WORLD HEALTH ORGANIZATION

FIFTY-SEVENTH WORLD HEALTH ASSEMBLY A57/17
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Human organ and tissue transplantation

Report by the Secretariat

1. At its 112th session in May 2003 the Executive Board discussed a report by the Secretariat prepared in response to a request by the Government of Colombia for the topic of human organ and tissue transplantation to be included on the agenda. The Board agreed that the Director-General should establish a group of experts who could work with the Secretariat in order to prepare a report setting forth a way forward for WHO regarding organ and tissue transplantation, including xenotransplantation,[1] for the Board's consideration in January 2004.[2] The ensuing consultations culminated in a meeting, hosted by Spain with support from the United States of America, held in Madrid from 6 to 9 October 2003, at which 37 clinicians, ethicists, social scientists and government officials from 23 countries, representing all WHO regions and all levels of economic development, closely analysed issues of global concern in ethics, access and safety in tissue and organ transplantation.

2. The report of the Madrid meeting[3] outlines the main concerns about allogeneic and xenogeneic transplantation identified during the consultation process and highlights points of consensus. The transplantation of organs, cells and tissues has become the treatment of choice for a wide range of both fatal and non-fatal diseases, resulting in high levels of demand for transplantation services, particularly in high- and middle-income countries. The consultations highlighted, however, that allogeneic (human-to-human) transplantation poses major challenges and that xenotransplantation, which offers a potential alternative to allogeneic transplantation in certain conditions, requires particularly rigorous oversight and management in view of its specific potential risks and related problems.

3. Following this work, the Executive Board at its 113th session in January 2004, considered a report[4] on human organ and tissue transplantation, and adopted resolution EB113.R5 for submission to the Health Assembly.

[1] Animal-to-human, or xenogeneic, transplantation.

[2] See document EB112/2003/REC/1, summary record of the second meeting.

[3] Ethics, access and safety in tissue and organ transplantation: Issues of global concern, Madrid, Spain, 6-9 October 2003: Report. Geneva, World Health Organization, 2004 (document WHO/HTP/EHT/T-2003.1; http://www.who.int/ethics/topics/en/madrid_report_final.pdf).

[4] Document EB113/14.

MAIN CONCERNS IN ALLOGENEIC TRANSPLANTATION OF ORGANS, TISSUES AND CELLS

Lack of comprehensive data and oversight

4. Although several countries have introduced compulsory registration of transplant procedures and some voluntary registries also exist, there is no comprehensive system to collect data on the different types of transplantation and their outcomes. The lack of documentation makes it difficult to estimate the extent of ethically unacceptable practices or the relative efficacy and safety of transplantation for the treatment of various conditions and in various settings.

Insufficient supply of cells, tissues and organs from deceased donors

5. The need for cells, tissues and, in particular, organs remains unmet globally. Inadequacies in clinical expertise and infrastructure, an inability to fund the surgery and follow-up treatment, and resistance to post-mortem donation resulting from local legal, religious and cultural factors contribute to this shortfall.

6. In the case of kidney transplantation, the use of organs from live donors produces better results medically than kidneys from deceased donors. The use of deceased donors as sources is preferred, however, because a broader range of human material can be obtained, and the risks and burdens inherent in operating on a living donor are avoided. To maximize donations from deceased donors, an effective coordinating organization, adequate medical and logistic infrastructure, appropriately trained staff and governmental involvement are needed.

Safety and ethical issues in living donation

7. The number of donations from live donors is increasing. Globally, just over half the kidneys transplanted each year are obtained from living donors, while in most developing countries almost all kidneys come from living donors. Where appropriate medical care is available, the risks associated with live kidney donation are low but not negligible – in addition to operative complications, they include such long-term risks as failure of the remaining kidney. No reliable data are available on the risks to living donors in many settings, in particular when exploitation of donors may be suspected.

8. Donors who are genetically related to recipients can provide the best matches for transplant material, thereby lessening the need for immunosuppression and lengthening the survival of graft and patient at lower cost; typically, such donors are also easier to follow up. A genetic relationship between the donor and the recipient increases, but does not guarantee, the likelihood of altruistic motivation; nor does it preclude coercion or financial incentives.

9. Although non-related donors may also act altruistically, strong evidence exists of such donors being remunerated directly or indirectly, even in countries that have adopted laws against the purchase and sale of organs in accordance with Guiding Principles on Human Organ Transplantation endorsed in 1991.[1] Patients from countries where waiting lists are long or where organs from deceased donors are not available travel abroad in order to purchase a transplant. This “transplant tourism” is present in all WHO regions, with patients often travelling to low- or middle-income countries. Donors usually come from the poorest and most vulnerable parts of the population. Transplant tourism appears to be extensive and active steps will be needed in order to prevent it.

[1] See document WHA44/1991/REC/1, Annex 6.

