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Is Informed Consent Necessary for Research on Stored Human Samples?

Depolanmış İnsan Örnekleri Üzerinde Yapılan Araştırmalarda Aydınlatılmış Onam Almak Gerekli midir?

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ABSTRACT

Informed consent is always required before patients can be treated in health centers as well as participating in any kind of research. This requirement often poses a serious challenge to researchers in situations where existing guidelines are not clear about the ownership of donated or discarded human biological samples in hospital archives. The current regulations demand that when doing research, the major bioethical principles of autonomy, beneficence, non-maleficence and justice should always be respected and adhered to. There is increased value of stored biomaterials due to advancement in biotechnology which has also contributed to increased debate on whether researchers should seek informed consent from the individual donors before such materials can be used for research. In enforcing these bioethical principles, most guidelines focus on research involving direct contact with human beings, and no much attention is given to stored or discarded body parts and biomaterials that end up being used for research in later years. There are some hypotheses that can be tested by doing research on the stored biological samples, especially by students or scientists attached to various University hospitals, research-centers and laboratories. We attempt to provide some scenarios and reviewed guidelines that can help provide a consensus as to whether it is strictly necessary to have informed consent for research on stored or discarded human body parts and who should claim ownership of collected human biomaterials for research or potential commercial purposes.

Key words: Discarded Human biomaterials, ownership of human biospecimens.

ÖZET

Aydınlatılmış onam sağlık merkezlerinde çeşitli araştırmalara katılmak için gerekli olduğu kadar

hastaların tedavi edilebilmesi açısından da her zaman önceden yapılması gerekli bir işlemdir. Hastane arşivlerinde biyolojik örneklerin imhaya ayrılması veya saklanması hakkında mevcut kılavuzlar yeterli olmadığı zaman bu gereklilik araştırmacılar için ciddi bir sorun teşkil etmektedir. Mevcut düzenlemelerle talep edilen; araştırma yaparken yararlılığa, adaletli olmaya ve kişisel temel biyoetik prensiplere her zaman saygı duyulmalı ve uyulmalıdır. Biyoteknolojide ilerleme nedeniyle saklanmış biyomateryaller çok değerlidir fakat bu aynı zamanda araştırma için kullanılan materyallerin alındığı donörlerden aydınlatılmış onamın alınıp alınmaması hakkındaki tartışmaların artmasına neden olmaktadır. Bu biyoetik kuralları uygulamak, çoğu kılavuz insan ile doğrudan teması kapsayan araştırmalara odaklanır, vücut parçaları ve biyomateryallerin yıllar içinde araştırma için kullanılabileceğine dikkat edilmemektedir. Bazı hipotezlerde, saklanmış örneklerden araştırma yapılabileceği ve çeşitli testlere tabi tutulabileceği söylenir, özellikle çeşitli üniversite hastanelerine, araştırma merkezleri ve laboratuvarlara bağlı öğrenciler veya araştırmacılar tarafından. Biz bazı senaryolara ve yenilenmiş kılavuzlar ile saklanan veya atılan vücut parçalarının ticari veya araştırma amacıyla kullanılmalarında aydınlatılmış onamın gerekliliğini öne sürenler ile bir uzlaşma sağlamaya katkıda bulunmayı amaçlıyoruz.
Anahtar kelimeler: İmhaya ayrılmış insan biyomateryalleri, insan örneklerinin mülkiyeti.

Introduction

Informed consent is always required before patients can be treated in health centers as well as participating in any kind of research. This requirement often poses a serious challenge to researchers in situations where neither research guidelines nor health authorities are clear about the ownership of donated or discarded human biological samples in hospital archives. It has been pointed out that when doing research, the major bioethical principles of autonomy, beneficence, non-maleficence and justice should be respected and "balanced"[1]. There is increased value of stored biomaterials due to advancement in biotechnology[2] which has also contributed to increased debate on whether researchers should seek informed consent from the individual donors before such materials can be used for research[3].

In enforcing these bioethical principles, most guidelines focus on research involving direct contact with human beings[4-7], and no much attention is given to stored or discarded body parts and biomaterials that end up being used for research in later years. There are some hypotheses that can be tested by doing research on the stored biological samples, especially by students or scientists attached to various University hospitals, research-centers and laboratories. The research interests of such people should not be stifled due to lack of clarity on ethical issues regarding the use of the stored human samples. Some internal ethical review

boards (IRBs) often simply waver informed consent on use of those biomaterials that have been 'stripped of' their unique identifiers (e.g. codes) such that the information or data collected from them cannot be traced back to the original source or donor[8]. Therefore, this has led to the suggestion that perhaps laboratory-based researchers should not be required to have informed consent in order to collect data from archived human bodies or biomaterials, provided the source cannot be identified[2,9].

In this opinion review article we try to present scenarios or guidance using some previously existing references and international guidelines that may help to answer the question of whether it is really necessary for laboratory investigators to always have informed consent for use of stored or discarded human samples for research.

