The updated WHO Guiding Principles on Human Cell Tissue and Organ Transplantation as approved by the 124th Executive Board in resolution 124.R13 includes Guiding Principle 10 dedicated to the necessity of detailed assessment of transplantation procedures as well as of the outcome of transplanted human cells, tissues and organs. In the commentary of Guiding Principle 10 is the following sentence: "Internationally agreed means of coding to identify tissues and cells used in transplantation are essential for full traceability".

Work carried out during and after the two Global consultations has resulted in the development of two WHO Aide-Memoires specifying basic requirements in this field. The Aide-Mémoire on "Access to Safe and Effective Cells and Tissues for Transplantation" provides an overview for National Health Authorities, but also for all stakeholders, of all key aspects to be considered and requirements to be met for the setting up and/or the oversight of human cell and tissue transplantation services (WHO 2009).

European directive and CEN workshop

In 2004, a European Union Directive mandated a single coding system for cells and tissues [European Tissues and Cells DIRECTIVE 2004/23/EC (ECD)]. To this end, the European Committee for Standardization (or Comité Européen de Normalisation or CEN) evaluated various standardized coding systems for use within the European Union (CEN Workshop Agreement 2008). It was recognized that "...there are real problems with meaning-shift when using common terms between languages. For that reason many nomenclature schemes use a very rigid set of syntactical rules to ensure that the term being coded is capable of being interpreted faithfully in any language, whatever its real-world syntax and grammar". The report promoted ISBT 128 as the preferred option but they also proposed allowing member states to use two other variations (one with national ID numbers but ISBT 128 product descriptions and one without any internationally agreed component). They determined that one of the major benefits of ISBT 128 was that it could be used for four groups of biologics: blood, cells, tissues and organs. The CWA work analyzed existing relevant public activities at European, national, regional and international levels, and also considered relevant international activities. There were 3 candidates proposed by Member State (MS) and a panel recommended use of ISBT 128 as the basis for the EU coding scheme. Although it was considered a good match to requirements, it was not perfect in its current design. Further work was identified to meet the need for an additional component to be created to support both use of ISBT 128 and those organizations electing to retain existing coding schemes. This new component was temporarily named in the CEN report as the "key code". Because a donation event may result in tissues sent to different Tissue Establishments ICCBBA offered a new component, incorporating Country code, Responsible organization (e.g. Competent Authority) and Tissue Establishment, to be developed with the EU to meet international requirements. The Key Code would not invalidate existing ISBT 128 code structures but augment them. The "key code" could also be used with existing coding systems to provide unique identification and allow EU (potentially global) traceability of all materials from one donation event. Among the other CEN CWA conclusions were:

1. The ability to share coded data between different donor sectors in the future may help with risk prevention measures and provide clearer indications of donor suitability.
2. It may also reduce duplication and ensure better recall management.
3. It is feasible that with technological advances in regenerative medicine that the interfaces between blood, tissues, cells, and organs may become less defined.

The CEN solution supports the long-term migration to ISBT 128 whilst providing a short-term solution to unique identification through the use of the key code.

In transposing the EC Directive into national legislation, some countries (notably Poland and Austria) made the use of ISBT 128 for coding and labeling cells and tissues a legal obligation.

Mechanisms for providing globally unique identification

A number of mechanisms exist for providing globally unique identifiers, and in general when a large number of items have to be identified, they work on a layered principle. An overarching international

body assigns a portion of the identifier to reference an organization responsible for lower level assignment, and the sub-body assigns unique identifiers within its jurisdiction. Together the two parts provide a unique identification. An example is the telephone numbering system where a United Nations Agency, the International Telecommunications Union, assigns the 'country code' and the actual number of each telephone in the country is assigned by a 'national' body. (Although 'country code' is used in this context, it is not an exact match to country identification—for example the country code '1' covers both the USA and Canada.)

A similar mechanism is used by GS1, the supply chain standards body that maintains the GS1 standard used by many commercial organizations for bar coding their products. Using GS1, each type of product from a manufacturer can be uniquely identified using a Global Trade Item Number (GTIN). GS1 assigns one portion of the GTIN identifier to uniquely identify each manufacturer, and the manufacturer assigns the second portion to uniquely identify the type of product within their organization.

In the transfusion and transplantation field, ICCBBA uses a similar model by assigning a facility code to each organization that will assign ISBT 128 donation identification numbers (e.g. blood center, tissue establishment, competent authority) and the relevant organization assigning a sequence number.

In all the above cases the combination of the two elements provides a globally unique identification for the item or, in the case of tissues, the donation event.

The case for bar coding and electronic data transfer

Traceability depends not only on the use of unique identifiers, but also on the accurate transcription of those identifiers at all parts of the traceability chain. The risks of error during manual transcription of information are well documented, and in the blood transfusion field, which has some well-developed hemovigilance systems, cases of incorrect blood component transfused are a major source of adverse events, with administrative errors in identification forming a major cause of these. Use of electronic information capture provides a means of improving safety by eliminating the risk of manual transcription error, and speeding up the information transfer process.

Clearly not all countries have the necessary infrastructure to support the use of computerized systems throughout the transplant process, however where systems are available they should be used, and the ability to introduce such safety measures should not be impeded by the lack of bar coded information on the tissue product label. For this reason, any move towards adopting globally unique identification should be compatible with a well established standard coding system so that the progression towards automated data capture and computerized records can be achieved.

Coding systems

What is a coding system?

A coding system is a means by which distinct items within a system can be uniquely identified and consistently characterized to all participants within that system. It requires as a minimum a means to allocate identifiers in a manner that avoids duplication, and a standard reference for describing items.

