報告

無侵襲性出生前遺伝学的検査に関するサイエンスカフェ実施の考察

An Examination of the Implementation of a Science Cafe: Regarding Non-Invasive Prenatal Genetic Testing

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Abstract

胎児の染色体異常を検査とする無侵襲性出生前遺伝学的検査（NIPT）は，検査採血の容易さ，妊娠早期の検査実施，および高い信頼性により生殖の自己決定権を向上しうる．しかし，臨床的，倫理的，および社会的問題も同時にもたらした．我々はNIPTに関するサイエンスカフェを実施し，その結果を考察した．

このカフェでは，参加者に生殖や先天異常の情報を提供するとともに，NIPTに対する様々な姿勢や関連法についても説明した．アンケート調査の結果，参加者のNIPT受容性は，受容可能（27%），どちらかというと受容可能（32%），どちらかというと受容不可能（14%），受容不可能（1%），回答不能（26%）となり，既報の世論調査と比較すると，一部参加者がより慎重な姿勢となった可能性が示唆された．また，一部参加者は遺伝的疾患や知能の検査へのNIPT利用を受容しうると回答した．NIPTの更なる利用拡大に先立ち，生殖の自己決定権のより倫理的な行使には社会教育の充実が不可欠であるが，サイエンスカフェは親密な雰囲気下での情報提供と参加者間コミュニケーションの促進が可能であることから，有効な社会教育の一つとなりうる．

Although clinical use of non-invasive prenatal genetic testing (NIPT) to detect fetal aneuploidy may improve reproductive autonomy owing to early testing, its reliability, as well as the ease of obtaining blood samples, NIPT raises clinical, ethical, and social issues. We herein report the implementation of a science cafe regarding NIPT and examine the results.

In this cafe, we explained various attitudes toward NIPT and relevant policies as well as information regarding on human reproduction and congenital anomalies. The subsequent survey clarified the acceptability of NIPT among the participants as follows: acceptable = 27%, rather acceptable = 32%, rather unacceptable = 14%, unacceptable = 1%, and unanswerable = 26%. These results and considerations suggested the possibility that this science cafe increased caution among some of the participants with respect to NIPT. Meanwhile, the survey also revealed the possibility that some individuals may accept the use of NIPT to detect genetic diseases and assess intelligence. Prior to the further spread of NIPT, social education should be given for better exercising reproductive autonomy. From this perspective, a science cafe may be an effective approach, as it provides

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important information in a casual and intimate manner and promotes mutual communication among the participants.
Keywords: science cafe, NIPT, prenatal diagnostic test, reproductive autonomy, disability rights

1. Introduction

In 2012, a Japanese newspaper reported on a clinical study led by the non-invasive prenatal genetic testing (NIPT) consortium[1], which stated that "Several Japanese hospitals next month will start using a new prenatal blood test that can detect Down syndrome with an accuracy of more than 99 percent"[2]. There are some questions regarding this report. Although it stated that pregnant females may be tested for fetal trisomy 21, 18, and 13, it emphasized merely Down syndrome only (DS: trisomy 21). Moreover, the report heedlessly referred to sensitivity as "accuracy", and went on to state that such testing may "possibly lead to an increase in abortions". Thus, the terms "Down syndrome", "99% accuracy", and "abortion" have frequently been reported in the news with respect to NIPT, potentially misleading the public in Japan.

Subsequently, the results of a public opinion survey were reported regarding the acceptability of NIPT among the Japanese public[3]. Surprisingly, the general acceptance rate of NIPT was 79.3%. The major reasons for acceptance were as follows:

"NIPT is useful for preparing postnatal care."
"We should better understand fetal conditions."
"We should use this new diagnostic test."
"We can opt for abortion after the test."

Although the general acceptance of the respondents may be ascribed to the rapid increase in maternal age, which is associated with chromosomal abnormalities (aneuploidy) in the fetus, the public appears to be optimistic about the use of NIPT and relevant abortion. Meanwhile, the general rejection rate was 15.9%. The major reasons for rejection were the selection of life, emotional distress, unavailability of prenatal therapy, and high cost of the test. The rest (4.8%) marked "unanswerable" or "no reply".

