX in the municipalities applying TWC to parents, in comparison to that in the municipalities without TWC. This acceleration in the shift is, at least partly, considered to reflect the validity of TWC for informing parents about the revision 2013. This validity is supported by a previous report in the Japanese setting: Takeuchi et al. showed that providing a face-to-face explanation for subjects, categorized as TWC, improves understanding of the contents[12)].

When the target of TWC is too great, the need for human resources is thought to be an obstacle to applying TWC[19)]. It was shown in this study that the application of TWC to parents was associated with the number of live births in the municipalities, particularly those with individual immunization. In practice, when excess targets make successfully applying TWC difficult, an alternative strategy is required to achieve significant communication. Previous reports have shown the advantages of applying social marketing techniques to improve public health systems[20)21)]. Some reports have described the capability of applying social media to help parents to decide the vaccination plan for their children[22)-24)]. A suitable method to accomplish adequate communication with the target should be identified, with comprehension of the demographic features and behavioral characteristics of the particular targets.

If BCG is vaccinated in infants infected with tuberculosis, Koch's phenomenon appears within a few days[25)]. Recently, it was made public that a total of 126 cases of Koch's phenomenon were reported in 2013, which was markedly higher than the approximately 20 cases per year observed until 2012[26)]. Nevertheless, no cases involving the onset of tuberculosis were observed among the reports of Koch's phenomenon in 2013. Although further studies are needed to clarify contribution of the implementation of the revision 2013 on the increase in Koch's phenomenon, the shift in the month of immunization observed in this study was valuable for identifying factors related to the increase.

There are some limitations associated with this study. I did not examine either the use of the municipality as the information source by parents or whether the parents showed a substantial understanding of the information. It is likely that some parents used the municipality information other than candidates obtained in this study. Multiple factors would have affected the behavioral changes of the parents after the 2013 revision. Some papers have demonstrated that parents perceive the physicians as one of reliable information sources[14)27)]; however, it is assumed that the home guidance for parents before the start of the regular vaccination schedule is efficient to alter the timing of BCG vaccination. This speculation is supported by the previous finding in the Dutch setting: most parents that receive the information about vaccination schedule at a home guidance perceived health care workers as the sufficient source of vaccine-related information[17)]. In addition, this study focused on a limited geographical area, which might indicate regional bias. Future research should address these issues before the results of this study can be generalized.

Although there were some limitations in this study, the findings showing an association between changes in the months of age at which infants are vaccinated for BCG and the means of communication are helpful for establishing further examinations of effective communication in terms of public health systems to control tuberculosis.

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Conflict of interest

The author declares no conflicts of interest in association with the present study.

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2013年に行われたBCGの標準的接種期間の変更に伴う接種月齢の変化

佐々木渓円

要旨：〔目的〕日本では2013年に，Bacillus Calmette-Guérinの標準的接種期間から生後3～4カ月齢が除かれた。この接種期間の変更に対して，予防接種方法と保護者に対する市町村の情報伝達方法がどのように寄与したかを評価した。〔方法〕愛知県内の35市町村を対象として，2013年の各月の被接種者数に占める3～4カ月齢の児の割合を，接種方法（集団接種，個別接種）や保護者に対する双方向性の周知方法（TWC）の実施の点から評価した。TWCは，訪問指導あるいは乳幼児健康診査における説明と定義した。〔結果〕ほとんどの市町村で，3～4カ月齢で接種した児が段階的に減少した。接種方法の違いは接種月齢の変化に有意な影響を与えなかった。集団接種では，3～4カ月齢の児の割合に市町村間のばらつきが認められ，その差は時間経過とともに増大した。個別接種の市町村では，TWCの実施によって3～4カ月齢で接種する児の減少が促進された。〔結論〕集団接種の市町村は，接種月齢の変化に多様性が認められた。TWCは，個別接種における接種期間の変更を促進した。

キーワーズ：Bacillus Calmette-Guérin（BCG），予防接種，予防接種事業，集団接種，個別接種，コミュニケーション