The degree to which unique identification is required depends upon a number of factors. For a manufactured drug identification of the manufacturer and the unique lot number assigned by that manufacturer is sufficient to trace back to the manufacturing records for the batch. In this situation it is common to use a single identifier for all items in the batch. For donated biologics such as blood or tissue each donation has unique characteristics and is thus a 'batch' in its own right. In such cases there is a need for unique identification to be at the individual donation level, and for each product prepared from the donation to also be individually identified.

Uniqueness within a system requires that a boundary be defined to the system and controls need to be in place to ensure that the item does not travel outside the boundary. If, for example, the system is contained within a national boundary, then uniqueness at the national level is adequate, but as soon as an item travels beyond the boundary, the risk of duplication exists. For biologic products, which increasingly travel worldwide, global uniqueness is essential.

With the increasing use of computers, coding systems are commonly associated with information standards to allow the coding information to be electronically transmitted between computer systems.

Typically the coded information is presented in an electronically readable format such as a bar code. The information standard defines the technical specification for this electronic format thus ensuring that all computer systems can read and write the electronic information.

It is important to recognize that a coding system does not itself provide traceability, but provides the information infrastructure on which effective traceability can be built. Coding and traceability are not the same but one supports the other.

Coding systems and traceability

Previous experience gained from Blood in managing adverse events and reactions has led to a widespread understanding of the need for traceability—the ability to track from donor to recipient and vice versa in order to ensure that all individuals associated with an event or reaction can be identified.

There is frequently confusion regarding the terms 'coding system' and 'traceability system'. These are perceived to be the same, but in fact they are quite distinct. A coding system provides the necessary standards and control in order to ensure that each donation, and each product prepared from that donation, is uniquely identified, and that a common terminology is used. A traceability system maintains records on the activities associated with donated material from the time of procurement to the point of implantation.

Where the full lifecycle of donated material occurs within the boundary of a single traceability system, the identifiers and terminology used can be specific to that traceability system. However, as soon as traceability responsibility is distributed across several traceability systems there is need for an underlying coding system that provides global uniqueness of identification and internationally agreed terminology.

The EU Commission Directive 2006/17/EC defines traceability as follows:

> 'Traceability' means the ability to locate and identify the tissue/cell during any step from procurement, through processing, testing and storage, to distribution to the recipient or disposal, which also implies the ability to identify the donor and the tissue establishment or the manufacturing facility receiving, processing or storing the tissue/cells, and the ability to identify the recipient(s) at the medical facility/facilities applying the tissue/cells to the recipient(s); traceability also covers the ability to locate and identify all relevant data relating to products and materials coming into contact with those tissues/cells.

This definition focuses on the single path from donor to recipient; however, full traceability requires all tissue, and arguably all biologics (blood, cells, tissues and organs) from the same donor to be traced. Full traceability goes well beyond the single strand of information following the path of one product from donor to recipient, and becomes a complex web where multiple products are produced, pooled products are prepared, donors can make multiple donations of different biologic materials and multiple agencies can be involved in the procurement of tissues. Almost inevitably this means that the traceability path will travel through multiple traceability systems. There may be situations where traceability is required beyond a single donation where a donor may donate multiple components via multiple establishments throughout their life e.g. Cord blood, blood, sperm, hip bone, and on death, organs, corneas and multi-tissues. Should a finding occur, it may be essential to track previous donation history e.g. when HCV testing was introduced and regular blood donors were identified as having HCV, it was essential to be able to track previous donations (blood, cells or tissue) via traceability to follow up potentially infected recipients. This might mean creating a unique identity for individuals.

In addition, regulatory requirements on data retention mean that traceability records have to be retained in an accessible manner for long periods of time (European Directive requires information to be stored for 30 years from the time of clinical use).

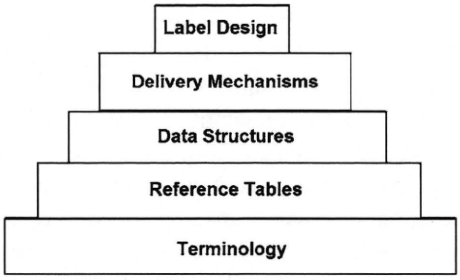
Retaining such large amounts of information for long periods in a format that allows rapid retrieval demands the use of computer data storage. In order to ensure a complete and secure information trail across the multiple computerized systems that may be involved, a means of uniquely identifying each donation, and each product prepared from that donation, is essential. Uniqueness at national or regional level is not sufficient when tissue can travel worldwide. A globally unique identification system is required, and this should extend across all biologic materials—blood, cells, tissues and organs.

A common coding system does not imply common traceability systems, however adopting a common coding system simplifies the interfaces between different traceability systems and reduces the risk of breaks in the traceability chain.

Nomenclature as a first step in harmonizing coding

Building an internationally standardized terminology that can be represented in an electronic form on a label is a complex activity. A useful model has been described based on a five-layer pyramid (Ashford 2006).

The base layer of the model, on which the others layers are built, is the Terminology. Taking individual terms and providing a clear and unambiguous definition, build the terminology. The 'granularity' or level of detail of this terminology is important. Too little detail will result in clinically distinct products having the same name, whereas too much detail will result in an explosion of different codes for what is essentially the same clinical product. In order to achieve the appropriate level of detail it is necessary to bring together an expert international panel. The production of an international dictionary provides a way of ensuring a common understanding of the information itself.



Once definitions have been agreed, then it is possible to start building the reference tables that provide the key lookup for the standard. These tables provide the mapping from the verbal description that is understood by users of the system, to the alphanumeric codes used in computer systems and electronic information carriers such as bar codes.

The Reference Tables ensure consistent interpretation of the coded information across multiple platforms. Because of the rapidly changing transfusion and transplantation environment these tables need to be flexible and readily updated within a strictly managed process.

