するための行政的な規制を整備しなければならない。規制には、患者の追跡調査を確実に行うための具体的な手段、感染症の報告義務を含む必要がある。
2．国際的な追跡調査のネットワークの構築が必要である。それには、異種移植の定義、ガイドライン等の国際的な共有が前提になる。
3. WHOの主な役割としては、1）各国の異種移植の規制に関する基本原則の確立、行政的規制の確立にむけた努力を援助すること、2）症例の登録を含む異種移植の国際的なサーベイランスシステムを構築すること、3）異種移植が公衆衛生上のリスクを持つことを明確にした、適切なインフォームドコンセントのモデルを示すこと、等とされた。

国立感染症研究所・遺伝子解析室
神田忠仁

資料１－２

WORLD HEALTH ORGANIZATION

WHO/HTP/EHT/T-2003.1

Ethics, access and safety in tissue and organ transplantation: Issues of global concern

Madrid, Spain, 6-9 October 2003

Report

NOTE BY THE SECRETARIAT

This report has been prepared on the basis of the draft report written by the two Rapporteurs of the meeting, Dr Farhat Moazam and Dr Jeremy Chapman, whose expert assistance is gratefully acknowledged.

The Secretariat would also like to thank the Chairman of the meeting, Dr Carl-Gustav Groth, for his valuable contribution both during and after the meeting.

The report was submitted to all participants for comments. The Secretariat is most grateful to them for their input during the meeting and their valuable comments on the draft report.

TABLE OF CONTENTS

Executive Summary

Transplantation of organs, cells and tissues are now effective therapies across a wide range of both fatal and non-fatal diseases. The excellent survival and success rates of transplantation of organs and cells, such as the kidney, liver and heart or haematopoietic stem cells in immunosuppressed patients, have led to high levels of demand globally. The success rates for transplantation of certain cells or tissues which do not require immunosuppression have also ensured that such procedures are frequently the treatment of choice in the respective therapeutic areas. It is, however, clear that ethically-unacceptable practices occur in a number of countries.

Neither measurements of activity in, nor outcome of, organ, tissue and cell transplantation is available globally. There are data from countries with compulsory registration of transplant activity and there are voluntary registries of some types of transplantation.

Despite the appropriate focus on prevention of disease, the global needs of patients for transplantation are not being met. The demand has outstripped the supply of organs, cells and tissues from both deceased donors and from the altruistic living relatives of patients in need. The alternative treatments and medical support for patients with end stage organ failure, especially renal dialysis, are expensive and limited in many countries. There is also a lack of clinical expertise in some regions and countries and an inability to fund transplantation to some extent in all countries. Thus in all Member States one or more influences prevent the sufficient supply of transplantation therapies and lead to pressure for non-altruistic living donation.

Deceased donation is meeting the needs of transplantation in few, if any, countries. Potential donors are reluctant to commit to donate after death and their families may refuse permission when approached after death. The use of executed prisoners as organ donors in some countries causes great concern that these donations are coerced. Member States employ different models of consent including: presumed consent or "opt out"; required requesting; "opt-in"; and mixtures of these three models. Independently from which specific model is chosen, information and voluntariness are of fundamental importance for the act of post-mortem donation.

Increasing use, over the past ten years, of living donation of non-regenerative organs has extended from kidneys to livers and even to the lung and pancreas in some instances, despite the hope that reliance on living donors could be reduced. There remains great concern that a market in body parts (especially the kidney) has flourished over the past few years with vulnerable persons being tricked or coerced into donating and some recipients travelling with their surgeons to countries where "donated organs may be purchased legally or illegally.

Human cells, human tissues and human organs provide different concerns. Tissues are processed and traded in many Member States by both for-profit and not-for-profit organizations. It is not clear the extent to which donors or their families are aware of the profit that is created through this trade. Human cells, in particular haematopoietic stem cells, on the other hand, are widely and increasingly exchanged globally between donors and patients through arrangements made by not-for profit organizations which isolate and protect the anonymity of both patient and donor.

