The Ethics of Research Using Biobanks

Reason to Question the Importance Attributed to Informed Consent

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Background: During the past decade, the use of stored tissue has become an object of increased ethical query. A Swedish biobank and a biotech company have been praised for solving the ethical problems with explicit informed consent procedures, and we decided to investigate donors’ perceptions of the system.

Methods: A questionnaire was sent to a randomized sample of 1200 donors who had donated blood and signed informed consent forms.

Results: The response rate was 80.9%. Of the respondents, 64.5% were aware that they had consented to donate a blood sample, 55.4% thought that they had consented to donate phenotypic information, and 31.6% believed that they could withdraw their consent. Among respondents, 3.9% considered informing donors about the research objective as the most important ethical issue in relation to biobanks, and 5.6% were unsatisfied with the information they had given. There was 85.9% acceptance of surrogate decision making by regional research ethics committees.

Conclusions: Considering that the donors in this study were not always aware of their donation but generally were not unsatisfied with the information they had received, and that they did not rate being informed about the research objective as an important issue, informed consent seems to be an inadequate measure of public acceptance of biobank-based research.

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The last decade has seen growing ethical concern about the use of stored human tissue for research, particularly with respect to population-based genetic research. In 1999, it was reported that Medical Biobank in Västerbotten County in Sweden and a biotech company, UmanGenomics, Umeå, which had been given all commercial rights to the biobank, had developed an ethics policy basically solving the problems with this type of research. The key element in this policy was informed consent, and all donors were reported to have signed a consent form. International bioethical debate has also centered on the use of informed consent in tissue-based research, usually founded on the assumption that consent procedures are the most important issue from the donors’ point of view.

Medical Biobank was established in 1985 in Västerbotten County, northern Sweden, and contains more than 78000 samples from 68000 people (as of June 2003). All inhabitants in the county are offered medical health examinations at the age of 40, 50, and 60 years, and during the examination they are invited to donate a blood sample and complete a questionnaire for future research. Although initially praised for its ethics, this biobank project has recently been subject to ethical questioning because of a conflict about unresolved ownership issues. Leaving this conflict aside, this study assessed the ethical model with respect to its content rather than the ownership problems. To achieve this, we approached the donors and explored how they perceived themselves to be informed, how they viewed surrogate decisions, and how they ranked donors’ information about research objectives in relation to other ethical issues concerning biobank-based research. Thereby, the study adds to the paucity of empirical research about informed consent in relation to biobanks (an overview has been published recently by Ring and Lindblad). Because other studies already have explored whether people would be willing to let their tissue be used for research and whether commercial involvement is an impediment to participation, we focused our attention on donors’ perceptions of selected aspects of the
informed consent procedures that have been praised in this Swedish system.

### METHODS

During the autumn of 2002, a random sample (N=1200) of people who had donated blood to Medical Biobank since its inception in 1985 were sent a questionnaire. Most respondents had signed an informed consent form that was introduced in 1990 as the project was broadened from one municipality to cover the whole county. It was not possible to exclude the few who had not signed a consent form without compromising confidentiality. As with most health care data in Sweden, the samples have been stored with codified social security numbers. These numbers were used by local authorities to retrieve the current addresses of respondents. Our questionnaire was followed by 2 reminders. This allowed us to distinguish between 3 groups of respondents (early, middle, and late) for our dropout analysis. As background questions, we asked about health care experiences, age, and sex. Data entry and analysis were conducted using the Epi Info (version 6.04; Centers for Disease Control and Prevention, Atlanta, Ga) software program. For comparing differences of proportions, we used the \( \chi^2 \) test.

The categories of answers reflect 29 semistructured qualitative interviews with individuals recently asked to donate blood for Medical Biobank. Open-ended questions were used to generate an understanding of the donors' concerns about genetic research. These included various considerations of what we might term 'eugenics' uses of genetic knowledge, in particular, the potential for selective use of abortion. In the questionnaire, we used more explicit phrases, such as "selective use of abortion," rather than complex concepts like eugenics, which could not be expected to be understood by all respondents. Similarly, we found that informed consent was a concept that not all respondents could be expected to comprehend. We therefore approached the issue by directing questions at different aspects of informed consent procedures (e.g., awareness of the actual donation, knowledge about the right to withdraw the sample from further research, and importance attributed to being informed about the research objective) and inferred the attitude regarding informed consent from responses to these questions.

