

The Patient's Consent*

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ABSTRACT

What does the patient's consent to research entail and what does it mean? How do the researcher and ethics committees strike a balance between ensuring that consent would be free and informed, and yet not hinder bona fide research with impracticalities or costly bureaucracy? The issues involved are examined substantially from perspectives in genetics. Selected guidelines published from various authorities on consent in medical treatment, for the research use of human biological samples and in reproductive studies were used to provide a streamlined overview of the best practices.

Keywords: consent, ethics, genetics, research, tissue

INTRODUCTION

Any practitioner of medical research or care knows that patient's consent is required for virtually all research participation as well as for many medical and surgical procedures, including screening programmes. Although the issues of consent for medical care are somewhat different from those concerning research, I think there are more commonalities between them than there are differences. While I intend to expound on the subject of patient's consent chiefly in the context of research, there are instances which relate to medical care similarly. I shall approach the subject from my perspective as a medical geneticist.

THE MEANING OF "CONSENT"

Among the myriad definitions for consent, the UK Joint Medical Genetics Committee (JMGC) defines consent as "a process to ensure that a person understands the nature and purpose of giving a sample or undergoing a treatment".¹ It suggests an emphasis on taking time and effort (on the part of both patients/

subjects and researchers/carers) to ensure the potential research subjects understand the methods and motives, and the potential risks and benefits of the study before they agree to participate. Entailing much more than just getting a signature on a piece of paper, consent-taking requires care, thought, sensitive handling and patience to facilitate a reasonable degree of understanding. In providing people with information about their condition, it is sometimes necessary to remember that they have a right to know as well as the right not to know, and be sensitive to whether detailed and explicit information, or the lack thereof, will cause undue confusion or anxiety.

Whether it is reasonable to ask for, or to give, consent to any procedure (therapeutic or research) depends upon the balance between the potential good and the potential harm that may happen to the subject from participating. In principle, people who are being treated are expected to gain some benefit from that treatment. Those participating in research are, in principle, relatively less likely to gain personal benefit. Precisely because of this, there is a tighter limit on the degree of hazard to which they can be subjected, and it is that much more important to be sure that they understand any dangers that may exist and that they give meaningful agreement to participate. There is a

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stricter threshold in research than in care, and consent can very seldom, if ever, simply be taken for granted as 'implied' in the way that it frequently is for minor participation in medical treatment. Few, if any, busy doctors get formal patient consent for every clinical examination, or for taking every blood sample, in the course of treating people. The fact that the patient has come to you for a consultation — and that you are now taking that blood sample in order to obtain a diagnosis — the act of holding out an arm for that purpose in front of you is taken to imply that they consent to your taking the blood sample. In the research context, such "implied consent" is not good enough.

CONSENT MUST BE FREE AND INFORMED

The Human Genetics Commission, in its report *Inside Information — Balancing the Interests in the Use of Personal Genetic Data*, emphasises two critical characteristics of valid consent — it must be freely given and it must be properly informed.² Consent is a process of communication, and its validity rests on the mutual understanding that it creates between the medical professional and the subject. The Department of Health, UK, prescribes that "consent can be written, oral or non-verbal. A signature on a consent form does not itself prove the consent is valid". There are many situations where people can be persuaded by someone that they trust (or even perhaps fear slightly) to put a signature on a piece of paper, even though they have little understanding of what they are signing.

Consent must not be coerced. It is easy to forget how many different people may bring pressure to bear on someone to participate in a medical procedure — their family, employers or insurance companies — but the most likely culprit is the attending medical professional. Often, this is a person that patients see as having some authority, frequently someone to whom they entrust their health and to whom they believe they are indebted for services already rendered or about to be rendered. Unless it is made explicit to them, they may feel that the extent to which they receive proper care depends on them being cooperative in agreeing to take part in research. To avoid this, the professional must go an extra mile to point out that the quality of care they will deliver is not contingent on the patient agreeing to take part in a research programme; that refusal to participate in research will not lead to victimisation, but that the professional will continue to do their very best for the patient. Even if gratuitous refusal to participate in a favourite research project does cause a slight twinge of annoyance, it is absolutely critical that medical professionals behave professionally towards

their patients and recognise their inalienable right to be properly treated.