The next level is described as the 'Data Structures'. These are only really of interest to the software developers who write or read electronic information, but they are an essential element as they provide the context and define the structure for each piece of information. The data structures make it possible for completely different and independent computer systems to communicate effectively and safely, and prevent erroneous interpretation.

The Data Structures package information in a manner that allows it to be transferred in many different formats. The means by which the information is transferred from one place to another is the delivery mechanism.

There are a number of different delivery mechanism types. The most familiar is probably the linear barcode. This relatively simple encoding system is highly effective, but can only hold a relatively small amount of information. Demands for more information, combined with limitations on space for small containers, are driving the need for alternatives.

Two-Dimensional (2-D) or Reduced Space Symbology (RSS) codes can hold more information in a much smaller space. Radio Frequency Identification (RFID) Tags have the benefit of not requiring 'line of sight' access to read. An effective coding system is one that can be adapted for use in all these media without the need to make changes to the underlying layers of the model. The final layer of the model is the Labeling layer. Labeling provides the means of physically attaching the information to the product, and for presenting the human readable interpretation of the information.

A critical element of the labeling strategy is to ensure consistency between information stored in electronic format and that which is human readable on the label. Demand printing of bar coded labels can achieve this as both sets of information are printed at the same time.

Management of a coding system

A coding system in a rapidly developing field such as transplantation must be able to adapt to the changing information needs of the environment and thus an appropriate management system is an essential part of an effective coding system. The tasks of the management organization will include:

1. Assignment of identifiers to tissue establishments in order to ensure global uniqueness of identifiers;
2. Maintenance of an internationally agreed terminology to describe tissue products;
3. Development and maintenance of the information standard documentation;
4. Regular updating of reference tables to reflect the development of new products and processes;
5. Communication with all stakeholders to keep them informed of changes;
6. Promotion of the standard as the global solution for transplantation.

To achieve its objectives the management organization will need to bring together experts from around the world to build the necessary consensus on terminology and will need technical committees for appropriate stakeholder engagement in the development of the standard. It will need to be a robust organization with sufficient staffing and resources, and will require a mechanism to cover its costs of operation.

Currently ICCBBA is the only organization providing a truly international coding system for biologics. Looking at the running costs of this not-for-profit organization, as presented in their annual report, one can make an estimate of the cost of providing these management arrangements. In 2008 this organization operated on a budget of just under $1 m US and provided the management of the ISBT 128 Standard for blood, cellular therapy, and a limited number of tissues. This is a relatively low cost considering that across all three fields of blood, cellular therapy and tissue there are now more than 3,700 ISBT 128 licensed facilities in 66 countries and ICCBBA estimate that more than 40 million products are labeled to the ISBT 128 Standard each year. There are 237 Tissue and Cell facilities in more than 30 countries currently registered with ICCBBA (ICCBBA 2009) and 27 of these have registered since the start of 2009.

Progress toward international standardization for coding: the current situation

Blood

National standards to ensure uniqueness of donation identification were introduced by many countries in the 1980s and 1990s. In some cases these were associated with the use of bar codes such as ABC Codabar. Some of these systems have been updated and continue in use today; however, there is widespread recognition of the limitations and weaknesses of Codabar as a bar code symbology and of the need to move towards an international standard. The experience in the Gulf War with units of blood labeled with Codabar but with multiple errors, demonstrated its limitations (see below).

European blood banks began adopting ISBT 128 in the late 1990s and countries in Asia and the Middle East followed. In North America, the AABB established it as a standard in 2008. It has been implemented across Canada and approximately 60% of the US blood supply with the remainder to be implemented following other software upgrades. In China, blood banks in three provinces are using ISBT 128 along with the hospitals they serve. The Japanese Red Cross uses its own coding system for blood within Japan.

Today ICCBBA reports that ISBT 128 is used for blood transfusion coding and labeling in more than 3,400 blood centers and transfusion laboratories in 49 countries worldwide and that more than 40 million blood components are identified with ISBT 128 each year. A recent survey indicates that this figure will continue to rise in the coming years (Ashford et al. 2010).

In Germany an alternative standard (Eurocode) was developed for blood transfusion use in 1998. This standard has been implemented in some blood services in Germany but has not gained widespread recognition. Other countries, such as Japan, have used their own coding systems, which are efficient within the country but are not translatable across national boundaries.

Cellular Therapy

In 2005 the Boards of Directors of AABB, American Society for Blood and Marrow Transplantation (ASBMT), American Society for Apheresis (ASFA), European Group for Blood and Marrow Transplantation (EBMT), Foundation for the Accreditation of Cellular Therapy (FACT), ICCBBA, International Society of Blood Transfusion (ISBT), International Society for Cellular Therapy (ISCT), ISCT Europe, Joint Accreditation Committee of ISCT and EBMT (JACIE), National Marrow Donor Program (NMDP) and the World Marrow Donor Association (WMDA) released a Consensus Statement confirming their

support for the international use of *ISBT 128* in the coding of hematopoietic progenitor cells and other therapeutic cell products and announcing the establishment of a co-sponsored International Cellular Therapy Coding and Labelling Advisory Group.

This group began working to expand ISBT 128 for use in the field of cellular therapy. While a number of facilities had used ISBT 128 for cellular therapy products since the late 1990s, this group greatly expanded the terms and definitions to meet evolving needs. Their work was published in a variety of journals (Ashford et al. 2007).

Beginning in 2008, ISBT 128 terminology was required by FACT, JACIE, and AABB standards for labeling cellular therapy products. The requirement by these organizations for full ISBT 128 labeling (bar codes and label design) is still a few years off to allow for enhancement of computer systems. However, some cellular therapy facilities that also handle blood are already in the process of implementing the full label and nearly 200 facilities in 36 countries are registered with ICCBBA (2008).