Xenotransplantation represents a potential opportunity to ensure a constant supply of organs and tissues for transplantation. However, the scientific hurdles to successful xenotransplantation in humans currently mean that it should only be undertaken under strict clinical trial conditions. There are substantial potential risks to human health from the transmission of xenogeneic infectious agents through xenotransplantation. Careful international monitoring of these clinical trials and of each subject is thus essential to ensuring the safety not only of subjects but also of their families and the broader human population. These issues transcend currently accepted norms of subject consent and medical responsibility for monitoring of the consequences of xenotransplantation.

It is clear that some Member States have not assumed or have been unable to assume an appropriate level of responsibility in each of the areas of transplantation. There are a number of roles for which the World Health Organization is best placed to ensure that minimum levels of human access, safety and ethical practice are adopted universally.

WHO roles could include:

(1) Encouraging the development of transplantation therapies in Member States in an ethically appropriate manner.

(2) Initiating an ongoing programme on transplantation at WHO and establishing a WHO Expert Advisory Panel for transplantation.

(3) Facilitating the development of a core of technical and ethical standards for the management of the safety, quality and efficacy of human material for transplantation that can serve as a model for Member States.

(4) Encouraging Member States to develop a legal framework and national policy and plan on transplantation activities, especially ensuring coordination of the procurement of human material from deceased donors.

(5) Facilitating communication between regulators and providers on the international circulation of human cells and tissues for transplantation, in particular for matched haematopoietic stem cells.

(6) Collecting data on the extent of paid organ, cell and tissue donation.

(7) Creating a global map of the known infectious risks and the safety measures that are applied to donors and donations in different countries and regions of the world.

(8) Helping Member States to develop capacity for national regulatory approaches to quality and safety in particular by encouraging the creation of international support networks.

(10) Encouraging nations to support consensus on basic principles of xenotransplantation safety and oversight:

- Defining the nomenclature of different types of xenotransplantation.
- Identifying countries in which xenotransplantation occurs.
- Supporting the approach that regulation must be in place in all countries in which clinical trials of xenotransplantation occur.
- Developing general recommendations for obtaining informed consent in situations that may represent a risk to the general public and in which individual rights and the public good may come into conflict.
- Fostering agreement between Member States to control travel for the purposes of xenotransplantation.
- Implementing an international xenotransplant surveillance system.

(11) Rewriting and updating the Guiding Principles, published by WHO in 1991, especially concerning:

- Measures to ensure safe and voluntary altruistic donations from living donors.
- Financial transactions and coercion.

Dr Daar noted that the primary challenges of xenotransplantation remain scientific at the present time, but added that the challenges also include ethical, legal and social issues. There are many significant concerns that require public debate prior to the first scientifically successful application that have been identified. These include animal welfare, equity of access to therapy, management of the small risk of xenozoonoses with large potential public health consequences, as well as short and long term surveillance needs. The form of consent needed for the patient and his contacts must take into account not only individual issues but also public issues, thus taking on the nature of a "Ulysses" contract, the contract that Ulysses made with his crewmen to restrain him, regardless of how much he objected, when he faced the Sirens. Dr Daar believed that the Canadian experience of public engagement has been instructive and has halted clinical xenotransplantation in that country at the current time. What is needed is "public engagement rather than public education" when considering policies. There is a need for agreement on risk evaluation methodologies and the application of global governance with harmonization of databases and archives to minimize global risks and maximize knowledge and research.