Any treatment, or any research, must involve weighing up the potential benefits (to the person in front of you and also to the rest of humanity) against the potential hazards of the procedures involved. Similarly, a sensible balance needs to be struck between the amount of time spent in the consenting process, the amount of detail required, and the potential hazards (and benefits) of what is being proposed. Collecting a saliva sample for a survey of something with no serious health consequences to the person concerned, can be treated more cursorily than a research programme involving brain biopsies from seriously ill people, however worthy the scientific objectives of the study might be!

CONSENT ISSUES RELATING TO GENETIC INFORMATION

In the JMGC consultation paper, certain information was thought to be helpful for subjects undergoing genetic tests, and should be discussed during the consent-taking process. It emphasises that some sorts of information gleaned in the course of research (or clinical management), may be of importance to other family members, so that both the researcher and the research subject need to be alert to this possibility and understand how it will be handled.

Where the research involves materials taken for "testing", samples may on occasion accumulate for a year or more before they are utilised, for many valid practical reasons. The tissue donors, on the other hand, would normally and eagerly want to know what the findings of tests conducted on their samples are. Ensuring that the research subject (or the patient) has a realistic idea of what sort of information might be fed back as a result of the test, and what the timescale of this might be, will be helpful to all.

In situations where one might, as a by-product of the test, discover something unexpected (for example, a mutation with potentially serious consequences for the offspring of the research subject), it is important to anticipate this and to tell the research subject whether such information will be relayed to them, by whom and how. Planning how the unexpected will be managed and ensuring that everyone understands the rules, saves stress and aggravation when the unexpected eventually happens (as it often does).

Where information is of potential importance to other family members, it is essential to clarify during the consent-taking process, whether you have permission

to share this information with those involved in the care of other family members. In general, people who learn something important about their family background naturally want this information to be conveyed to other family members for their benefit. Occasionally, there are exceptional situations, but it is not appropriate for us as researchers and doctors to sort out internal family issues. The imperative for us is to be sure that we do the maximum good and the minimum harm, by having clear understanding and knowledge as to what is expected of us.

GUIDELINES FOR CONSENT

There are quite a number of published guidelines dealing with various ethical aspects of consent-taking. Of these, I selected three documents for a study of the salient elements in the consent-taking process for medical treatment, for the use of human biological samples for research and finally, for research into reproductive issues.

Consent for Medical Treatment

The UK Department of Health published a *Reference Guide to Consent for Examination and Treatment* in 2001, bringing out the following points:³

1. The person giving consent must be “competent” — that is, capable of understanding the conversation, comprehending its meaning and its importance, and therefore giving a meaningful opinion on whether to proceed. If the person that you are dealing with is not competent (perhaps a young child, or someone whose mental capability or consciousness is impaired in some way) then someone else who has responsibility for them may consent on their behalf.
2. Consenting is a continuous process — people can at any time withdraw, from treatment or from research participation, even if their reasons for doing so do not seem very satisfactory. This right of withdrawal is the ultimate guarantee that continued participation is a voluntary act. It should be made clear to the patient that withdrawal from a research programme does not mean he will no longer receive the same standard of medical care. The better the communication at the time that consent is obtained, the better the understanding as to how all possible consequences and results might be handled, the less likely it is that people will want to withdraw. If the issue is complicated and serious, it is critical that the researcher (or doctor) takes proper time to discuss with the subject, in clear and simple language. It is equally important for the researcher or doctor to allow enough time for the subjects to sort out any thoughts and confusion in their minds, and clear any doubts through asking questions. Wherever it is possible, the subject should be provided the necessary information in simple written form, and then asked for consent a few days later; the subject is given time to go through the information carefully and gather all the questions which he might not have been able to remember to ask the first time. The following points are worth remembering:
 - i) Unexpected decisions do not necessarily mean that a patient is incompetent; perfectly competent people may sometimes disagree with you
 - ii) Take time, and give the subject time to think about things
 - iii) Do not talk all the time — LISTEN as well
 - iv) Ensure that they, and you, know about their freedom to withdraw consent
3. The formal age of consent. The formal age of consent is usually about 16 to 18 years of age, although different jurisdictions have somewhat different rules. Children younger than this may however often have a good understanding of the issues and a valid opinion of their own, and even quite young children may have enough understanding to be entitled to express an opinion about research participation. It is always safer to ensure that a child who is old enough to understand what is going on, knows what is going on. The best situation, where a child has sufficient understanding, is to get consent from both the young person and their legal parent or guardian. It can be awkward where there are differences of opinion within a family, and a researcher should avoid these situations if it is at all possible. It is an act of desperation for a researcher to try to arbitrate between warring family members; better by far to try to recruit a different subject.
4. Adults who are not competent to consent for themselves represent a difficult legal problem, at least in the UK where technically no one is allowed to consent on behalf of an adult, even if they are not able to speak for themselves. In practice, a consensus must be reached with people who can be expected to be acting in the best interest of the adult concerned. “Best interests” may be quite broadly interpreted to include research which may

benefit other people — their family, or the community at large — which they, were they competent, might have wished to support.