We questioned the observation of such a high rate of acceptance of NIPT. At present, it is difficult to discuss various issues surrounding NIPT in Japan. Meanwhile, the general public may not sufficiently understand the clinical, ethical, and social implications of NIPT. Indeed, public understanding of issues related to the disabled population and clinical use of such prenatal tests is insufficient worldwide. For instance, various facts about individuals with DS remain to be known. First, although individuals with DS nearly always have physical and mental disabilities, there is wide variation in their abilities (Faragher and Clarke 2013). Second, recent developments in healthcare have facilitated the participation of disabled individuals in social activities, and have achieved the marked improvements in life expectancy (50-60 years on average). Third, 99% of DS persons are satisfied with their lives (Skotko et al. 2011). However, approximately 92% of females whose fetuses were prenatally diagnosed with trisomy 21 opted to terminate their pregnancy, according to an analysis of metadata from the UK, US, New Zealand, France, and Singapore (Mansfield et al. 1999). To our knowledge, there are no reliable reports regarding the relationship between prenatal testing for trisomy and the rate of relevant abortions in Japan. However, a preliminary report on NIPT showed that approximately 95% of Japanese females opted for abortion after receiving a definitive

diagnosis of trisomy 21, 18, and 13[4]. Therefore, elective abortion is usually the first option following a diagnosis of fetal trisomy 21. Although the United Nations declared March 21st World Down Syndrome Day in 2011, it is crucial to provide the public with accurate clinical and social facts about DS in order to ensure improved current and future reproductive autonomy (Purdy 2006). Other congenital anomalies should also be sufficiently understood throughout society.

In view of this background, we developed a science cafe (Dallas 2006) in which various attitudes toward NIPT and relevant policies were explained in addition to information regarding human reproduction and congenital anomalies. In the cafe, we conducted a survey of the acceptability of, potential subjects of, and further requirements for NIPT. We herein report the implementation of a science cafe regarding NIPT and examine the results.

2. Non-invasive Prenatal Test (NIPT)

2.1 A New Prenatal Test, NIPT

NIPT, which provides fetal genetic information via DNA sequencing of cell-free fetal (cff) DNA fragments in blood drawn from pregnant females has advantages over conventional prenatal blood tests such as quadruple tests, in terms of its higher rate of sensitivity, lower false-positive rate, and the ability to perform testing as early as 10 weeks of gestation (Allison 2013). In addition, NIPT helps females to avoid definitive but invasive tests, such as amniocentesis and chorionic villus sampling, which are associated with a risk of miscarriage.

2.2 Current Clinical Use of NIPT

Private enterprises in the US (Allison 2013) and China[5] have provided NIPT to detect sex chromosome aneuploidies as well as trisomy 21,18, and 13 since 2011. Some large-scale clinical studies of testing for trisomies are currently ongoing or have recently been completed in China (Dan et al. 2012), the UK[6], and the US (Ehrich et al. 2011 ; Palomaki et al. 2012). In the UK, NIPT for fetal sex determination is currently available to pregnant females who are carriers of sex-linked genetic conditions[7]. In addition, an Israeli health maintenance organization has already initiated the reimbursement of the cost of testing for conditions such as trisomy 21 (Petherick 2013). Therefore, the use of NIPT as a component of prenatal care is spreading worldwide.

In Japan, the NIPT consortium initiated a clinical study to collect supporting data for genetic counseling in order to implement NIPT in April 2013[8]. Currently, maternal blood samples collected through physicians who participate in the study are subject to NIPT to detect trisomy 21, 18, and 13.