National and international policies – Dr Eda Bloom

Dr Bloom began by defining and providing illustrative examples of xenotransplantation, according to the USA definition of xenotransplantation as "any procedure that involves the transplantation, implantation or infusion into a human recipient of either (a) live cells, tissue or organs from a non-human anima source or (b) human body fluids, cells, tissues or organs that have had ex-vivo contact with live non-human animal cells, tissues or organs". This definition was developed to encompass the broader range transplantation circumstances that pose a risk of transmitting xenogeneic infectious agents to humans. She also stated that "xenotransplantation has specific issues" that set it apart from organ and tissue allotransplantation. These issues include the possibility of transmission of known and as yet unrecognized xenogeneic infections from animals to humans. For example, based on the findings that porcine endogenous retroviruses (PERVs) could infect human cells in vitro, in 1997 the USA halted all clinical trials in porcine xenotransplantation until those conducting the trials provided data to demonstrate their ability to perform appropriate tests and updated their Informed Consent documents to reflect the PERV risks. Dr Bloom gave an account of the collaboration on xenotransplantation within the USA among the components of the Department of Health and Human Services. The US Food and Drug Administration has produced three guidance documents on xenotransplantation and there is a Public Health Service Guideline on Infectious Disease Issues in Xenotransplantation. Dr Bloom summarized the OECD consultation on xenotransplant surveillance systems in 2000, which reached consensus on a number of areas, especially on the development of an international surveillance network. She stated that potential roles for WHO might include the development of consensus on basic principles of safety and oversight with the encouragement of nations to support those principles, development of agreement to monitor and control the travel of recipients for xenotransplantation and implementation of a xenotransplantation surveillance system. WHO may also help to identify countries in which xenotransplantation occurs and encourage regulation with an accepted minimal framework for oversight. There is also a need for the development of general recommendations for obtaining informed consent in

situations that may represent a risk to the general public and the holding of international consultations to consider when public health risks may override individual rights.

Brief presentations

Xenotransplantation in Mexico – Dr Arturo Dib-Kuri

Dr Dib-Kuri gave a brief report of xenotransplantation activities in Mexico. Research in this area has occurred within Mexican universities in collaboration with institutions in other countries such as New Zealand. Clinical work has included the transplantation of pig islet cells with barriers into humans with Diabetes Type 1. After two years there have been no instances of infection and patients have shown "some decrease in insulin requirements". Mexico has a strict law for the safety and protection of human subjects, with the requirement for mandatory submission of progress reports every month.

Council of Europe approaches to xenotransplantation – Mr Karl-Friedrich Bopp

Mr Bopp reported that short recommendations were introduced in 1997 to draw Members' attention to xenotransplantation procedures, followed in 1999 by Recommendation 1399 of the parliamentary assembly calling for a moratorium. An expert working party was subsequently established (under two standing committees, CDBI/CDSP) to produce Recommendation (2003) 10 on xenotransplantation which is to date a "state of the art" document. This will include definitions similar to those used in the USA and include requirements and conditions for regulation and implementation of xenotransplantation, including close and continuous surveillance of recipients.

Japanese approaches to xenotransplantation – Dr Tadahito Kanda

Dr Kanda reported that the first Japanese Public Health Guidelines on the issue of potential infections related to xenotransplantation were published on 9 July 2002. The guidelines made note of the prior treatment of patients with cells exposed to mouse keratinocytes and supported the accumulation of data from all human clinical trials as the most effective basis for understanding the risks. Dr Kanda recommended "flexibility" in formulating global guidelines depending on the nature and type of xenotransplantation. He also emphasized the need for an international database on infections following xenotransplantation.

Canadian approaches to xenotransplantation – Dr Maura Ricketts

Dr Ricketts provided a brief account of the approach that Canada has taken towards xenotransplantation. At present xenotransplantation is a regulated procedure in the country. The first draft for Proposed Canadian Standards was completed in 1999, followed by workshops on xeno-surveillance in 2000. Public involvement was sought through a Public Advisory Group. As a result of these processes, cessation of all clinical trials and a moratorium on xenotransplantation was called for in 2000. In 2002, the Issue Analysis was completed, recommending the implementation of precautionary measures prior to any clinical trials; final Canadian regulations are awaited. According to Dr Ricketts, the "Canadian approach" recognizes the urgency of establishing effective regulation and surveillance plans prior to the first effective clinical application, especially because of the potential for rapid and widespread dissemination of such an application.

General discussion – Consensus points

There was consensus that there was a need to act internationally prior to clinical evidence demonstrating success of xenotransplantation to ensure that "guidelines are in place as soon as possible" in all states in which xenotransplantation occurs. In view of the continuing shortage of allografts, xenograft organ and tissue transplants have the potential for tremendous good by providing "an unlimited supply" of organs and, if the approach is proven successfully, may be rapidly and widely used. It has the potential for "changing the world". A cautionary note was expressed by some that xenotransplantation is an expensive high technology endeavour that will be accessible to only some rather than to many and that it thus has the potential to "widen the gap" between the affluent and the poor nations. It also has the potential to introduce novel infectious diseases into the human population.