### RESULTS

Of the random sample (N=1200), 51 had moved away or died, leaving a sample of 1149 individuals, of whom 930 answered our questionnaire (response rate, 80.9%). The male and female response rates among respondents were 44.8% and 55.2%, respectively, which represented a slightly higher response rate among women compared with the sex distribution of all donors (49% male and 51% female). Excluding 1 question in which only 857 respondents specified their opinion, the internal dropout varied from 0 to 17 (mean, 8.6) (Table). For our dropout analysis, we added a question concerning respondents' interest in the issues contained in the questionnaire. Of 917 respondents to the question, 75.6% stated that they found it important to express their views, 12.3% said that they did not find it important, and 12.1% said that they did not know.

An introductory letter informed the respondents about the fact that they had donated material for Medical Biobank, and with the use of the 2 questions reproduced in Figure 1, we then explored whether donors thought of themselves as having actively consented. There was a slight sex variation, and older persons tended to be more aware of their informed consent than younger respondents. More than 64% (64.5%) were aware that they had consented to donate a blood sample; 55.4% thought that they had consented to donate phenotypic information. More respondents with negative experiences with health care services tended to say that they did not actively consent or that they did not remember.

We asked whether respondents knew that they could withdraw their informed consent to donate: of 918 respondents, 290 (31.6%) answered positively, 511 (55.7%) answered negatively, and 117 (12.7%) were not aware that they had consented. Concerning the donors' perceptions of the information they had received, 503 (54.8%) were satisfied, 51 (5.6%) were not satisfied, 340 (37.0%) could not remember whether they had received any information, and 24 (2.6%) stated that they had not received any information. More older people and people with positive

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### Table. Relative Importance of Different Issues*

<table>
<thead>
<tr>
<th>Issue</th>
<th>Issue Is Important (n = 921)</th>
<th>Issue Is the Most Important (n = 857)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All population groups get equal access to research results</td>
<td>651 (70.7)</td>
<td>270 (31.5)</td>
</tr>
<tr>
<td>The research is easily made useful for concrete objectives</td>
<td>560 (60.8)</td>
<td>199 (23.2)</td>
</tr>
<tr>
<td>Corporate interests do not determine the research outlook</td>
<td>506 (54.9)</td>
<td>121 (14.1)</td>
</tr>
<tr>
<td>Confidentiality is protected</td>
<td>528 (57.3)</td>
<td>106 (12.4)</td>
</tr>
<tr>
<td>Research results are not used to offer selective abortion</td>
<td>302 (32.8)</td>
<td>73 (8.5)</td>
</tr>
<tr>
<td>Much research is done, including privately sponsored research</td>
<td>294 (31.9)</td>
<td>48 (5.6)</td>
</tr>
<tr>
<td>The donor of tissue is informed about the research objective</td>
<td>281 (30.5)</td>
<td>33 (3.9)</td>
</tr>
</tbody>
</table>

*Data are given as number (percentage) of respondents. The options were generated through semistructured interviews. There was also a possibility of selecting “Other” (n=18) and “Do not know” (n=7). Seven respondents (0.8%) selected “Other” as the most important issue.

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*Figure 1. The level of awareness of respondents' donation of blood and questionnaire information, depicted with differences between sex, is shown. There were 917 respondents to both questions. In the first question, the sex difference was significant (P<.001), while it was not significant in the second (P=.24). The Swedish word for "consent" (införstådd) can also be translated as "agree to" or "accept."*
experiences with health care service tended to believe that they could withdraw their consent to donate. To reveal donors’ attitudes regarding surrogate decisions, we described the procedures for allowing researchers’ access to samples in Medical Biobank and asked whether the respondents were prepared to let Medical Biobank and the regional research ethics committee make decisions concerning when and how the donors’ blood was to be used. Donors were then invited to specify any conditions they would like to attach to their answers. The results are depicted in Figure 2 together with the conditions. There was 85.9% acceptance of surrogate decision making by research ethics committees. Acceptance of surrogate decision making was correlated with having positive experiences with health care service, being satisfied with the information provided, knowing their right to withdraw a donation, and being aware that they had donated blood and questionnaires to Medical Biobank.