2.3 Ethical and Social Issues

Although NIPT may contribute to improving reproductive autonomy, its use raises various concerns regarding genetic counseling, informed consent, elective abortion, and disability rights (Allison 2013 ; Benn and Chapman 2009). Due to the ease of drawing blood, even females with a low risk of affected fetuses are likely to undergo NIPT. Uncertainties abound in such cases. Although NIPT has a high rate of reliability, it also carries a risk of false-positive and false-negative results (Allison 2013). There are no perfectly accurate clinical tests. If a test result is positive or false-positive, the females confront the decision as to whether to maintain or terminate the pregnancy. Some females may lose the quality of self-affirmation (Steele 1988), while others, without undergoing definitive tests, choose

to undergo abortion in order to avoid a state of mental or emotional suspense. Moreover, pregnant females would be surprised if they chose to continue their pregnancy in cases of false-negative results. It must therefore be carefully confirmed whether the females truly understand the implications of the test prior to giving consent to undergo NIPT. Therefore, the quality of genetic counseling prior to NIPT may need to be improved. When fetal aneuploidy is definitively diagnosed by physicians based on the test result, post-test counseling is also crucial because the diagnosis may lead the females to terminate the pregnancy without sufficiently understanding the clinical and social facts of the disability. In addition, the extensive use of NIPT may affect the disability rights, intentionally or unintentionally assuming a posture against existing disabled persons who deserve respect.

3. Implementation of the Science Cafe and the Survey

3.1 Outline of the Science Cafe

We held a science cafe entitled, "Science Intervening in Life", given in Sapporo on December 21, 2013. The total number of the participants was 90. We provided an overview of human reproduction, congenital anomalies, and various prenatal tests, including NIPT. In addition, we offered an overview of assisted reproductive technology (ART), considering that some females who undergo ART procedures receive prenatal tests. We also explained the outline of the Maternal Protection Law and the Act on Comprehensive Support to the Disabled. Furthermore, we explained various attitudes toward NIPT in terms of the reproductive autonomy of pregnant females and the social context.

Following a one-hour session of providing this information, the participants were required to respond four questions in addition to demographic survey, such as sex, age, and occupation.

Question

1. Do you accept the use of NIPT to detect fetal aneuploidy?
2. Which patients should be allowed to undergo NIPT to detect genetic diseases other than aneuploidy?
3. For what purposes do you accept the use of NIPT if the test is made available to detect non-medical traits?
4. What do you think about further requirements for the ethical use of NIPT?

Demographic characteristics of the respondents were investigated to confirm whether the cafe theme, which is liked to gender issues in a specific age, might impact the survey response. Question 1, which was similar to an item in a previous public survey[3], was incorporated into the present survey to clarify the science cafe participant's acceptance of NIPT as well as preliminarily compare the results of this survey with those of the previous survey. If the respondent selected a negative votes or "unanswerable" for question 1, they did not need to reply to question 2 and 3. No payment was given in this survey. Subsequently, a facilitator and a guest speaker discussed the topic with the participants for about half an hour.

3.2 Results

Of the 90 participants, 66 responded to the questionnaire survey. The demographic characteristics of the respondents are shown in Table 1. The gender composition of the respondents was 56% female and 44% male. The distribution of the age groups showed that fewer participants were under 20 or over 70 years of age. This is considered to be an appropriate distribution, considering the content of the science cafe. Regarding occupation, many of the respondents were employees of a company (18%) and teachers or faculty (14%), excluding "others".

Table 1. The Demographic Characteristics of Survey Respondents in the Science Cafe.

Characteristics	n	Percentage
Sex: male	29	44
Female	37	56
Sum	66	100
Age (year): <20	3	5
20-29	11	17
30-39	14	21
40-49	11	17
50-59	14	21
60-69	10	15
≧70	3	5
Sum	66	100
Occupation: high school student	2	3
College student	6	9
Graduate school student	4	6
Employee of a company	12	18
Government employee	5	8
The self-employed	3	5
Teacher or faculty	9	14
Researcher	2	3
Others; house wife, health care provider etc.	19	29
No reply	4	6
Sum	66	100

*Of 90 total participants, 66 people responded to this survey.

The results for question 1 are shown in Figure 1. The acceptability of NIPT was lower than that reported in the previous opinion survey[3]. Namely, the rate of a response of "acceptable" was 27% (44.2% in the previous survey). In contrast, the rate of a response of "unanswerable" was 26% (4.8% in the previous survey). The frequencies of the other options were similar to the rates observed in the previous survey. According to these results, this science cafe appears to have formed a different social group from that noted in the previous public opinion survey, although a careful examination is needed to interpret the findings of the comparison between the two surveys.