Currently, national coordinating centers assign donor numbers to cellular product donations. As an example, the NMDP assigns a donor number for each unrelated donor of bone marrow, cord blood or peripheral blood stems cells. If the donor gives three products over 3 days, each has the same donor number and the date makes the identifier unique for each product. In the future, products should be labeled with ISBT 128 donation numbers. Products from a donor who donates on multiple days will have a different donation identification number on each product. The donor number, which is assigned by NMDP, is in the donor record, but does not appear on the product as the unique identifier. Currently, the donor number is unique only within the country and thus the unique identifier on the product is unique only within the country. There is a need to move to the system of a donation identifier on each product to be unique internationally.

Tissues

Currently identification systems for tissues range from the use of tissue bank assigned identifiers, which are only unique within the specific tissue bank to use of ISBT 128 globally unique identifiers.

In the USA, a typical numbering system is based on the year of tissue recovery followed by a sequence number, thus the first recovery of 2009 is identified as 09/001. Many tissue banks use this system thus there will be tissue grafts from multiple donors carrying the same identifier. Only when the tissue bank name is associated with this identifier is national uniqueness ensured. This duplication of identifiers presents major challenges for traceability. The Center for Disease Control is investigating the use of a national donation event identifier to overcome these difficulties.

In Italy, tissue donors are assigned an identifier at the national level by the Italian competent authority. All tissue processors, procuring tissue from the donor, use this identifier. The number is unique nationally, but does not meet an internationally agreed format and is thus unlikely to be compatible with traceability systems outside Italy.

In the UK, the National Health Service—Blood and Tissues assigns an ISBT 128 identification number to all tissues it procures. This number is unique globally and is in an international standard format, and therefore can be read and understood by all laboratories, inventory management and traceability systems that support ISBT 128.

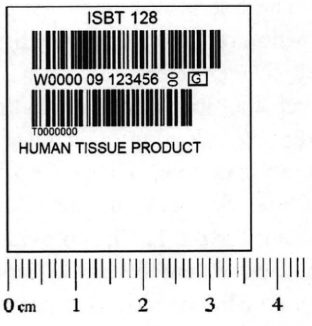
Most of the hospitals in China are using coding systems for cells, tissues and organs. These coding systems are usually different from one hospital to another; however, the coding for patient ID is unique in every city originally for insurance purposes. This is how a patient and his/her medical history can be traced within/among one/different hospital(s). There is little use of ISBT 128 at this stage.

Attempts at standardizing nomenclature have had limited success throughout the world. For the most part, individual Tissue Banks have their own labeling and coding scheme, which is not readable by recipient hospitals and surgery centers except through manual entry. Exceptions do exist, for example, The National Health Service Blood and Transplant Tissue Services in the United Kingdom was the first to recognize the importance of international standardization of coding for tissues. They worked with ICCBBA to develop appropriate terminology and to adapt the ISBT 128 Standard to the needs of tissue banking. They fully implemented ISBT 128 for tissue in 2003 (Fehily et al. 2004). Since then, facilities in other countries, including Poland, Finland and Denmark have implemented the standard. Austria has a

regulatory requirement to implement it for tissues but have not yet done so.

ICCBBA has set up a European Tissue Technical Advisory Group (ETTAG) and is in the process of establishing an international advisory group for eye banking. The ETTAG will focus on the specific challenges facing European countries implementing ISBT 128 and will work with the EC to develop the key code identified in the CEN report. In the US, ICCBBA has been working with the North American Tissue Technical Advisory Group (NATTAG) of the AATB to establish common terminology for tissue products, the first step in the standardization process. When this expert panel reaches consensus, their document will be circulated for comment among AATB members. Comments will be taken into consideration and final draft shared for international comment. When international consensus for terminology attained, terminology will be added to *ISBT 128 Standard Terminology for Blood, Cellular Therapy and Tissue Product Descriptions.*

Additionally, ICCBBA has developed a proposal for a two-phase implementation of ISBT 128 that may be a model for implementation in countries that are unable to move directly to full ISBT 128 labeling. The proposal uses a small ISBT 128 label (approx 35 mm × 35 mm) and, as a first phase, would carry a bar coded and eye readable ISBT 128 identification number with a generic product code indicating the product to be human tissue but without further definition. The ISBT 128 number could be in addition to any local numbering for an interim period allowing time for local systems to be updated to use the new number format.



Once terminology has been agreed, the second phase incorporates the product code onto the label with minimal design change. The proposal also introduces the possibility of using 2-dimensional (Datamatrix) codes as a means of encoding more information in the space available.

Organs

As with tissue, in some countries, organ donors are assigned an identifier at the national level by the competent authority such as in Italy, or a government designated authority, such as the United Network for Organ Sharing (UNOS) in the U.S. This identifier is used by the organ recovery agency and is assigned to all organs recovered from a particular donor. The number is unique nationally, but does not meet an internationally agreed format and is thus unlikely to be compatible with traceability systems outside of the country of origin or countries that participate in the assigned system, such as Eurotransplant. This number is also not universally shared with the tissue recovery agencies that recover tissue from the same donor. Thus, the linkage is broken and communication is difficult. If an adverse event is recognized by one program, usually in the organ transplant recipient, mechanisms are lacking to convey this information to the multiple agencies involved outside of the organ transplant community. This was a serious gap recognized by the CDC in designing the TTSN.

One example of such a coding system that is currently being used for solid organ donors is the alphanumeric scheme used in the United States since the inception of the Organ Procurement and Transplantation Network (OPTN) in 1987. UNOS maintains a computer system (UNet^{SM}) where all information about organ donors, candidates and actual organ recipients are stored. When an Organ Procurement Organization (OPO) has a potential deceased organ donor, they access the UNet^{SM} system and generate a unique six-character alphanumeric Donor ID. The OPO uses UNet^{SM} to make electronic offers to the transplant programs of the candidates on the list. When an organ is transplanted, the transplant program uses UNet^{SM} to enter information on the recipient and the donor and the UNOS Donor ID links the two within the computer system.