5. Sometimes, an independent third party should seek the patient's consent for research. In treatment, it is usually best for the person carrying out the treatment to seek consent — a patient's consent to surgery is an agreement of trust between himself and the surgeon. In research, it may be rather different. Particularly if the person undertaking the research also (as often happens) has responsibility for the clinical management of the patient, then refusing consent may seem like a bad idea if the person asking is the person to whom you are obligated for your continuing health. In this situation, discussing consent with a more disinterested intermediary, may have advantages. Whoever takes consent must be properly qualified and trained in taking consent, and must know enough about the research programme to portray it fairly, but a more open conversation may be possible with someone less intimidating than the most senior consultant in the hospital! It is most important to emphasise that medical care should not be adversely influenced by a decision relating to research participation; failing to clarify this is a significant potential cause of coercion to consent.

Consent for the Use of Human Biological Samples in Research

Biological samples are, in essence, chemically or physically coded information about a person's body and its function. Thus they are not very different from clinical information. There are obviously specific pragmatic issues concerning the actual process of obtaining the sample, which need to be dealt with during consent. This is particularly important information for the research subject if the procedure involved would cause major inconvenience or risk to the subject. There are pertinent points in the UK Medical Research Council's guidelines that are not covered above:⁴

1. Samples should be treated as gifts — this is thinly veiled code for saying that people who donate samples for research should not be entitled to financial compensation, even if the sample forms part of a project that produces something of great commercial value, and someone else gets very rich in the process. It is extremely rare that any one sample is critical in such a discovery process, and the problems engendered in attempting to put in

place a fair system for dividing eventual profits amongst all those who contribute in any way to a programme of discovery and development are just too complex to contemplate.

2. All new samples taken specifically for research use should have the donor's consent. This is widely accepted, however, there are two types of sample collection that give rise to further consideration:
 - i) So-called "legacy" collections — groups of samples, perhaps from patients with some specific disorder, that have been painstakingly accumulated over long periods of time. In the past, consent requirements were less clear and so were the consent records for many of these collections. It is frequently either impossible or very impractical, to go back to the sample donors and ask for consent again. In some cases, where samples were taken many years ago and the people concerned may have wished to put that episode far behind them (such as the loss of a child), it is ethically questionable to reopen the whole issue by asking for further consent. One simple solution is not to use such collections at all, but some of these have considerable value and it will take a long time to replace them. If samples have been taken (and given) in good faith, for the benefit of knowledge and the betterment of medicine, it is unethical to throw them away for no valid reason. Although opinions differ, my personal view is that provided data in the outcome of the research is fully anonymised so that anyone who is not professionally involved in the research cannot access identifying details, and provided the work has been ethically reviewed and approved, it is legitimate to continue to use such legacy collections.
 - ii) The second type of sample which warrants specific consideration is "leftover" material — parts of samples taken in the process of routine clinical care (remnants of tissue from biopsies and blood) which are surplus to clinical requirements. Good pathology departments have systematically stored histological sections, tissue blocks, serum samples and so on, from large numbers of diagnostic samples, over very long periods of time. The samples were given for clinical use, and no research consent had been taken for them. Provided results using such material are anonymised, there is virtually no additional

hazard to the research subject (since the sample is being taken anyway for diagnostic purposes, and no one should use material for research which would actually put the diagnostic test at risk). In my view, provided appropriate protocols for protecting confidentiality are in place, the value of these collections for research purposes far outweighs the risk of harm to any individual that might result from their use. I therefore favour continuing to make such sample collections available for legitimate and approved research. It would be a good idea to devise some mechanism to avoid this problem recurring in future, by ensuring that those whose samples are taken for medical purposes understand that materials surplus to diagnostic requirements may be used for research, teaching, audit, quality control, among others. In the most general terms, the extent and nature of the consenting process should be appropriate to the very low level of personal hazard. Because of the large numbers of samples taken in this way, whatever process is devised has to be very simple or it will be unmanageable. This could, for example, be a notice given in writing to all patients admitted to a hospital setting out the policy for anonymised use of remnant tissues for research, audit and teaching purposes.

