ETHICS AND EPIDEMIOLOGY
What Ethical Issues are Japanese Epidemiologists Facing? Results of a Questionnaire Study for Members of the Monbusho Research Committee on Evaluation of Risk Factors for Cancer by Large-Scale Cohort Study.*

Subcommittee of Ethical Issues

In 1993 questionnaires concerning ethical issues were mailed to 34 committee members of the Monbusho research committee of a large-scale cohort study which started in 1988 including 32 rural communities and 4 occupational groups. The questionnaire survey revealed the following results.

1. In all cohorts, "informed consent" for health questionnaires was carried out, though the methods varied.
2. Although the method varied, informed consent for collection of blood was obtained in 28 (77.8%) of the 34 cohorts. The committee decided that the collected specimens without consent is not used for study.
3. The protection of privacy was deliberately planned and has been carefully carried out in the cohort study.
4. The committee members' concerns for ethical issues has increased after joining the cohort study.
5. The attitudes of informed consent for collection of blood at mass screenings showed wide differences among research objects and researchers.

These results suggested that the research members had a considerably high concern for ethical issues and that ethical considerations in epidemiological studies should be continued in Japan. * J Epidemiol, 1996; 6 : S141-S146.

Recently the International Ethical Guidelines for Ethical Review of Epidemiological studies1-2) was published. It implies that ethical issues in epidemiological studies are attracting world-wide concern. Although some discussions of these issues have been carried out since 19903-5), these are a lot of ethical problems which should be studied and resolved in epidemiologic societies in Japan.

The Monbusho Research Committee on Evaluation of Risk Factors for Cancer by Large-scale Cohort Study (Monbusho ECC), started in 1988, in cooperation with the Steering Committee Grant-in Aid for Cancer Research from the Ministry of Education, Science and Culture. The research team on the Monbusho ECC consists of 34 members of epidemiologists and biostatisticians, and five established oncologists as adviser evaluate the projects and outcomes, and also give advice and suggestions. The number of the participating study fields in this study is comprised of 50 areas (cities, towns and villages), of which the geographical locations are scattered throughout Japan, except Shikoku island. Some cohorts are consisted of plural area and other are only one area or the parts of the area. The sizes of the numbers of study subjects and the proportion to the total population age 40-79 years in each area were not the same. In took three years for the study team to establish the cohort group exceeding 100,000 altogether, because of financial problems and provisions regarding participation in the study. More than 25,000 industrial workers mainly living urban area were joined this cohort study, as most of the study field were rural area in Japan. The industrial cohort is being followed up separately and will be analysed. To accomplish this long follow-up study smoothly, several subcommittees were set up, such as the planning and steering subcommittee, the data collection, the summing-up and analyses, the serum bank, the industrial study, the ethical issues and the genetic problems subcommittees. The subcommittee for ethical issues has been operating since 1990. Main tasks of the subcommittee for ethical issues in the initial stage were as fol-

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1. To get consent of the subjects and participating areas, after explaining the purpose and procedures of the study.
2. To exchange contract of cooperation by the document between the principal investigator and the relevant person in participating area.
3. To obtain signature of the subjects on the form of the questionnaire.
4. To keep confidentiality of personal data or other data in collection, data processing and outcomes.
5. To get informed consent of blood donation to the blood bank for the use in the near future separately.
6. To discuss other general ethical issues which will occur in the Monbusho ECC.

After establishment of the cohort, ethical issues which occurred in the follow-up have been discussed and regulation have been made for the study.

A questionnaire survey was performed by the subcommittee in order to determine the methods of privacy protection and of obtaining informed consent used, and to see how the researchers’ concern for ethical problems changed due to participation in the Monbusho ECC study, and to elucidate what kinds of ethical issues Japanese epidemiologists are facing.