There was a consensus that WHO can play a significant role and could consider the following:

- Encourage nations to support consensus on basic principles for xenotransplantation safety and oversight.
- Identify countries in which xenotransplantation occurs and support the approach that regulation must be in place in all countries in which clinical trials of xenotransplantation occur.
- Develop general recommendations for obtaining informed consent in situations that may represent a risk to the general public and in which individual rights and public good may come into conflict.
- Develop and encourage nations to support agreement to monitor and control travel of recipients for xenotransplantation.
- Implement an International Xenotransplantation Surveillance network along the previously discussed lines.

Session 9 – Efficacy, access and allocation

Pakistan and live renal transplantation: Moral dimensions of access and allocation – Dr Farhat Moazam

Dr Moazam provided a background to the nature of health service delivery and insufficient government dialysis and transplant programmes. The void is being filled by a rapidly expanding private sector, many using unrelated paid donors. In the absence of health insurance, the costs of dialysis – US$ 40- 50 per session, transplant US$ 8000-10 000 and medications at US$ 300 per month - remain beyond the means of the majority. She contrasted this with the success of the Sind Institute of Urology and Transplantation (SIUT), a "unique" model of "government-community partnership" (40% financial support from the government, the rest from donations and endowments), that utilizes indigenous moral norms of culture and religion to promote renal transplantation. Pakistan presents a deeply religious, family centred, hierarchical, collectivistic culture with several generations pooling resources for survival. SIUT relies on cultural and religious emphasis on obligations and duties to the extended family rather than autonomy and rights of individual members. It accepts only genetically related donors with the belief that healthy family members have a duty to come to the aid of kin in danger of losing their lives. Reluctant

- The primary motivation for, and instigation of, illegal donation is presumed to be poverty.
- There is assumed complicity of a small minority of trained physicians and surgeons, but they have been identified in only a small number of cases There is extreme difficulty in documenting illegal trafficking events reliably and either substantiating or refuting the rumour.
- It was agreed that organ trafficking should be seen as an increasingly common criminal activity with individual, social, economic and political repercussions, akin to transnational trafficking in humans for other purposes (such as children for sexual abuse or adoption, males for forced labour, and women for prostitution). The laws in Member States should therefore address issues of the supply, receipt, and brokerage of trafficked organs and tissues.
- The conceptual difference between removing disincentives and giving incentives was highlighted. It is not clear when the first process, which was deemed to be acceptable, becomes the second. Local realities may influence these issues in different ways. It was not clear, for example, whether offering free health insurance (to cover post-operative complications) is an unacceptable incentive for donors in a country that has poor public provision of health care. No consensus was reached on these issues.
- Potential solutions that were considered included:
  - Giving organ trafficking the same international legal status as child sexual abuse in both donor and recipient countries.
  - Limiting organ transplantation to publicly-funded and managed hospitals.
  - Abolition of insurance reimbursement for live kidney donation that is undertaken in another country (where organ trafficking is known to occur).
- Some participants suggested that the commercial traffic in organs, cells and tissues should be regulated by individual countries based on their own situations, rather than prohibited globally. However, the majority of participants, especially those from developing countries, strongly supported the view that the entire practice of commercialization of organs must continue to be declared illegal and unethical if there is to be a global reduction in the human toll from donation.

Xenotransplantation

Breakout group report

It was agreed that no nation should undertake any xenotransplantation in humans without an appropriate regulatory framework and surveillance. It was agreed that prompt action is needed in advance of the first successful xenotransplantation because of the high speed with which such a therapy may be disseminated.
WHO could therefore:

- Develop and encourage nations to support consensus on basic principles of safety and oversight.
- Provide existing national documents as models for countries that do not have current documents.