3. All research using human samples must be approved by an ethics review committee or institutional review board (IRB). There still are people who make their own judgement that the project which they are about to start is too innocuous to require an ethics review. There must be a reasonable lower limit, below which IRB submission is really superfluous. One such case may be a clinician who simply wants to look back over half a dozen cases that they have treated to see whether there is something in common between them. However, anything at all structured in the way of research using patient information or patient material should go to an IRB. You may present an outline of your research project to the chairman of the IRB to obtain a prompt opinion on whether the project warrants an IRB review. Nonetheless, the necessity for a review or no review is a decision better taken by the IRB than by the researcher.

4. When to provide feedback to the research subjects. In principle, information of medical relevance which emerges during a research study should be fed back to the participants. Where issues come to light as a result of the research which has obvious impact on the health of the subject, it is important to have established mechanisms for ensuring that the subjects, and those who care for them medically, are appropriately informed. However, in many other situations, the whole purpose of undertaking the research is that the results which are obtained are (at least until the research is completed) rather hard to interpret. For example, tests to look for mutations in a particular gene may be very difficult to interpret until much is known about the range of variation which can occur at that gene locus without causing pathology. Furthermore, research studies (although carried out in a careful and professional way) are nevertheless likely to be somewhat more subject to administrative and laboratory error than diagnostic laboratory assays subject to standard operating procedures and stringent quality controls. For both these reasons, it may be misleading and inappropriate to feed information from research studies back to the subjects, since it may cause undue anxiety, and may even lead to inappropriate medical action to avoid hypothetical hazards. A study involving a large number of people (for instance, the UK BioBank project aims to recruit 500,000 subjects) giving personal information to each research subject, can consume a considerable amount of resource; it is usually not enough to just post a result, but a proper discussion is needed to allow full appreciation of the interpretation of the results obtained.

For all of these reasons, it is sometimes in everyone's best interests to do the counter-intuitive thing and agree that there will be no feedback of individual results to research subjects. Whatever decision is taken, it is very important that there is clarity of understanding between researcher and subject as to what the position is with regard to feedback of individual results. Particularly where it is decided not to give individual results to subjects, it is good practice to send regular updates to all research participants on the general progress of the study and the nature of the results being obtained as a result of their cooperation.

(The Council's guidelines also include a checklist for researchers on seeking consent for the research use of human material.)

Consent Issues in Reproductive Research

The World Health Organisation's *Guideline for Obtaining Informed Consent for the Procurement and Use of Human Tissues, Cells and Fluids in Research* encompasses some special information and considerations:⁵

1. Liability and compensation for non-negligent injury. The WHO recognises that in this field of research, the sampling process itself may entail significant risk.
2. "Restricted consent". They introduce the question of "restricted consent" — people may well consent to samples being used for some types of research but not others. This is more likely to occur within emotionally laden fields such as reproductive biology than it is, for example, in drug trials.
3. Financial disclosure. They make the important point, that if a researcher is paid for recruiting research subjects, particularly if personal reimbursements are related to the number of subjects recruited, research subjects are entitled to know this. There are some fuzzy borderline issues such as where researchers are not personally reimbursed but are given research funding, for use in their department, or are given hospitality in the way of paid fares to meetings. Nevertheless, research subjects have some right to know if the advice they are receiving from the researcher carries a vested interest.
4. The use of foetal tissue. In many jurisdictions, there are special rules regarding the use of foetal tissue. The UK Polkinghorne *Code of Practice on the Use of Foetuses and Foetal Material in Research and Treatment* separates the process of obtaining

research consent from the person who is clinically in charge of the woman and her pregnancy.⁶ This is to avoid any possible pressured termination of pregnancies in order to provide aborted material for research purposes.

CONCLUSION

While I have dwelt on the components that make a good consent process, it is equally important not to let this process go to extremes; excessive emphasis on the complexities of appropriate consent should not be allowed to strangle harmless and reasonable research. Good research is ultimately a benefit to all humanity, and the great majority of people who are asked to participate in research do so willingly, are glad of the opportunity to do so, and come to no harm through doing so. Striking this balance between not taking our research subjects for granted, but not becoming so fixated on the process as to inhibit research or to make it impossibly expensive and complex, is the task before IRBs and researchers.

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