

REFLECTION DOCUMENT

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The practice of human cell (HC) and human tissue (HT) transplantation has reached a global dimension. The international circulation of HC/HT or their products and the involvement of multinational companies in HC/HT processing and distribution has an impact on the way we practice medicine, trade health goods and services and regulate such activities on a global level.

National oversight and monitoring are mandatory for any activity relating to HC/HT transplantation. But there is also a need for common global requirements for HC/HT transplantation concerning its medical, scientific, legal and ethical aspects.

When defining a common normative basis for activities related to HC/HT transplantation, the perspective of the donors, their legal or nominated decision-makers or their next-of-kin is primary. Without them, there would be no HC/HT transplantation. But it is also important to consider the perspective of the recipient, to discuss the role and limits of cultural and religious factors which affect the practices of HC/HT transplantation and to be aware of global differences in health care systems and available resources.

1. Lack of clear basic definitions in HC/HT transplantation

a. Ownership of the human body, its parts or products is not clearly defined from a legal, economic, cultural and philosophical perspective.

- In many countries, there are no legal frameworks for HC/HT transplantation. Existing frameworks are based on a variety of legal definitions of HC/HT in which tissues may be regarded as organs, specific entities, medical devices or pharmaceutical products. It is important to consider that legal definitions influence processing and distribution of HC/HT as well as oversight of activities involving HC/HT.

- Property rights of HC/HT are inexplicit from a legal perspective. In the deceased in particular, it is not clear whether the HT belongs to the deceased individual, to his or her next-of-kin, or to society.

- From an economic perspective, it is unclear at what point the human body is transformed into a product. When HC/HT products are sold, does this imply the sale of a good with a certain value? Or rather, is a priceless object associated with monetary value through investment of other goods and services, the cost of which is recovered to allow continued supply?

b. The term “donor” is often ambiguous and may refer to either the donor him- or herself, to his or her legal/nominated representative and/or to the donor’s next-of-kin.

- While the donor him- or herself is able to decide whether they wish to donate tissue and give informed consent, it is important to acknowledge that in some cases, next-of-kin may know little or nothing about the donor and his or her wishes. And even if they know, next-of-kin do not always decide according to the hypothetical will of the deceased (substituted judgement), but may also take decisions based on their own interests.

In the following, a broad notion of “donor” as the donor him- or herself, to his or her legal/nominated representative and/or to his or her next-of-kin is adopted.

2. Donation and procurement of HC/HT

a. Both living and deceased donation of HC/HT should be voluntary and unpaid.

- Because payment for HC/HT donation may unduly induce donors and will likely result in exploiting or taking of unfair advantage of the vulnerable and poor, donation

of HC/HT from both live donors and from the deceased should be unpaid. However, donors may receive compensation for travel expenses, loss of earnings and/or other expenses actually incurred.

b. The criteria applied in the identification and selection of potential donors should be made explicit and clearly communicated to the general public

- It is important to note that in today's practice, potential donors are not only identified according to medical eligibility: The theoretical number of medically eligible HC/HT donors by far exceeds the number of people who actually donate. This can be either due to potential donors declining consent, or to factors other than medical eligibility that influence donor identification on the part of medical, nursing and/or tissue procurement personnel. Which additional factors influence donor identification in practice frequently remains unclear.

- Donor registries may facilitate a more systematic identification of potential donors, if security and privacy of data can be guaranteed.

c. Procurement of HC/HT should be coordinated with the procurement of organs, if applicable.

- When consent has been given for both organ and HT procurement from a deceased person, priority decisions may be necessary. Should organ or HT procurement have priority? And should a procured organ be used as an organ for transplantation, if medically appropriate, or processed into a profitable HT (e.g. processing of heart valves or the entire heart)? Because the scarcity of organs is more marked than the scarcity of HT, procurement of organs should be generally prioritized over procurement of HT for transplantation.

3. Consent for donation of HC/HT

a. Consent for donation is crucial.

- The body of a living person is not a public good, and the remains of a deceased person are usually not considered a public good either. HC/HT can only be procured after consent for donation has been given either by the person, his or her legal/nominated representative or his or her next-of-kin. If informed consent can be presumed rather than be required as an explicit statement largely depends on public awareness and individual education about HC/HT transplantation and opting out procedures.

- Consent for donation does not justify all clinical practices. In particular, HT procurement in living donors can inflict irreversible and severe harm on the individual. Only safe clinical practices that do not cause serious harm to the individual can be considered for living donation.

- Prior to actual procurement of HT, withdrawal of consent should be possible at any time. In rare cases such as hematopoietic stem cell donation, however, withdrawal of consent may be highly problematic (e.g. when the recipient is already conditioned), and this should be made clear to the donor.

b. It is a particular challenge to sensitively provide appropriate information on HT procurement, processing, distribution and transplantation when obtaining informed consent from relatives in the deceased donor situation.