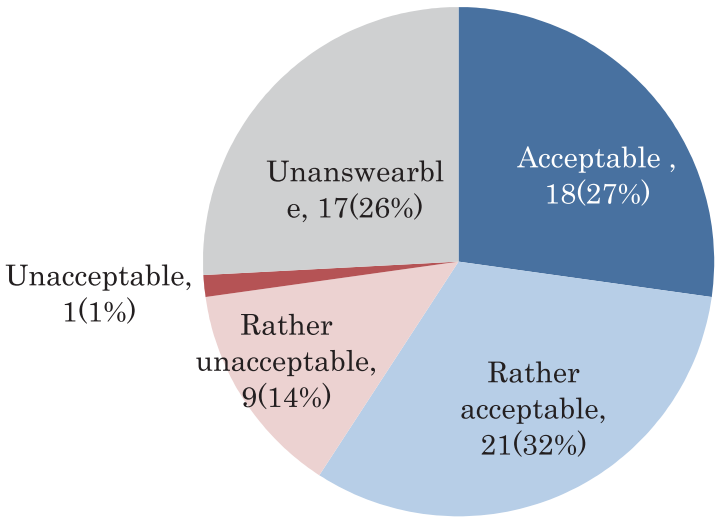

Figure 1. Results of the Survey of the Acceptability of Non-Invasive Prenatal Genetic Testing in a Science Cafe
Of the 90 total participants, 66 responded to the survey following a one-hour explanation of various attitudes toward NIPT and relevant policies as well as information regarding human reproduction and congenital anomaly.

Next, the answers to question 2 revealed that most of the respondents who opted for "acceptable" or "rather acceptable" in question 1 accepted the use of prenatal testing to detect severe congenital (51%) or late-onset (41%) genetic diseases (Table 2A). Moreover, many of the participants rejected the use of prenatal testing for non-medical purposes (31%, Table 2B). Interestingly, some of the participants accepted the use of testing for intelligence (21%). Conversely, only one respondent opted for testing of "resemblance to parents".

Table 2A. The Result of a Survey on the Acceptable Subjects of Non-Invasive Prenatal Genetic Testing for Genetic Diseases Other than Aneuploidy

Options	Votes Cast	
	n	Percentage
Congenital severe genetic diseases	35	51
Late-onset severe genetic diseases	28	41
Both of the options listed above are unacceptable	1	1
Unanswerable	4	6
Sum	68	100

*Of 66 total respondents, 39 people responded to the survey.
*A respondent was allowed to cast votes for up to two options, excluding "Both of the options listed above are unacceptable" and "Unanswerable."

Table 2B. The Result of a Survey on the Acceptable Purposes of Non-Invasive Prenatal Genetic Testing for Non-medical Traits

Options	Votes Cast	
	n	Percentage
Sex discernment	10	16
Resemblance to parents	1	2
Physical abilities of a certain standard	4	6
The senses of a certain standard	7	11
Character with a certain tendency	6	10
Intelligence of a certain standard	13	21
All of the options listed above are unacceptable	19	31
Unanswerable	2	3
Sum	62	100

*Of 66 total respondents, 39 people responded to the survey.
*A respondent was allowed to cast votes for up to two options, excluding "All of the options listed above are unacceptable" and "Unanswerable."

With respect to the results of question 4 (Table 3), most of the respondents did not consent to either the statutory regulations of the test or the more severe conditions for abortion. Instead, many of them recommended improving consulting services such as genetic counseling (20%). In addition, the respondents suggested the further need for social education regarding the advantages and disadvantages of prenatal testing (13%) and various congenital anomalies (12%). They also responded that people with various viewpoints should further discuss the subjects of, and requirements for, this prenatal test (8%). Furthermore, the participants suggested that the disabled should be more included (13%) and supported (12%) in society, taking into account the impact of the test on disability rights. The establishment of a system to ensure the quality of the test was requested (8%). This response may be ascribed to the difficulty in understanding the statistics of the test. Some of the participants wished financial support or insurance coverage for the prenatal test (8%).