An Overview of Informed Consent in Medical or Biomedical Practice

Informed Consent in Research means authorization by an individual to be recruited into any kind of research involving collection of information by an investigator. It is also required in medical practice before a patient can be given any medical care by the medical practitioner[10], either for diagnostic or therapeutic purposes[11]. In both of these scenarios, the potential research participant or patient must get adequate information about all the details of the procedures, risks and benefits that they might experience by participating in a particular study or during the course of receiving treatment for their disease condition[10,12]. Although verbal consent is often acceptable when receiving medical treatment, the informed consent in research must also be documented with a signature on the consent form either in handwriting or in finger print form[11]. As far as receiving informed consent for human biological samples is concerned, the following concepts must be taken into consideration: "ownership of the human body or its parts; possible commercial use of the human body or its parts; and obtaining the informed consent for use of human biological samples"[13]. The ethical requirement of having to seek for informed consent before conducting any kind of research involving human beings is usually enforced by the local Institutional Ethics Review boards, and the various Medical Councils or Associations ensure that medical ethics is upheld by all their health professionals while dealing with patients.

Major Issues Regarding Ethics of Using Human Biomaterials

We start this section by reviewing Carlo Petrini's guidance on issues regarding, but not limited to; who can own the human body; possible commercial use of the human body and how to get informed consent for use of stored human biological samples for research purposes. This

will eventually help us to come to a consensus on whether informed consent is always necessary in order to use the stored human body parts or biomaterials for research and commercial purposes.

Who can Claim Ownership of Human Body or its Parts?

Research involving the use of human biospecimens (human body parts, tissues or cells and materials such as body fluid samples) is extremely important, especially in this era of advanced biotechnology due to the potential commercial value associated with it. Human body parts or biomaterials are also routinely used in teaching of medical students and other health professionals or scientists. According to Carlo Petrini, there are ethical issues regarding the "ownership of the human body or its parts and their possible commercial use" which calls for proper guidelines to be drafted and followed strictly[13].

The NIH (National Institutes of Health) guidelines for human biospecimen storage and tracking in research entail all human biospecimens/samples "including nucleic acids and other direct derivatives from human tissues" [14]. They also consider extracted DNA or derived cell lines which can be traced to a particular human subject as "independent biospecimens"[14]. These guidelines are applied specifically to: (a) "identified specimens" that can be associated to any available human identifier e.g. medical record number or address; (b) "Coded specimens" that are identified by some random numbers which can still be associated with the source of the sample by the researcher; (c) "Unlinked specimen" which have been stripped of their identification numbers making it impossible to link them to their source; (d) "Unidentified specimens" which were previously collected without any form of identification[14]. It is also emphasized that these guidelines always apply irrespective of whether (i) the specimens had been collected for clinical care or for research purpose; (ii) the original donor is alive or deceased[14]. However, the guidelines do not apply to "tracking or reporting of biospecimens or their derivatives obtained from commercial sources such as human cells or tissues purchased from a vending company", even though they were originally obtained from human body parts[14].

The ownership of the human body biospecimens can sometimes stir up some serious ethical and legal debates[13], even though the "Universal Declaration of human rights" already prohibits all forms human slavery[15]. The processing or modification of dead human bodies or body parts has caused some controversy in the past, as to who should be the rightful owner [13]. Legal disputes have been heard where treated human bodies or biospecimens have been

awarded to people who processed them with chemicals such as spirit for instance, in a bid to preserve them after acquiring them[13]. Petrini Carlo further points out that the current legal understanding is that once the biospecimens (e.g. cells and tissues) have been removed from the dead human body, "the recipient" becomes the rightful owner, even if he/she is not the original source of the specimen[13]. Moreover, if the recipient treats such biospecimens for instance in a bid to preserve them or prepare them for viewing, he/she is also granted some kind of "ownership rights"[16]. We certainly think that someone has to take charge of these stored biological specimens, even though the guidelines don't seem to categorically describe such a person as the rightful owner. Such a person could be the hospital director where the specimens are archived, or the bio-depository manager of major research center/laboratories with huge specimen bank(s) that could be accessed by the public.

Possibility of Getting Some Commercial Benefits from Human Body Parts

The potential commercialization of the human body or its parts has already been highlighted in the past[13] and is currently taking place in some developed countries such as the United States of America. This starts right at the point of collection of the biospecimens (e.g. blood or plasma)[17], by handing out some kind of incentive(s), as a way of providing motivation to potential donors. It is extended to the vending of commercial products formed from these original biospecimens in form of hemotherapeutics (i.e. blood replacement therapies such as plasma, platelets and vaccines) manufactured by some pharmaceutical companies. Disease out-breaks involving high fatality rates such as the most recent Ebola cases in West African countries provide a great opportunity for investigators and pharmaceutical companies to collect human samples which are often used for commercial purposes, especially in vaccine development. In such cases the first companies to collect and process these samples claim ownership where they end up taking the lead in commercializing such samples either to other pharmaceutical companies that may be involved in drug or vaccine development or other interested investigators.