- HT procurement, processing, distribution and transplantation are complex and continuously changing procedures, and providing comprehensive information on current practices does not seem appropriate in a situation of grief. Information should rather be given with regard to the donor's informational needs. A sensitive approach by professionals who are educated to work with the bereaved and are both confident and comfortable discussing donation with families is crucial for obtaining valid consent for donation. Follow-up support for the bereaved and their information needs should be addressed in the consent discussion as well.

- It is particularly controversial whether information relating to profit-making should be provided. Some suggest a nuanced approach that distinguishes between involvement of for-profit and not-for-profit organizations in HC/HT processing and/or distribution. It is important to note that profits can be made in both organizations, but are then distributed differently. For-profit organizations generally distribute profits among shareholders while not-for-profit organizations invest surpluses into the improvement of services (but do not distribute surpluses among stakeholders). It is reasonable to assume that the public expects not-for-profit organizations to be involved in HC/HT processing and/or distribution or similar services; however, this is not the case for for-profit organizations. For this reason some suggest that information should be provided about involvement of for-profit organizations but can be withheld when not-for-profit organizations process and/or distribute HC/HT. In any case there can be no valid consent if the consenting party is deceived or donates under the assumption of different conditions, e.g. concerning profit-making or access.

- There is a lack of empirical studies on informed consent for HC/HT donation, in particular with regard to the perspective of the bereaved family (relating to procedural questions of obtaining consent, follow-up of donors and non-donors, etc.).

c. Public awareness and individual education are prerequisites for an effective donation system and for any system presuming informed consent for donation.

d. The discussion about informed consent for HC/HT donation has to take into account existing legal frameworks.

e. Inducements can unduly influence the decision for or against HC/HT donation or constitute a conflict of interest for the next-of-kin.

4. Reporting of testing results

a. It is a sensitive issue whether donor confidentiality of testing results should be maintained even if this affects the health of third parties (e.g. in HIV-positive test results).

The issue should be anticipated as far as possible as part of the consent process. Reporting of testing results is more appropriate if treatment of those affected is possible and likely, and can be legally mandatory if the disease is notifiable.

5. Stewardship of donated HC/HT

a. Tissue and cell establishments have a responsibility to act as stewards of a donation that was entrusted to them, ensuring that the maximum possible benefit for patients results from the donation.

b. The procurement, processing, and distribution of tissues and cells should honour the intentions/expectations expressed in the consent to donate.

- Donors have a right to specify future use of donated HC/HT. Donor wishes should be respected with regard to (1) potential clinical uses – life-saving, life-enhancing or cosmetic – and other uses of donated HC/HT, such as research and training; (2) involvement of for-profit organizations in processing and/or distribution of HC/HT; and (3) potential international circulation and use of donated HC/HT. Directed donation involving discriminatory choices, in particular relating to race and religion, should not be possible.

- In addition to respecting the wishes of individual donors, general priorities for clinical uses of HC/HT should be set in accordance with the general intention of donors to help others in need. One of several reasons to justify oversight and regulation of HC/HT practice is to assure that the choices of organizations involved in HC/HT transplantation are compatible with donor intent.

c. Questions like profit-making have to be discussed in the light of their compatibility with donor's wishes.

6. Profit-making in HC/HT processing and/or distribution

a. The categories "public/not-for-profit" and "private/for-profit" should not automatically be attributed a moral notion; important criteria are stewardship of the donated HC/HT, efficiency, transparency, accountability, fair pricing and responsiveness to health needs of the local or national population and allocation on the basis of clinical need.

- According to most existing legal and regulatory documents, the involvement of for-profit organizations in processing and/or distribution of HC/HT is neither forbidden nor mandatory. HC/HT processing and distribution have many business features, such as technical processing, quality and safety management, distribution of processed HC/HT, etc. Maintaining some market forces in such activities is likely to result in efficient organizational structures and investment in high-quality facilities and/or research and development, and efficient use and high-quality processing of donated HC/HT as well as continuous improvement of services is also an ethical imperative. Therefore, involvement of for-profit organizations in HC/HT processing and possibly distribution can be justified.

- In practice, both not-for-profit and for-profit organizations process and/or distribute HC/HT and some make considerable profits by doing so, depending on national regulations. But the distinction between not-for-profit and for-profit organizations is often blurred because not-for-profit organizations may own for-profit organizations or collaborate with such entities. In addition, not-for-profit and for-profit organizations have to be viewed in the context of national health-care systems. In some countries, tissue establishments do not receive public funding. In other countries, not-for-profit institutions cannot meet existing medical needs and patients may have to rely on services of for-profit institutions to access necessary medical care. This is why

stewardship, efficiency, transparency, accountability, fair pricing and responsiveness to health needs of the local or national population, aiming for equity in access, are often more important for evaluating practices than judging the for-profit or not-for-profit nature of involved organizations.