Finally, we asked which factors the respondents considered important in research involving biobank material and asked them to select 1 factor as the most important one. The response pattern is listed in the Table, demonstrating that the respondents rate informing donors about the research objective as the least important issue among the listed options. The donors were invited to consider the issue in relation to the sample already donated; hence, the result primarily concerns attitudes regarding renewal of informed consent for new research objectives.

The response rate to our survey was high. We found significant differences between early and late respondents in response to the question of whether they believed it important to express their views regarding issues contained in the questionnaire. We take this as an indication that people abstained from answering the questionnaire not because of difficulties with understanding the questions or because they held views inadequately covered by the response categories but because of lack of interest in the issues.

Considering that most respondents had signed an informed consent form, it is noteworthy, though perhaps not surprising, that a considerable number of them were unaware that they had consented to donate a blood sample and let their questionnaire with phenotypic information be used for research objectives. Furthermore, it shows that it cannot be taken for granted that people understand that a questionnaire can be used for research. More striking, however, is that only 5.6% of the respondents stated that they were not satisfied with the information provided, despite the low levels of awareness. This indicates that few blamed the health care centers for the fact that they were unaware of their donation.

Regarding donors’ interest in informed consent procedures, a study based on 504 telephone interviews with US residents found that most respondents would require their consent for research on clinically derived, personally identifiable samples. The answer to a hypothetical question like this can be interpreted as an attitude, and a similar attitude is reflected among the 446 respondents in our survey who said they would appreciate information about projects involving their samples (Figure 2). There is, however, a striking inconsistency in relation to our other findings, namely, that most donors were prepared to let the regional research ethics committee make decisions about the use of their blood and that information about the research objective was seen as the least important ethical issue in biobank-based research. The discrepancy could reflect the way in which questions are asked. When asked whether one would like to provide informed consent, this issue is already singled out as the most important one. In contrast to other research, including the US-based study already mentioned, we approached the issue from several angles and then asked the respondent to rate the importance attributed to his or her information levels in relation to other issues that had emerged in qualitative interviews. This gave the most surprising result of the study, and it calls for more research on what concerns the donating public in different settings. This will be the only way of determining whether the high expectations associated with informed consent in research conducted in the United States reflect a culture more concerned with questions of autonomy, or merely surveys resting on assumptions about donors’ interests in information as a means for enhancing their autonomy. We must rethink the donor informed consent procedures in tissue-based research: perhaps information about research objectives is seen more as a service than a safeguard (ie, it is nice to have but not important), which would imply that bioethicists should work to ensure safeguards other than informed consent. In fact, it has been suggested that we focus attention on the establishment of tissue-trustee infrastructures, rather than consent issues, to ensure the confidence of the donating public, and the findings of this study lend empirical support to that proposal.

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Finally, it is worth considering the cultural specificity of these findings. The Swedish health care delivery is mediated by a welfare state, and solidarity with weaker groups has been a value permeating Swedish health politics for a century. This might explain the high degree of concern about equal access to research results (Table). If future studies reveal that people in different contexts hold very divergent views about what constitutes important ethical issues, we might have to reconsider the universal applicability of ethical guidelines emphasizing informed consent in tissue-based research without prior context-specific empirical investigation of donors’ perceptions of their interests.

CONCLUSIONS

Despite effective informed consent procedures being given as a reason for deeming this particular Swedish biobank and a biotech company ethical, the donors are not well informed. However, only a small number report their information levels to be of particular importance when biobank-based research is assessed in relation to other issues pertaining to research politics and ethics, and few of them are unsatisfied with the information they have been given. This study calls for reconsideration of the importance attributed to informed consent in debates about ethics of biobanks and genomics companies and for in-depth exploration about what is at stake for donors in various contexts.

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