- Devise a means to involve national authorities in the regulation of xeno-transplantation, with as clear as possible a message to Member States.
- Provide a means for interaction and communication among nations.
- Produce a WHA resolution that countries would not perform xenotransplantation unless they have a framework for regulatory activities, including animal husbandry, patient and animal testing and follow-up activities, including a recommendation to prohibit "xenotourism" (travel abroad to obtain a xenotransplant).
- Review and revise as necessary and/or redistribute 1998 WHO recommendations.
- Identify funding and external partner(s) to assist in this, such as professional/scientific associations (Transplantation Society, International Xenotransplantation Association) and other international organizations (EU, CoE, OECD).
- Recommend that each country develop their own protective measures, as part of their own national recommendations. Any physician seeing a patient who has undergone a xenotransplantation procedure in another country should have the responsibility to report that procedure to their own national public health authorities, respecting the privacy and confidentiality regulations of their own country. The physician and the patient should then follow the relevant national regulations and guidelines of the country in which they are resident.
- Any physician performing a xenotransplantation procedure on a patient returning to another country should report that procedure to their own national authority, which should report to the home country of the recipient.
- A xenotransplantation surveillance system should be developed.
- Countries should develop national surveillance systems to keep track of individual xenotransplantation events.
- WHO could come up with concrete recommendations based on the WHO/OECD/Health Canada meeting of October 2000 for developing a system that would be widely applicable and practical.
- The surveillance system/WHO should be informed of any syndrome or infection thought to be contracted from xenotransplantation.
- The IAEA could be approached for funding for international support of assays involving radioisotopes.
- WHO could identify countries in which xenotransplantation occurs.
- WHO could develop a recommendation for biological specimen archives to be developed as part of any surveillance programme.
- WHO could compile a database including numbers and types of xenotransplantation performed in Member States.
- WHO could conduct and publish in the World Health Report a survey of where xenotransplantation occurs, to include a rigorous quantitative estimate of xenotransplantation events in each country.
- WHO could develop general recommendations for obtaining informed consent in situations that may represent a risk to the general public.
- WHO could explore how/whether informed consent procedures could be adapted for the circumstances of xenotransplantation, including obtaining consent from close patient contacts and the acceptance of the need to comply with subsequent monitoring and follow-up.

General discussion – Summary of consensus points

There was consensus that there was a need to act internationally in advance of clinical evidence demonstrating the success of xenotransplantation to ensure that "guidelines are in place as soon as possible". In view of the continuing shortage of allografts, xenograft organ and tissue transplants have the potential for providing "an unlimited supply" of organs and, if the approach is proven successful, may be rapidly and widely used. It will be important to "proceed with caution" since the potential health gains are very significant but are balanced against the potential health risks. There is thus a need for more research, surveillance and oversight. A cautionary note was expressed by some that xenotransplantation is an expensive, high technology endeavour, that will be accessible to only some rather than to many and that it thus has the potential to "widen the gap" between the affluent and the poor nations.

There was consensus that WHO could play a significant role by providing leadership to facilitate global networking and cooperation and could consider the following:

- Encourage nations to support consensus on basic principles for xenotransplantation safety and oversight.
- Identify countries in which xenotransplantation occurs and support the approach that regulation must be in place in all countries in which clinical trials of xenotransplantation occur.
- Develop general recommendations for obtaining informed consent in situations that may represent a risk to the general public and in which individual rights and public good may come into conflict.
- Develop and encourage nations to support agreement to monitor and control travel of recipients for xenotransplantation.
- Implement an international xenotransplantation surveillance network as previously discussed.

International regulation of human tissues and cells for transplantation

Breakout group report

Human cells and tissues provide benefits to patients which, to meet their needs, must be provided through ethical processes which maximize access, equity and safety. It was felt that:

- WHO could promote discussion between regulators to create an agreed definition of cells and tissues and to provide model regulatory framework options for Member States.
- WHO could provide guiding principles for the transparent regulation of ethical, organizational and technical aspects of tissue and cell transplantation, in order to increase both access and safety for patients.
- WHO could advocate the development of sustainable models of regulation, capacity building, training and surveillance, facilitating regional and global cooperation.