- It has to be recognized that transparency with regard to profits can be a problem even if official data exist.

b. There may be conflicts of interest between a profit-making orientation and appropriate procurement of and equitable access to HC/HT. For-profit organizations should not be involved in the promotion of donation, the interviewing of donors and donor families or the procurement of tissues, and regulation should aim to minimize conflicts of interests in the distribution of HC/HT.

- While there is consensus that for-profit organizations should not be involved in procurement of HC/HT, there are also concerns that the profit-making orientation of for-profit organizations can compromise equitable access to HC/HT.

c. Involvement of for-profit organizations in HC/HT processing and/or distribution can be acceptable (1) if donors are informed accordingly; (2) if the quality, safety and price of products are at least comparable to not-for-profit organizations; and (3) if the profit-making orientation does not compromise equitable access to cell and tissue services.

d. Autologous/private cord blood banking is not an evidence-based practice today, but a speculative private investment. It should only be offered (1) if proper informed consent is guaranteed, also with regard to the current lack of evidence for the practice; (2) if the cord blood is procured and processed according to safety and quality standards of allogeneic/public cord blood banking; and (3) if cord blood is stored in a sustainable manner.

- A particular concern is a lack of quality control on all levels of autologous/private cord blood banking. As private institutions, these banks are often not subject to common regulatory frameworks. The quality of cord blood stored in private banks may be too uncertain to be actually used by some transplant clinicians.

7. Allocation and international circulation of HC/HT

a. National oversight and prioritization rules are necessary to avoid shortages of HC/HT and to guarantee equitable access to cell and tissue services.

- Patient need should be the most important criterion in the allocation of HC/HT, because donors generally give HC/HT with the intention to help others. Allocation according to patient needs implies that there is a priority of use for life-saving over life-enhancing over cosmetic purposes in transplantation practice. Factors such as scientific evidence, “reciprocity” of services between procurement and processing institutions and waiting time can be equally important factors for allocation of HC/HT. While there is consensus on the need for national oversight and the relevance of explicit allocation criteria, it is controversial how allocation factors should be weighted and whether the scope of allocation rules should be institutional, national, regional, or international. Factors like ethnicity, nationality or religion should not play a role in HC/HT allocation.

- Several factors implicitly affect the allocation of and access to HC/HT and require consideration in the regulation and oversight of these activities. These are most importantly (1) the legal status of HC/HT which defines requirements for processing and thereby affects the balance of for-profit and not-for-profit involvement; and (2) the HC/HT establishments themselves which may process HC/HT according to profitability of different products (e.g. processing of skin into highly profitable acellular dermis products instead of supplying it as minimally processed skin for burn care).

b. International circulation of HC/HT can help address patients’ needs on a global level but can at the same time lead to inequities.

- Both for-profit and not-for-profit organizations may experience a conflict of interest between providing access to HC/HT to the local population and making profits by exporting HC/HT internationally. HC/HT should be circulated internationally only if local, national or regional needs are met.

- International circulation or trade of HC/HT does not necessarily imply scarcity of HC/HT.

- Despite the international circulation of HC/HT, transplant tourism also occurs in the field of HC/HT transplantation. Wealthy patients from resource-poor countries go to wealthier countries for HC/HT transplantation services, indicating the need to improve local access to appropriate transplantation services.

c. Building of tissue banking and hospital infrastructures should be fostered in parallel to be able to provide equal access to care.

8. Recipient consent

a. Consent by or on behalf of the recipient must contain information that a planned intervention contains human material. Recipients or their surrogate decision makers also need to be informed about the specific risks of the HC/HT product designated for use, if any, and therapeutic alternatives.

- Internationally, HC/HT recipients or their surrogate decision makers may be unaware that a planned intervention contains human material.

9. Quality and safety

a. There is a need for graduated quality and safety standards for HC/HT transplantation. Minimal quality and safety requirements must be met to guarantee the safety of recipients even if this implies a reduced availability of HC/HT.

- This requirement endorses the WHO Aide Mémoire for National Health Authorities (2006): Access to Safe and Effective Cells and Tissues for Transplantation.

b. Follow-up of living HC donors and HC/HT transplant recipients as well as data collection and scientific outcome evaluation are integral and mandatory elements of any HC/HT transplantation procedure.

c. Traceability should be included in regulatory systems of cell and tissue transplantation.

- Considering that many organ donors are also HT donors, it is desirable for the traceability of organs and tissues to be coordinated in a common surveillance system with universal donor identification numbers.

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