MATERIALS AND METHODS

After a preliminary survey, a questionnaire was made by the subcommittee. The questionnaire consisted of two parts: the first part was questions about each cohort for the Monbusho ECC, including population size, methods of privacy protection, methods of obtaining informed consent and methods of data collection. Second part was the questions for each researcher’s concern for ethical issues related to Monbusho ECC such as attitudes for informed consent at mass screening, or publication procedure.

The questionnaire was mailed to the 34 committee members. The first part was answered by the committee members about each cohort. A total of 36 cohorts, 32 local communities and 4 occupational groups were accounted for. Among the committee members, 7 members have no cohorts and 4 members have more than 2 cohorts. The second part was requested to answer by both the committee members and the associate members who are cooperating with the committee members. A total of 39, that is 29 committee members, and 10 associate members who were requested by committee members responded for this questionnaire.

RESULTS

Ethical Considerations for Each Cohort

Among these 36 cohorts, 26 (72.2%) were consisted of less than 5000 members. Ages of the cohorts subjects were included at least 40 years old and over, and under 80 years old.

In the process of the Monbusho ECC, various kinds of methods were used to obtain informed consent. Table 1 shows the methods of obtaining informed consent for the Monbusho ECC. More than half (63.9%) cohorts obtained informed consents by subject’s signature on the questionnaire at home.

| Table 1. Methods of obtaining informed consents for questionnaire (multiple answers) |
|--------------------|------|------|
| 1. Participant’s signature in the presence of interviewer | 9 | 25.0 |
| 2. Oral agreements with interviewer | 1 | 2.8 |
| 3. Participant's signature on the questionnaire at home | 23 | 63.9 |
| 4. A written contract on consent of the representative of the field with the committee member | 3 | 8.3 |
| 5. Oral agreement of the representative of the field with the committee member | 11 | 30.6 |
| Total | 36 | 100 |

Researchers’ Concern for Ethical Issues

From the 39 respondents, 8 (20.5%) were under 40 years old and 6 (15.4%) were over 60 years old. Only one was a female and 32 (82.1%) were physicians.

Figure 1 shows the researcher’s concern for ethical issues. Before participating in the Monbusho ECC, more than 30% of researchers had weak or very weak concern for autonomy, informed consent, benefit restoration and risk minimization. However, after participating in the project, more than 70% of them had strong or very strong concern for every item. The change of concern for ethical issues increased after participat-
Table 2. Methods of privacy protection (multiple answers)

| Method                                                                 | n  | %   |
|-----------------------------------------------------------------------|----|-----|
| a. On collecting information                                          |    |     |
| 1. On site interview by licensed person (physician, nurse etc.)       | 10 | 31.3|
| 2. Self administered questionnaire at home combined with interview by licensed person | 13 | 40.6|
| 3. Telephone interview by licensed person (physician, nurse etc.)     |  4 | 12.5|
| 4. Interview at home by licensed person                               |  3 |  9.4|
| 5. Other's                                                            |  2 |  6.3|
| Total                                                                 | 32 | 100 |
| b. On transportation of questionnaire from home to committee member's office |    |     |
| 1. Using sealed envelope                                              | 17 | 63.0|
| 2. Collected by only licensed person (physician, nurse etc.)          |  7 | 25.9|
| 3. Name of participants was hidden in cover page instead of sealed envelope |  3 | 11.1|
| Total                                                                 | 27 | 100 |
| c. On data processing                                                 |    |     |
| 1. Using code number rather than name for subject identification      |  8 | 30.8|
| 2. Date processing by authorized person                               | 18 | 69.2|
| 3. Making a contract for confidentiality with the data processing company |  1 |  3.8|
| Total                                                                 | 27 | 100 |

Table 3. Methods of obtaining informed consents for collecting blood samples (multiple answers)

| Method                                                                 | n  | %   |
|-----------------------------------------------------------------------|----|-----|
| 1. Subject’s signature in the presence of interviewer                 |16 | 52.1|
| 2. Oral agreement with interviewer                                    |  9 | 32.1|
| 3. A written contracts on consent of the representatives of the field with the committee member |  3 | 10.7|
| 4. Oral agreement of the representatives of the field with the committee member |  8 | 28.6|
| Total                                                                 | 28 | 100 |