When a disease transmission is reported to the OPTN Patient Safety System, UNOS staff can easily access the information about all other recipients of organs from the donor and contact the transplant programs that performed the transplant. The OPO is

responsible for contacting the tissue organization that recovered and/or processed the tissue recovered from the donor. Note that UNet^{SM} is not used to generate a UNOS Donor ID in the case of a tissue-only donor. There is currently no single coding system in the United States that is used for all organ and tissue donors.

Software and instruments

To maximize the safety and efficiency benefits of electronic data capture it is important to ensure that instruments and software used throughout the pathway from donor to recipient are able to read and correctly interpret the information provided in electronically readable format. The cost of modification of software and instruments to accommodate locally designed systems is high. Manufacturers will only include support for a coding system as a standard feature of their product if the market is sufficiently large. This presents a major obstacle for any new coding system—as illustrated by the case of ISBT 128 where it took almost ten years from the development of the standard until a significant number of manufacturers would support it as a standard feature. Today, fifteen years after ISBT 128 was developed, almost 100 vendors of software, instruments, and containers and labels are licensed with ICCBBA and support the ISBT 128 Standard. Many of these suppliers provide products that are used across all sectors (e.g. blood grouping machines, infectious disease screening systems). Several of the major software systems providers in the blood transfusion field that support ISBT 128 are now marketing systems to support cellular therapy and tissues.

Coding systems for cells, tissues and organs: lessons learned and a path forward

Lessons learned and the value of a coding system common to substances of human origin

A number of lessons from the past decade can be applied to issues of traceability and coding. The safety and traceability benefits of uniform identification combined with electronically readable information were recognized in the blood transfusion field as far back as 1976 when a system using Codabar bar codes was introduced in 16 blood centers and transfusion services in the US as part of a test program coordinated by the American Blood Commission. Following the success of this program the ABC-Codabar standard was widely adopted in the US and in several other countries (Brodheim et al. 1980; Thatcher 1981). Whilst highly successful for many years, this standard was designed for use in a 'local' context at a time when there was little movement of blood or samples outside the local blood center region, transfusion records were stored for periods of only a few years, and only a small range of blood components was prepared.

With the rapid growth in component therapy, combined with the move to larger and more centralized blood centers and testing facilities, the ABC-Codabar standard was unable to cope with the more complex demands. Donation identification 'uniqueness' was constrained to the local provider (i.e. two different blood center providers could use the same 'unique' identifier). Locally introduced 'fixes' to accommodate new codes into the old structure undermined the original elements of commonality in the standard. As previously noted, the Gulf War emphasized the weakness of this system and stimulated the development of a new, internationally recognized machine-readable system.

There continues to be resistance to changing to an international standard due to a variety of reasons. There are inherent costs related to changing coding and labeling including software and hardware investments along with the inherent resistance to any change per se. This applies to both suppliers and customers who have to coordinate their systems to be compatible. There is also a small fee to register the individual institution in order to identify the sources of materials. Nevertheless, cost savings are also achieved over the long term, including personnel costs realized by adopting a standardized coding system. As an example, Diana Teo (Director of Singapore Blood Services) in the ICCBBA annual report is quoted: "ISBT 128 has provided us with an organized and consistent system of labeling for our blood and blood components. This has enabled better monitoring and more efficient management of our blood inventory. The unique format of the donation identification and product code has also contributed towards blood safety. Ultimately, the change to

ISBT128 has been of benefit to our blood program in Singapore."

There has also been resistance to the adoption of a 'blood' standard for tissue products, however the ISBT 128 system has already been demonstrated to meet the needs of tissue banking, and ICCBBA have gone to considerable lengths to engage with the tissue and cell communities by appointing experts from these fields to their Board of Directors and establishing technical advisory groups in these fields. The benefits of a single coding system for products of human origin, both in terms of simplified handling within the hospitals, and improved biovigilance, are clear.

Currently, tissue that is received into a hospital inventory can come from as many as 40 different suppliers, each with a different labeling system and most of which are not machine-readable. This adds significant burden to the management of inventory requiring significant labor investment to log in each tissue both as received and when distributed within the hospital environment. This obviously increases risks to patient safety as it creates opportunities for error and increases the difficulty of traceability as well as the costs associated with these.

Recommendations for a path forward

There is currently a wide diversity in the identification and coding of tissue and cell products. Identification numbers are very often only unique to the cell processing laboratory or tissue bank of issue and are not always provided in an electronically readable format. Product terminology is generally not standardized even at the national level. Label design and content is varied although regulatory requirements ensure essential information is present. However, there is a slow but steady trend towards the implementation of ISBT 128. Two hundred and thirty-seven Tissue and Cell facilities in more than 30 countries are currently registered with ICCBBA to use ISBT 128, and 27 of these have registered since the start of 2009. Across all three fields of blood, cellular therapy and tissue there are now more than 3,700 ISBT 128 licensed facilities in 66 countries.

The international consensus on cellular therapy coding and labeling has set a clear direction for the global adoption of ISBT 128 for CT products. Interest in the tissue banking sector continues to grow, particularly with the recognition of the essential need for globally unique identification of tissues, however the lack of clarity over the European Commission's position on coding is hampering adoption in some European countries.

Effective traceability and biovigilance in the global context depends upon the use of globally unique identification for all donated biologic products. Where technological development permits, such identification should be provided in a standard electronically readable format to eliminate the risk of manual transcription errors. The ISBT 128 system has already been adopted in many countries, is well established, and is reliable.