資料２－１

厚生労働科学研究研究費補助金
厚生科学特別研究事業

異種細胞との共培養による皮膚の移植に関する安全性調査

平成１４年度　総括研究報告書

主任研究者　吉倉　廣

平成１５（２００３）年　４月

厚生労働科学研究費補助金（厚生科学特別研究事業）
総括研究報告書

異種細胞との共培養による皮膚の移植に関する安全性調査

主任研究者　吉倉　廣　国立感染症研究所長

研究要旨
異種移植の実施に伴う公衆衛生上の感染症問題に関する指針」（平成１４年７月９日付け医政局研究開発振興課長通知）の作成に引き続き、現在国内外において異種細胞と共培養皮した皮移植膚につき、その製造方法、使用の実態等を調査した上で、上記指針の適用上問題となる処を精査し、その結論を取りまとめた。

分担研究者
神田忠仁　国立感染症研究所遺伝子解析室長

A. 研究目的

免疫抑制剤等技術の進展により人から人への同種移植は定着し、待機患者が増加する一方で、慢性的に臓器の提供数が少ない点が問題となっている。そのようなことから、近年のバイオテクノロジーの進歩とあいまって、異種移植という新しい治療法の開発が促された。しかし、異種移植に用いる細胞、組織又は臓器に随伴した異種動物由来感染症の発生及び伝播の可能性が否定出来ず、これに対応する為に各国でガイドラインの作成が検討されている。我が国では、昨年、「異種移植の実施に伴う公衆衛生上の感染症問題に関する指針」が班研究（主任研究者吉倉廣）により取りまとめられ、平成１４年７月９日付け医政局研究開発振興課長通知にて周知された。本研究班では、現在、国内外において実施されている培養皮膚移植につき、その製造方法、使用の実態等を調査した上で、上記指針の適用上問題となる処を精査し、取りまとめる事とした。これは、移植用培養皮膚はヒト由来であるが、異種細胞と共培養により製造される為、異種移植に該当する為である。

B. 研究方法

国内外において実施されている培養皮膚移植につき、その製造方法、使用の実態等を調査し、「異種移植の実施に伴う公衆衛生上の感染症問題に関する指針」（平成１４年７月９日付け医政局研究開発振興課長通知）の皮膚移植への適用に関する討議を行い（別添２）、最終文書とした。

C. 研究結果

（１）国内外において実施されている培養皮膚移植の実態調査

培養皮膚のうち、異種細胞を利用しているものがあるが、それらの製造方法を具体的に調査するため、共同研究者国立感染症研究所神田忠仁が 2003 年２月 25-26 日の２日間、米国の Genzyme Biosurgery (Boston, MA) と FDA CBER (Rockville, MD)で、調査をした（別添１参照）。

（２）上記調査結果を踏まえ、京都大学再生医学研究所井上教授、自治医科大学小澤教授、国立感染症研究所神田室長、国立動物衛生研究所清水所長、神戸大学法学研究科丸山教授、主任研究者感染症研究所吉倉所長、厚生労働省医政局研究開発振興課の出席のもとに、「異種移植の実施に伴う公衆衛生上の感染症問題に関する指針」（平成１４年７月９日付け医政局研究開発振興課長通知）の皮膚移植への適用に関する討議を行い（別添２）、最終文書とした。最終文書では、(i) 指針「3.3 インフォームドコンセントの方法及び内容」、「5.1 移植患者(1)、(5)、(7)」「5.4 移植患者の記録」「6.1.2 感染症発生時の報告」については皮膚移植に該当する個所を選択し、これを計画書で明記した上で実施すること、(ii) 培養に使用する細胞のワーキングセルバンクにつき、別添１の内マイコプラスマなど適切な微生物検査を予め決めておき品質管理を行うこと、(iii) 最終製品中の異種フィーダー細胞の存在有無の確認、(iv)最終製品の一部試料の冷凍保存、などの指針の適用法を示し

写

資料２－２

医政研発第0709001号
平成１４年７月９日

各都道府県衛生主管部(局)長　殿

厚生労働省医政局研究開発振興課長

異種移植の実施に伴う公衆衛生上の感染症問題に関する指針について

臨床研究の実施においては、人の尊厳、倫理に関して各実施機関の倫理審査委員会での承認等を受ける等適切に実施することは言うまでもないが、異種移植においては、さらに、異種動物に由来する感染症について留意することが必要であることから、平成12年10月31日厚科第575号・研発第21号「異種移植の臨床研究の実施に関する留意事項等について」により、適切な対応を求めているところです。