Figure 1. The researcher’s concern for ethical issues
To add some volume of blood

1) Detection for AIDS or syphilis
2) Examination of DNA
3) Examination of liver function test for special purpose
4) Examination of ordinary liver function test

To use the residual blood of ordinary examination

1. not necessary to obtain informed consent
2. oral agreement of a representative of the examinees with the study team leader
3. written contract on consent of the representative of the examinee with the study team leader
4. oral agreement of the examinee after informed study outline
5. signature of the examinee after informed study outline
6. oral agreement of the examinee after informed items of examination
7. signature of the examinee after informed items of examination

**Figure 2.** The attitude of obtaining informed consent for collection of blood sample at mass screening

**Table 4.** Future ethical problems in the research project (multiple answers)

| Problem                                      | n  | %   |
|----------------------------------------------|----|-----|
| a. Leakage of privacy                        | 8  | 20.5|
| b. Problems of informed consent              | 13 | 33.3|
| c. Intervention of administration            | 3  | 7.7 |
| d. Countermovement of study subjects         | 3  | 7.7 |
| e. Problems of authorship for publication    | 14 | 35.9|
| Total                                        | 39 | 100 |

DISCUSSION

Although there have been many reports on bioethics in Japan, the research on the ethical issues of epidemiological studies has been very limited.

Although the respondents were limited to only the members of the Monbusho ECC and most of them belong to universities or research institutes, the respondents have had enough experiences in epidemiological studies and have good leadership in Japanese epidemiological society. Thus, the results may not be applicable to the whole Japanese epidemiologists but their attitudes and opinions may reflect the recent ethical issues conceived by most of Japanese epidemiologists.
There may have been some misunderstandings between the questioners and the respondents. For example, the questioner intended to elicit multiple answers as often as possible, but the respondents selected only one. The questionnaire should have been examined more carefully before use.

The privacy protection is one of the most worrisome ethical issues in recent Japan. Local authorities are endeavoring to establish it and the research committee have been paying attention to it since the beginning of the Monbusho ECC.

The personal data have been computerized with identification code number and mailed to the central office without subjects names. The researchers’ concern for privacy protection on data processing was the highest among other ethical issues at the beginning of this study.

The International Guideline stressed individual consent, but it is a growing concept in Japanese society. Although most of the study subjects have been accustomed to participate in mass screening programs and have had a cooperative relationship with each of the research members, some community leaders and doctors who are in charge of health care of the communities have an opinion that the confidence between health care providers and inhabitants or employees may be disturbed if written informed consent is strictly required at health check-up. This is the reason why many committee members didn’t adopt the signature method for obtaining informed consent.

However, a younger generation including researchers tends to think that individual signature of informed consent is essential for this type of epidemiological study. As show in Table 5, many researchers expressed an opinion that liver function test dose not require informed consent, but a few researchers were against that opinion even in cases where residual blood sample are used. They insist that the individual subjects have a right to know the results of the examination of their samples. What kind of methods for informed consent should be applied to individual subjects is a serious ethical issue in present Japan and is necessary to be examined continuously.

REFERENCES

1. CIOMS : International Guidelines for Ethical Review of Epidemiological Studies Geneva, 1991.
2. CIOMS : Translated International Guidelines for Ethical Review of Epidemiological Studies Clin. Eval. 1992 ; 20 : 563-578 (in Japanese).
3. Inaba Y. Epidemiology and ethics. Jpn. J. Cancer Clin. 1994 ; 40 : 374-378 (in Japanese).
4. Nakamura K. Health survey and informed consent. Digest of Science of Labour. 1994 ; 49 : 512-515 (in Japanese).
5. Yamamoto S. Ethical issues in preventive medicine with special emphasis on epidemiological research and practice. Supp. J. of Epid. 1992 : S1-S6.

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