In most cases mapping from existing local or national numbering systems to an ISBT 128 number should be relatively simple. The ISBT 128 Facility Identifier can be assigned at the level of individual tissue banks or organ procurement organizations, or at the level of a national coordination body. The remainder of the identifier is made up of a two-digit year code, and a six-digit sequence number. As an example, a tissue bank in the USA may currently identify tissue donations using a year code (09) and sequence number in the year (001), giving the first donor of 2009 the number 09/001. If this tissue bank were assigned the ISBT 128 facility code of W9999, then the number would map into an ISBT 128 number as W9999 09 000001, where W9999 is the facility code, 09 is the year and 000001 the sequence number for the year.

Recognizing that existing systems will need to be modified to change from current numbers to globally unique identifiers a two phase proposal from ICCBBA could be considered as an interim step.

Previously concerns have been expressed about the status of ICCBBA, in particular whether the organization is a commercial entity, and whether it is 'US-centric'. In response to such queries, ICCBBA has confirmed that they are a tax-exempt not-for-profit organization under Section 501 (c) (3) of the Inland Revenue Code which requires that the organization must not be organized or operated for the benefit of private interests, and no part of their organization's net earnings may inure to the benefit of any private shareholder or individual (IRS.gov 2010). In addition, an international volunteer Board of Directors governs ICCBBA with current members from Canada, China, Denmark, Egypt, Italy, the Netherlands, and

the USA, and the Executive Director is based in the UK. Other resistance/perception issues include:

ICCBBA is not under the auspices of government and there is perceived risk of the system collapsing if ICCBBA fails without funding guarantees.

There are issues around who ultimately owns and controls the standard and has ultimate power over it. Another issue is the fact that the tissue banking field is competitive (and in some cases commercial) with slight variations in products using patented technologies creating unique marketable 'edges' which conflicts with the principle of commonality and product equivalence. Finally the labeling system 'looking the same' is against the principle of product branding, and highly processed grafts having unique trade names rather than product descriptions further exacerbates the issue.

Nevertheless, International standardization of terminology helps to reduce the risk of misunderstanding when product is shipped internationally and would greatly assist in the analysis of adverse events and reactions. To date the most comprehensive international terminology for biologic product descriptions is held by ICCBBA for use in the ISBT 128 Standard. However, there are some areas, most notably in reproductive tissues, eyes and organs, where the terminology has yet to be fully defined. In addition, efforts are needed to create communication pathways between the different transplant communities where a donor is shared, such as with organs, tissues and cornea programs. The identification of an adverse event, that may impact other recipients of biological components from the same donor, must be communicated to all stakeholders to improve patient safety and outcomes.

It is recommended that:

- Efforts be made to encourage the introduction of a standardized international coding system for donation identification numbers, such as ISBT 128, for all donated human biologic products.
- Focus on global traceability for all donated human biologic products.
- Encourage communication between international stakeholders to develop consensus on common grounds.
- Promote suitable international forums to be established to expand the international terminology for donated human biologic materials.
- Any move towards adopting globally unique identification should be compatible with a well established standard coding system so that the progression towards automated data capture and computerized records can be achieved.

References

Ahn J, Cohen SM (2008) Transmission of human immunodeficiency virus and hepatitis C virus through liver transplantation. Liver Transplant 14(11):1603–1608

Albee FH (1912) Discussion of Carrell A: the preservation of tissues and its application in surgery. JAMA 59:527–528

Ashford P (2006) ISBT 128—improving security by international standardization. ISBT Sci Ser (1):242-245

Ashford P, Distler P, Gee A, Lakester A et al (2007) Terminology and labeling of cellular products: 1 Standards. Bone Marrow Transpl 40:1075–1083

Ashford P, Fearon M, Bedford R (2010) Report on the joint IBEPAG/ICCBBA survey on import/export and blood component labeling. Vox Sang 98:85–86

Billingham RE, Medawar PB (1951) The technique of free skin grafting in mammals. J Exp Biol 28(3):385–402

Blood Products Advisory Committee (1997) Center for Biologics and Evaluation. In: Proceedings of BPAC meeting, June 20, 1997 http://www.fda.gov/ohrms/dockets/ac/97/transcpt/3304t2.rtf. Accessed 11 Dec 2009

Brodheim E, Ying W, Hirsh RL (1980) An evaluation of the Codabar symbol in blood banking automation. Vox Sang 40(3):175–180

Bush LF, Garber CL (1948) The bone bank. JAMA 137: 588–594

Carel A (1912) The preservation of tissues and its application in surgery. JAMA 59:523–527

CEN Workshop Agreement, CWA (2008) 15849. CEN Workshop Agreement on 'Coding of Information and Traceability of Human Tissues and Cells' CWA_Coding-for-T-and-C_v2000_20080522.doc. ftp://cenftp1.cenorm.be/PUBLIC/CWAs/e-Europe/Tissues_cells/CWA15849-2008-publishedtext.pdf. Accessed 6 Nov 2009

Chaney A (2006) "Body Brokers", Random House

CIBMTR Progress Report (2008) January–December

DeBoer HH (1986) The history of bone grafts. Clin Ortho Relat Res 226:292–298

Eastlund T, Strong DM (2004) Infectious disease transmission through tissue transplantation. In: Phillips GO (ed) Advances in tissue banking, vol 7. World Scientific Publishing Company, Singapore, pp 51–131

Eisenbrey AB, Eastlund T (eds) (2008) Hospital tissue management: a practitioner's handbook. AABB Press

Federal Register (2005) 70(106):32620–32624

Fehily D, Ashford P, Poniatowski S (2004) Traceability of human tissues for transplantation—the development and implementation of a coding system using ISBT 128. Organs Tissues 2:83–88

Feyerick D (2009) Mayors, rabbis arrested in corruption probe. CNN.com/crime. http://edition.cnn.com/2009/CRIME/07/23/new.jersey.arrests/index.html. Accessed 4 Sept 2009