The difference in voting between female and male respondents was not significant (Table3). The age groups shown in Table 1 were further categorized into 3 groups considering the average ages of female's first childbirth and menopause (Table3). The difference in voting among the three age groups was not significant again.

Table 3. The Result of a Survey on Further Requirements for the Ethical Use of Non-Invasive Prenatal Genetic Testing

Options	Votes Cast	Votes by Sex[1]			Votes by Age (year) [2]			
	n	Female	Male	P value	<30	30-49	50<	P value
1) Enhancement of consulting services, such as genetic counseling for pregnant females and couples	31	20	11	n.s.(0.19)	5	16	10	n.s.(0.096)
2) Financial support or insurance coverage of prenatal tests	13	9	4	n.s.(0.26)	2	7	4	n.s.(0.52)
3) Establishment of a system to ensure the quality of prenatal tests	12	8	4	n.s.(0.41)	4	3	5	n.s.(0.43)
4) Enhancement of social education with regard to the advantages and disadvantages of prenatal tests	21	15	6	n.s.(0.86)	8	7	6	n.s.(0.89)
5) Promotion of inclusion of the disabled in school, work and leisure	21	10	11	n.s.(0.35)	3	9	9	n.s.(0.70)
6) Enhancement of education or enlightenment concerning a diversity of congenital anomalies in school or society	19	9	10	n.s.(0.37)	6	8	5	n.s.(0.23)
7) Supporting the disabled regarding healthcare, welfare, education and work	19	11	8	n.s.(0.85)	4	8	7	n.s.(0.94)
8) Statutory regulations on the development of for-profit provision of prenatal tests	3	2	1	n.s.(1.0)	1	0	2	n.s.(0.42)
9) Setting more severe conditions for elective abortion under the Maternal Protection Law	4	2	2	n.s.(1.0)	2	0	2	n.s.(0.15)
10) Active discussions involving people with various viewpoints regarding the subjects of, and requirements for, prenatal tests	12	5	7	n.s.(0.27)	2	5	5	n.s.(1.0)
Others	2	1	1	n.s.(1.0)	0	1	1	n.s.(1.0)
Sum	157	92	65		37	64	56	

Of 90 total participants, 66 people (37 females, 29 males) responded to the survey.
A respondent was allowed to cast votes for up to three options.
1 Option 1-7,10: χ^2 test. Option 8, 9, 11: Fisher's exact test (extended).
2 Option 1: χ^2 test. Option 2-11: Fisher's exact test (extended).

4. Discussion

4.1 Possible Effect of the Science Cafe

This science cafe appears to have formed a different social group from that observed in a previous public opinion survey (Figure 1). The rate of a response of "acceptable" in this cafe was lower than that reported in the previous survey. Conversely, the rate of a response of "unanswerable" was higher. Both the responses of "unacceptable" and "rather unacceptable" were similar between the two surveys.

Note that the subjects differed between the previous public opinion survey and our survey in the science cafe. Regarding the subjects collected in the previous public survey[3], random sampling of 3,000 people was conducted to form a model of national voters. In addition, the number of respondents was 1,800 in the previous public survey. Moreover, the gender composition of the respondents in the previous survey was 49.4% female and 50.6% male. In our survey, slightly more females responded to the questionnaire than males (56% versus 44%).

However, prior to this survey, we explained various attitudes toward NIPT and relevant policies

as well as information regarding on human reproduction and congenital anomalies in the cafe. A previous report suggested that after scientific information was provided, such a small-group discussion helps participants to form their own opinions in a deliberative poll (Sugiyama 2012). In the previous public opinion survey, such information was not provided to the subjects[3]. Under such circumstance, non-attitude may be hidden by a random choice of answers to avoid appearing ignorant (Converse 1964). Due to this difference, although there is some speculation, the science cafe respondents' attitude toward NIPT was likely to be formed based on the provided information. Moreover, in the science cafe, the response of "unanswerable" accounted for one-fourth of all responses (26%). Taken together, these observations and considerations suggested the possibility that the science cafe made some of the participants cautious with respect to NIPT.