Due to the gradual decline in public or social altruism, it was found necessary to encourage the payment of incentives to potential donors, just like research participants in medical research[18], as a means of recruitment and retaining them to become a continuous supply of raw materials for those essential medical products or hemotherapeutics[17]. This method of collecting biospecimens for purposes of producing urgently needed hemotherapeutics received a lot of criticism from purists and ethicists, but it is still an important means of blood

supply in the developing world[19]. Moreover, replacement blood components such as platelets are also still being harvested from "compensated donors" in certain parts of the developed world where compensated whole blood donation is not allowed[17].

Despite the above potential commercial use of the human body, there are legal or "authoritative documents" such as the Council of Europe on bioethics[13] still insisting that the human body cannot be used for commercial purposes or as a source of profit[20, 21]. This same Council of Europe document also indicates that the removed human body parts (e.g. blood and other tissues) may be used for purposes other than the reason for removing them, as long as a proper informed consenting process has been followed with the donor[21]. This exception in the general rule is enough in our opinion to justify the use of human body parts in research and in the production of commercially viable products such as hemotherapeutics, therapeutic cell lines and vaccines. However, according to Petrini Carlo, this also requires taking into consideration "those guidelines that regulate the patentability of biological human samples" and the storage of biospecimens in public bio-depositories (e.g. hospital tissue sample archives) for future research or public altruism [13]. It is such patent guidelines that we think should protect the commercial interests or benefits of everyone involved in the collecting, processing and vending of the commercial products made from human biospecimens.

Getting Informed Consent to use Human Body Parts (or Samples) for Research

Seeking informed consent from potential donors is a way of respecting human dignity and autonomy. Most guidelines have emphasized seeking of a proper informed consent as the most important ethical issue in the use of human body parts for research and for any potential financial or commercial rewards realized from them[22,23]. Donors of human body parts always sign an informed consent before the removal of the biospecimen either for diagnostic or therapeutic reasons in health facilities around the world, even though there are still some variations in the nature informed consent sought[24]. When it comes to collecting and storage of human biospecimens for future research and production of potentially commercial products from these specimens, a much more detailed consenting process is required with a number of options presented to the potential donor[24] before committing someone into signing the informed consent form without any kind of coercion.

Besides participating in research for the immediate direct benefits, most people might also be very willing "to authorize the use" of their biospecimens for future research if given the

opportunity to express this desire of making such a contribution[24]. The world health organization (WHO) guidelines for informed consent in this case also recommend that the potential donor must be given the option of declining to consent to any future use of their biospecimen either in research or in production of potential commercial medical remedies, as well as the option of setting certain terms of restrictions[25]. Petrini Carlo also suggested a criteria that can be used in dealing with the ethics associated with the collection of biospecimens for future research with potential commercial gains[13], by making reference to recommendations from the American Medical Association (AMA) that made guidelines to be followed by physicians intending to collect such biospeciments[23]. According to these guidelines, it is clear that informed consent must be sought always "before patients' organs or biomaterials can be harvested; potential commercial applications must be disclosed to patients before a profit is realized on products developed from the biospecimens; human tissue and its products may not be used for commercial purposes without the informed consent of the patient who provided the original cellular material; profits from the commercial use of human tissues and its products may be shared with patients, in accordance with lawful contractual agreements; and diagnostic and therapeutic alternatives offered to patients by their physicians should conform to standards of good medical practice and should not be influenced in any way by the commercial potential of the patient's tissue"[26].

It has also been suggested following some debates regarding the use of stored samples that patients' or potential donor's informed consent forms should contain information showing exactly what kind of future research is going to be conducted on the biospecimen(s) that they are going to donate to enable them make a well informed decision[2]. We think that since the guidelines regarding Informed consent are not clearly defining the duration for which the human samples can be kept, it would be unreasonable to expect investigators to start by searching for the people who donated their samples so many years in the past. So, it would entirely be dependent on the guidance that such a researcher gets from the person claiming ownership of the specimen at that moment to clearly indicate which biomaterials can be used for research since they already got informed consent for them at the time of donation, and leave out those which are not accessible for research.

Conclusion

The common understanding is that every investigator requires proper informed consent before using human biospecimens for research purposes. However, the informed consent forms to be signed, should give the potential donor all the available options with enough

information showing all the potential uses of the biospecimen(s) that they are being asked to donate, before they come to making an appropriate decision of whether they want to donate or not. So, the question of whether all laboratory investigators require informed consent to use stored or discarded human biological samples, we think can be answered depending on who claims ownership of the biospecimen at any particular moment in time. In a situation where the investigator wants to conduct some research on stored specimens in a bio-depository where no direct informed consent can be obtained from the original donors, it is presumed that the informed consent that was given by the donors at the time of harvesting the biospecimens would suffice, as long as the donor consented to the use of their biospecimen for future research of any kind. And for those biospecimen donors, who would have consented to the use of their biospecimens for research, but with certain restrictions, for instance, not consenting to the use of their biospecimens for production of any commercial medical products or cosmetics, then the management of the bio-depository has to be very discrete and careful about who can conduct research using such 'restricted biospecimens'.

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