Fishman JA (2007) Infection in solid organ transplant recipients. N Eng J Med 357:2601–2614

Fishman JA, Strong DM, Kuehnert MJ (2009) Organ and tissue safety workshop 2007: advances and challenges. Cell Tissue Bank 10:271–280

Gandhi MJ, Strong DM (2007) Donor derived malignancy: a review. Cell Tissue Bank 8(4):267–286

IRS.gov (2010) http://www.irs.gov/charities/charitable/article/0,,id=123297,00.html. Accessed 2 Feb 2010

Guild WR, Harrison JH, Merrill JP, Murray J (1955–1956) Successful homotransplantations of the kidney in identical twins. Trans Am Clin Climatol Assoc 67:167–173

Health Canada News Release (2005) 2005-115 Tissue Recall in the United States, October 2005

Henkel J (1994) FDA consumer magazine, vol 28, September 1994

Herman AR (2002) The history of skin grafts. J Drugs Dermatol 1(3):298–301

ICCBBA (2008) ISBT 128 cellular therapy coding and labeling advisory group 2008—a year end review, Annual Report, 2008

ICCBBA (2009) http://iccbba.org/info_abouticcbba.html. Accessed Dec 2009

Internal Revenue Service (2010) http://www.irs.gov/charities/charitable/article/0,,id=96099,00.html. Accessed 2 Feb 2010

Ison MG, Hager J, Blumberg E et al (2009) Donor-derived disease transmission events in the United States: data reviewed by the OPTN/UNOS disease transmission advisory committee. Am J Transpl 9(8):1929–1935

Keller M, Grill M (2009) Inside a Creepy Global Body Parts Business. http://www.spiegel.de/international/europe/0,1518,645375,00.html. Accessed 4 Sept 2009

Moffat SC, Cartwright VA, Stumpf PH (2005) Centennial review of corneal transplantation. Clin Exp Ophthalmol 33(6):642–647

Mroz TE, Joyce MJ, Steinmetz MP, Lieberman IH, Wang JC (2008) Perspectives in modern orthopaedics. Musculoskeletal Allograft Risks and Recalls in the United States. J Am Acad Orthop Surg 3(10):559–565

Phillips G, Strong DM (1997) The contribution of the international atomic energy agency to tissue banking. Cell Tissue Rep 4(1):5–9

Strong DM (2000) The U.S. Navy Tissue Bank: 50 years on the cutting edge. Cell Tissue Bank 1:9–16

Thatcher R (1981) Recommendations of the task force on codes and machine-readable symbols. Vox Sang 40(3):144–155

Thomas ED, Lochte HL, Lu WC et al (1957) Intravenous infusion of bone marrow in patients receiving radiation and chemotherapy. N Engl J Med 157:491–496

Trotter JF (2008) Infectious disease risk factors of corneal graft donors. Arch Ophthalmol 126(2):235–239

Tugwell BD, Patel PR, Williams IT et al (2005) Transmission of hepatitis C virus to several organ and tissue recipients from an antibody-negative donor. Ann Intern Med 143:648–654

Warren J (2006) BTS stolen body parts scandal generating gruesome headlines, fears of infection; NY grand jury meeting. Transplant News, 16(1(Jan 13))

WHO (2005) Guidance on adverse event reporting and learning systems. http://www.who.int/patientsafety/events/05/Reporting_Guidelines.pdf

WHO (2006) Human organ and tissue transplantation. Transplantation 79:635

WHO (2009) Aide-Mémoire on Access to Safe and Effective Cells and Tissues for Transplantation. http://www.who.int/transplantation/cell_tissue/en/. Accessed Nov 2009

Wilson PO (1947) Experience with a bone bank. Ann Surg 126:932–946

欧州モデルに学ぶ，医療文化と臓器提供推進機関のあり方

篠崎尚史

東京歯科大学市川総合病院　角膜センター

Learning from European Model, Culture of Medicine and the Way in Promotion of Organ Donation

Naoshi Shinozaki

Cornea Center, Tokyo Dental College

1．はじめに

1960年代の免疫抑制剤の開発と共に急激に発展した臓器移植技術は，その後の生活習慣病の蔓延などにより特に腎不全を中心とする急激な患者数の増加を見た。これらの事象が，80年代になり先進国から発展途上国への臓器を求める様々な行為，即ち，臓器売買を拡大し，また，先進国内でも生体間臓器移植の拡大を呈した。1987年5月に開催された世界保健機関総会（WHA）で，国際的な実態調査と，ガイドラインの制定に向けた委員会の設置が決議された（WHA40.13）。この後，4年間の審議を経過し，1991年に9条からなる“Guiding Principles for Transplantation”（WHA42.5）が制定されるに至った。この協議に伴い，80年代後半から90年代には多くの国々で「臓器移植法」が制定され，本ガイドラインは多大な効果があった。

WHOガイドラインでは，死体からの臓器提供を主たるものとし，生体移植は補足的医療との位置づけであったが，前述の状況よりその比率，移植数は増加する一方であった。そのような中，臓器提供者数を優位に増加させる事に成功したプログラムが，スペインから発表された。国際的なプログラムとしては，“Collaborative”を中心とする米国政府機関のHARSAによるUNOSとの共同プログラム等が実施され，また，欧州では提供病院の啓発に注目し，移植コーディネーターの教育を主としたEDHEP（European Donor Hospital Education Program）や，ベルギーのDAP（Donor Action Program）等が実施された。しかし，その効果は対象とする医療機関での臓器提供数を一定程度，増加させたものの，契約等の制約により，国レベルでの増加をもたらすまでには至らなかった。