4.2 Future Subjects of NIPT

The results for question 2 revealed the possibility that some individuals accept the future use of NIPT to detect not only chromosomal aneuploidy as well as severe congenital or late-onset genetic diseases (Table 2A). Currently, some private companies provide only NIPT for testing of autosomal and sex-chromosome aneuploidies. However, the methodology of NIPT makes it possible that upcoming NIPT may provide fetal tests for monogenic diseases at least (Allison 2013). The present survey results suggested that the expansion of NIPT subjects is likely to occur in a social context. Although many of respondents rejected the use of prenatal tests for non-medical purposes, some respondents accepted the use of the tests to assess intelligence (Table 2B). This attitude may be associated with the potential for abortion following the fetal diagnosis of congenital anomalies. Meanwhile, a UK sociological study suggested that NIPT is viewed as not only a positive clinical application offering peace of mind in pregnancy but also a medical option justified for severe disorders only (Farrimond and Kelly 2013).

In order to further address these findings in a social context, further public dialogues are required if the provision of NIPT for non-medical purposes becomes realistic in the near future.

4.3 Ethical Use of NIPT

As shown in the survey results (Table 3), the participants constructively addressed the clinical, ethical, and social ramifications of NIPT because most of them did not vote for the statutory regulations of the prenatal testing and the more severe conditions for abortion. In another sociological study of UK public attitudes toward NIPT, regulating and monitoring provision were preferred in addition to monitoring introduction and clinical use (Kelly and Farrimond 2012). The differences in voting not only between female and male respondents but also among the three age groups were not significant (Table 3). Therefore, these results in this implementation of the cafe suggest public attitudes that do not depend on the differences of sex and age. The participants considered ethical use of NIPT from various viewpoints. The need to improve genetic counseling was required. Further requirements need for social education regarding the prenatal testing and congenital anomalies as well as further social inclusion of, and support to the disabled were particularly emphasized. Based on these results, we further considered requirements for the ethical use of NIPT from the viewpoint of pregnant females and society.

NIPT may allow for expectant females to better prepare for the risk of miscarriage and disability. In

such cases, obstetricians, in cooperation with pediatricians and other specialists such as cardiovascular surgeons, must provide healthcare information about the disabilities, particularly focusing on post-test genetic counseling. Patient groups may also provide the females opportunities to come in contact with the disabled. Hopefully, these females would then better understand and initiate preparations for complications, education, and work for disabled children. Physicians can subsequently provide follow-up postnatal care for such children.

Conversely, for females who wish to have only healthy children, NIPT may lead to the need for decision-making regarding whether to maintain or terminate the pregnancy. As suggested by the science cafe participants (Table 3), pre-test genetic counseling requires further improvement, as even pregnant females in low-risk groups are likely to undergo the NIPT due to the ease of drawing blood. In so doing, the explanation should encompass the clinical implications of not only the sensitivity, specificity, and the false-positive and false-negative rates, but also the positive predictive value, the probability that a positive test reflects the age of the females being tested for the aneuploidy (Mersy et al. 2013). In addition, such explanation must be conducted in a sufficiently comprehensive manner. Although informed consent is ordinarily obtained following a document-based explanation, the use of additional slides, movies, or other e-learning tools may be useful. Furthermore, the right to opt for childbirth without receiving NIPT should be sufficiently recognized as well because the test might induce severe distress in the pregnant females. With respect to post-test counseling, unbiased up-to-date information regarding the disabled should be provided to both the female and her family members when the fetus is confirmed to have aneuploidy.

Nevertheless, public understanding of the pre-test or post-test counseling is likely to depend on their prior education within their family, school and/or community. If the pregnant female has an unsettled state of mind, the timing of counseling should be reconsidered, particularly in the first trimester which is associated with frequent physical and emotional changes. It must also be carefully confirmed whether the pregnant female truly understands the explanation provided and the meaning of her consent to undergo NIPT. Meanwhile, public understanding of congenital anomalies and the lives of the disabled is insufficient. Efforts should be made to increase awareness of these conditions.