今般、厚生科学研究費補助金厚生科学特別研究事業において、別添のとおり「異種移植の実施に伴う公衆衛生上の感染症問題に関する指針」が作成されました。ついては、貴管下関係施設における異種移植の実施に関し、移植患者、医療従事者等への異種動物由来感染症の感染及び伝播を防止するため、別添をご理解の上、十分な対策を実施するよう貴管下関係者に対し周知徹底をお願い致します。

戻る

別添

異種移植の実施に伴う公衆衛生上の感染症問題に関する指針

平成１３年度厚生科学研究費厚生科学特別研究事業
主任研究者　　吉倉　廣（国立感染症研究所長）

［目次］

前書き

免疫抑制剤等技術の進展により人から人への同種移植は定着し、待機患者が増加する一方で、慢性的に臓器の提供数が少ない点が問題となっている。そのようなことから、近年のバイオテクノロジー等の進歩とあいまって、異種移植という新しい治療法の開発が促された。例えば、動物細胞を利用した体外灌流装置等が開発され、海外では多くの実施例の報告もあり、同種臓器移植までの橋渡し又は急変時の対応策として、期待されている。また、遺伝子改変によりヒトの補体活性化抑制遺伝子を挿入したブタが作られており、異種抗原を発現しないブタを作出する試みもあり、ブタの細胞、組織又は臓器をヒトに移植する可能性も現れてきている。

しかしながら、異種移植に用いる細胞、組織又は臓器に随伴した異種動物由来感染症については、ウシ伝達性海綿状脳症（BSE）からの新変異型クロイツフェルト・ヤコブ病（vCJD）等動物由来の感染症の発生や、ブタ細胞と共培養したヒト細胞にブタ内在性レトロウイルス（PERV）が感染したことを指摘する研究等があり、現時点では未知の感染症の発生及び伝播が起こらないことを保証できる段階になく、同種移植とは異なる予測困難な問題が残されている。異種移植に由来する未知の感染症に対する公衆衛生学的対応として、米国、英国を初めとするいくつかの国々において、指針が作成され、また国際機関においては国際的な情報交換及びサーベイランス体制の必要性が唱えられるなど、国際的に異種移植における感染症問題が注目されているところである。

医療機関等において通常行われる臨床研究は、それぞれの研究実施機関等に設置されている審査委員会（Institutional Review Board :IRB）において、技術的及び倫理的な面についての適切な審査が行われた上で実施されている。しかし、異種移植では、上記の問題への対応及び国際協調の観点から、その実施について、公衆衛生上、一定の指針を示す必要性があることから、特に指針を作成するものである。移植実施機関等において指針を参照し、最大限の感染症対策を行いつつ、国内外で異種移植に関係する問題が発生した際には的確な対応が取れるような体制を確立することが必要である。

国際的なサーベイランス体制については、国際機関において検討されているところであり、その具体的な進め方については、各国が協同して検討しようとしている段階である。国内においても、異種移植の実施に関する情報を得た場合の取扱い等については、国際動向に適切に対応することが必要である。

国内では、技術面、倫理面等について十分な審査を行うことのできる審査委員会を有し、且つ十分な技術力を擁する数機関で異種移植の研究が検討されている段階であり、まだ異種移植の実施が急増する状況にはない。今後、規制の変化、技術の進歩等により、幅広い医療機関において実施できるような状況になれば、指針の見直し、学会等での登録・情報収集、実施前の審査、感染症対策に関する移植実施施設の査察等新たな対応の実施についての検討が必要になると思われる。

本指針は、公衆衛生学的な見地から、異種移植に関係する感染症拡大に関する問題を扱うものであり、言い換えると異種移植に起因し出現するかもしれない感染症に対してこれを見逃し、感染が拡大することの無いようにすることを目的とする。従って、異種移植そのものの有効性、倫理性等の確保及び移植患者における感染症一般の予防を目的とするものではなく、また「遺伝子治療臨床研究に関する指針（平成６年２月厚生省告示第２３号）」他、臨床研究に関わる指針が適用される場合については、これらの指針を併せて用いることが重要である。