Safety, quality and efficacy of tissues and cells

10. The volume and complexity of activities relating to transplantation of tissues and cells are growing rapidly although in many countries this field remains unregulated by health authorities. Around the world, simple tissue banks that operate locally coexist with large-scale institutions selling cells and tissues in worldwide markets. The extent of international circulation of human tissues and cells for transplant purposes is not well documented but is believed to be large and growing. Definitions of human cell-based medical devices, biologicals and tissues for transplantation have not yet been agreed internationally, nor have minimum standards to promote the safety, quality and efficacy of cells and tissues for transplantation been established. Moreover, it is not known how public confidence in organ-donation programmes would be effected when tissue banks were making profits from the commercial use of material from human bodies freely donated.

Access to transplantation in resource-poor countries

11. Transplantation can save life and improve the quality of life, and it can reduce the total cost of care for patients with many conditions in low- and middle-income countries compared with alternative treatments, such as renal dialysis. These countries might benefit from the experience of similar countries with better access to transplantation through successful transplantation programmes, from guidance on needs assessment, and from regional and global partnerships in developing transplant programmes that are responsive to their identified needs.

MAIN CONCERNS IN XENOTRANSPLANTATION

12. Xenotransplantation has the potential to supplement the limited supply of human material for transplantation and may even become an alternative. However, xenotransplantation (including the use of living xenogeneic cells, tissues or organs, as well as human bodily fluids, cells, tissues or organs that have had ex vivo contact with living xenogeneic material) presents specific immunological problems for recipients. It also may transmit infectious agents of animal origin to the recipient and, hence, possibly to the general public; recent instances of human epidemics/pandemics arising from cross-species infections, such as severe acute respiratory syndrome, underline the public health risks of xenotransplantation. These risks are compounded by immunosuppression, nonexistent or inadequate diagnostic tools, and an absence of effective therapy. Additional basic and clinical research is needed on both the safety and the efficacy of xenotransplantation, which should proceed only with due oversight and surveillance. WHO, in conjunction with OECD, has issued guidance on such surveillance and response.[1]

13. Ethical questions in xenotransplantation include whether potential recipients (and possibly their family and other close contacts) have given voluntary, informed consent, and whether monitoring of recipients may be mandated along with containment measures when transmission of an animal pathogen is suspected. There are also special ethical issues associated with the use of animals as sources of material.

[1] OECD/WHO consultation on xenotransplantation surveillance: summary report, document WHO/CDS/CSR/EPH/2001.1; WHO guidance on xenogeneic infection/disease surveillance and response: a strategy for international cooperation and coordination, document WHO/CDS/CSR/EPH/2001.2.

14. In several countries xenotransplantation now features in clinical research or even forms part of medical practice. Xenotransplant experiments have been reported in countries with no regulatory oversight. Moreover, "xenotransplant tourism" by patients who are ready to pay for unproven interventions in countries without adequate controls potentially risks global dissemination of new pathogens and may undermine this fledgling field. Thus an urgent need exists to act internationally to establish mechanisms for the surveillance and effective regulation of xenotransplantation.

THE WAY FORWARD

15. The consultative process (see paragraph 1), with its extensive discussion, led to broad agreement on the role of governments and WHO in dealing with these concerns. The consensus was that Member States should give urgent attention to ensuring effective oversight of cell, tissue and organ transplantation (from the procurement and distribution of human material for transplantation to the follow-up of recipients and donors), being able to account for such material, and implementing safeguards against the risks posed by xenotransplantation. Member States should also put in place effective regulatory control and surveillance of transplantation activities including the follow-up of recipients and living donors. In the case of xenotransplantation, this supervision should be based on a specific framework that includes appropriate practices in animal husbandry, patient and animal testing, and follow-up activities. The latter should include the maintenance of archives of biological specimens in order to facilitate detection of any transmission of xenogeneic infectious agents. Only with such control and surveillance should xenotransplantation be allowed. A further conclusion was that WHO should facilitate communication and collaboration among Member States to control the international circulation of material for transplantation, to prevent transplant tourism that exploits poor, vulnerable donors, and to ensure effective surveillance of xenotransplantation.

16. Current practices and thinking challenge the 1991 Guiding Principles. The consultations indicated that WHO needs to update and complete its guidance to Member States, and that it should create a global evidence base in order to help to identify obstacles to be overcome, evaluate practice and validate potential model transplantation programmes. Besides working with Member States to gather data, WHO should explore opportunities to cooperate with international scientific bodies. Furthermore, strong agreement emerged from the consultations that any commercialization of organs should continue to be declared illegal and unethical, although other evidence indicates that some clinicians, patients and philosophers would allow payment for organs, a practice either allowed or not punished in a few countries already. Further work is needed to understand the ramifications of programmes that include a payment and to clarify the boundary between removing disincentives and sanctioning the purchase of organs. Data on the short-term and long-term safety of donation for living organ donors need to be assembled if guidance is to be issued. Finally, the safety, quality and efficacy of transplantation could be improved at the global level by the application of internationally agreed minimum standards, including common definitions and consensus on the balance of risks and benefits (such as the risks associated with specific transplantation procedures versus the consequences for patients not receiving a transplant).

ACTION BY THE HEALTH ASSEMBLY

17. The Health Assembly is invited to consider the draft resolution contained in resolution EB113.R5.

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