According to the World Health Organization, congenital anomalies, which affect approximately 1 in 33 infants worldwide, are caused by chromosomal, monogenic, multifactorial, and environmental/teratogenic factors[9]. Currently, NIPT provides information for only a portion of congenital anomalies. Despite its high reliability, NIPT carries a risk of false-positive and false-negative results, as well as test failure due to the low content of cff DNA in maternal blood. Due to these current limitations, NIPT may not detect all congenital anomalies. As some of the science cafe participants suggested (Table 3), further social education is needed to form an ethical consensus and increase scientific knowledge among the public, including prospective parents, regarding various congenital anomalies and the clinical limitations of prenatal tests, such as NIPT. However, thinking about prenatal tests involves careful considerations of ethical and social issues in addition to complex statistics. Giving a lecture tends to involve the unilateral provision of information. It is difficult to pay attention to each participant in a large symposium. A science cafe is one appropriate approach in this setting, as it can be used to provide information in a casual and intimate manner to facilitate the understanding of the participants. Moreover, a cafe can promotes mutual communication between participants with various viewpoints.

5. Concluding Remarks

In this cafe, we provided information regarding human reproduction and congenital anomalies. We also explained various attitudes toward NIPT and relevant policies. For these reasons, although there is some speculation, our survey research suggested the possibility that the science cafe made some of the participants cautious with respect to NIPT which is associated with clinical, ethical and social issues. Subsequently to the science cafe, those who opted for "unanswerable" may discuss the clinical, ethical, and social implications of prenatal tests with others at home or school, or in society in order to find the answers. Such dialogues may contribute to the ethical use of NIPT.

The use of NIPT may contribute to prenatal and postnatal care for childbirth in cases of aneuploidies if a healthcare team and/or the commitment of patient groups are available. Meanwhile, social education is essential for better exercising reproductive autonomy in most cases of prenatal care using NIPT. Such education would be all the more needed if the forthcoming NIPT expands the number of potential test subjects to monogenic or multifactorial disorders other than aneuploidies. Continuous public dialogues are vital to prevent abuses of the NIPT. In this manner, a science cafe, which can be used to provide information in a casual and intimate manner as well as promote mutual communication, may have significant benefit for prospective parents.

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Notes

1) According to the NIPT consortium (http://www.nipt.jp/), the clinical study was initiated on April 1, 2013.
2) The Japan Times. Published on August 31, 2012. "Japan to try prenatal detection test for Down syndrome".
3) The Hokkaido Shimbun. Published October 13, 2013. "Shin Syusyouzen Shindan Habahiroi Shiji" (The new prenatal test widely accepted). The acceptability of prenatal tests such as NIPT: acceptable 44.2%, rather acceptable 35.1%, rather unacceptable 11.7%, unacceptable 4.2%, and unanswerable or no reply 4.8%. In this survey, the method of double sampling for stratification was used so that random sampling of 3,000 people would form a model of national voters. The gender composition of the 1,800 respondents was 49.4% female and 50.6% male. The investigators met the subjects to conduct the public opinion survey.
4) The Japan Times. Published on November 23, 2013. "Most who test positive in new prenatal test opt for abortion". The article reported the proceedings of the clinical study led by the NIPT consortium during the first six months. A total of 3,514 females underwent the test. The 53 females out of 56 who received a definitive diagnosis of fetal trisomies chose to terminate pregnancy.
5) The BGI health website. (http://50.62.146.72/our-tests/genetic-testing-for-reproductive-health/nifty/)
6) The RAPID project: Study to evaluate new prenatal test for Down's Syndrome in the NHS. (http://www.rapid.nhs.uk/news/study-to-evaluate-new-prenatal-test-for-down%e2%80%99s-syndrome-in-the-nhs)

7) The RAPID project: NIPT for fetal sexing (http://www.rapid.nhs.uk/patient-information/fetal-sex-determination).
8) The statement in the NIPT consortium website (http://www.nipt.jp/).
9) The World Health Organization: Congenital anomalies Fact sheet N° 370 (http://www.who.int/mediacentre/factsheets/fs370/en/).

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