１　総則

１．１　目的

公衆衛生学的な観点から、異種移植に起因する未知の感染症に対して、感染及びその拡大を防止することを目的とする。

指針に示された方法以外の方法であって、公衆衛生上、指針に示された方法よりも感染症予防の観点から科学的に妥当なものがある場合には、その根拠を示した上で、その方法を採ることができる。

１．２　定義

１．２．１　異種移植

（１）本指針において、異種移植とは、次に掲げることをいう。

ａ　ヒト以外の動物に由来する生きた細胞、組織又は臓器をヒトに移植、埋め込み又は注入すること。

ｂ　体外において、ヒト以外の動物に由来する生きた細胞、組織又は臓器に接触したヒトの体液、細胞、組織又は臓器をヒトに移植、埋め込み又は注入すること（接触には、共培養による間接的な接触を含む。）。

（２）従って、動物由来のものであっても、それ自身が生きていない物、例えば、心臓弁、インスリン、血清アルブミン等の材料又は薬剤をヒトに使用することは、異種移植に含めない。

１．２．２　異種移植片

ヒト以外の動物に由来する物であって、異種移植において、ヒトに移植される、埋め込まれる若しくは注入される、又はヒトの体液等と接触する細胞、組織又は臓器をいう。

１．２．３　ドナー動物

異種移植に用いる異種移植片を提供する動物をいう。

１．２．４　ドナースクリーニング

動物が、異種移植片を提供するための適格性を満たしているかどうかを決定するための診断及び検査を行い、適格性を判断することをいう。

１．２．５　微生物学的監視

ドナー動物、移植患者及び医療従事者等に対して、血清学的検査等適切な方法を用いて、感染性病原体の感染の有無を継続的に調べることをいう。

１．２．６　医学的記録

移植患者についての、異種移植実施前後における健康状態及び微生物学的監視の結果を記録したものをいう。

１．２．７　健康管理記録

ドナー動物個体又はその集団若しくはコロニーの由来（交配に関することを含む。）、品種、医薬品の投与歴、飼育状態、微生物学的監視（検疫を含む。）等の結果を記録したものをいう。

１．３　基本原則

１．３．１　異種移植を実施する前提

ヒトの細胞、組織又は臓器を患者に移植する同種移植は、既に臨床の場で定着しているが、その需要に対して供給がはるかに少ない。そのような問題を背景に、異種移植についての研究が進展してきたところである。

しかし、異種移植については、ドナー動物に由来する病原体の移植患者への感染及び伝播による公衆衛生学的な危険性を、現在の医学では完全には排除し得ないおそれがあるため、サーベイランス等感染症対策を十分に行うことができることが実施の前提となる。

１．３．２ 薬事法との関係

薬事法の対象となる場合には、これに従うこと。薬事法に規定されない部分等については、本指針を参照されたい。

１．３．３　遺伝子治療

遺伝子を導入した異種移植片を使用する移植等のうち、遺伝子治療臨床研究に該当する場合、「遺伝子治療臨床研究に関する指針（平成６年２月厚生省告示第２３号）」等に従うこと。ただし、ドナー動物に由来する感染症に対して、その感染及び伝播を防止する目的から、併せて本指針を参照されたい。

１．３．４　その他の指針

薬事法及び遺伝子治療臨床研究に関する指針の他、遵守するべき指針等がある場合、当然のことながらそれらに従うこと。

１．３．５　個人情報の保護

異種移植に関係する者は、取り扱う際に知り得た移植患者に関する個人情報を漏らしてはならない。また、その職務を離れた後でも同様である。

１．４　指針の見直し

本指針は、科学技術の進歩、異種移植片等の取扱いに関する社会情勢の変化等を勘案して、必要に応じて適切な場で見直すことが必要である。

２　異種移植の実施及び審査の体制

２．１　異種移植チーム

２．１．１　異種移植チームの業務

総括責任者のもとで移植実施計画書を作成、遵守し、異種移植を実施すること。また、移植実施後の監視等を適切に実施すること。