2．国際的臓器提供推進モデル

1980年代後半になり，EDHEPやDAPのコアメンバーであったバルセロナ大学の麻酔科医師である，Marti Manyarich氏がこれらの手法を元に考案した，TPM（Transplant Procurement Management）が，バルセロナの医療機関を中心に活動を開始した。アクティブな教育を行った，臓器提供を専門とする医師や看護師を中心とする移植コーディネーターチームを救急現場に配備するプログラムである。90年代になり，その効果が顕著となり，1993年以降にはスペイン全体の臓器提供者数を飛躍的に増大させる事に成功した（図1）[2]。

スペインは臓器提供率を一気に引き上げて世界

別刷請求先：篠崎尚史　〒272-8513　千葉県市川市菅野5-11-13
TEL：047-324-5800　E-mail：info@eyebank.or.jp

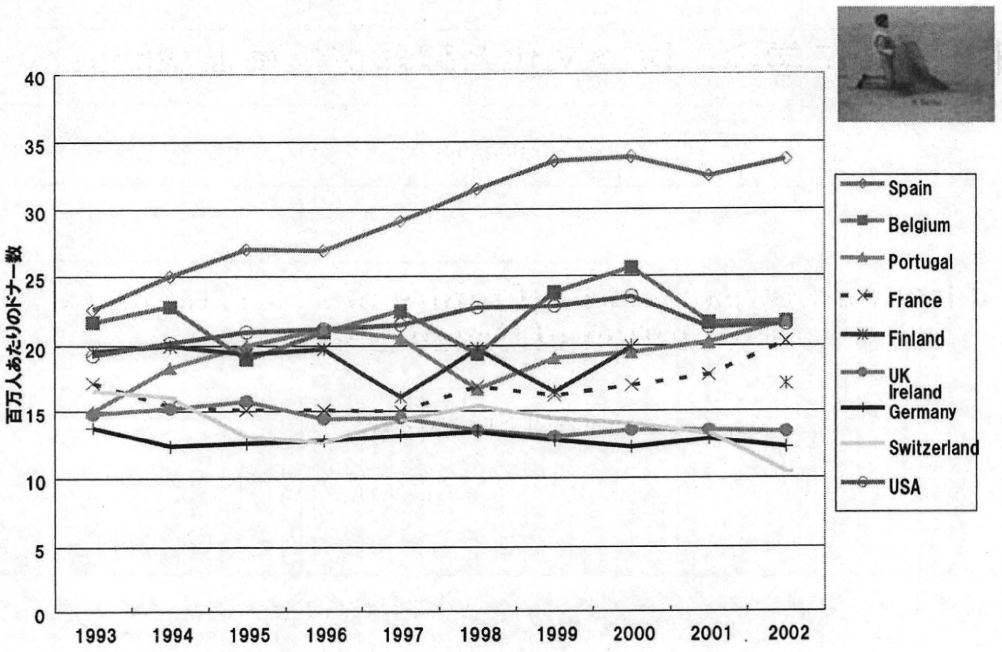


図1　欧州，米国での臓器提供数の推移.

TPMの各国の年次推移をグラフ化した[2].

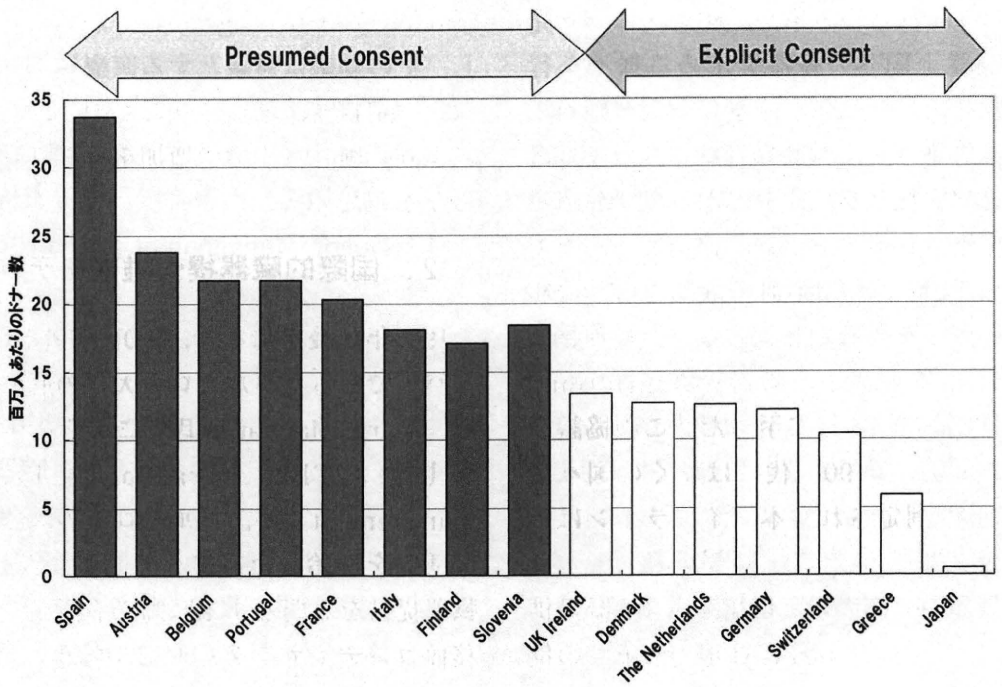


図2　臓器提供意思表示確認制度と臓器提供数.

TPMの2002年臓器提供者数をPresumed ConsentとExplicit Consentに分けて作成した[2].

最高の水準を現在も維持しており（図2，3），WHO移植課でも公式にスペインモデルを推奨するに至り，国際移植学会（TTS）では，2009年のシドニー総会で，外国人への臓器移植を禁止する法整備に貢献した中国の黄副部長と共に，名誉表彰を授与している。臓器提供を推進するには，

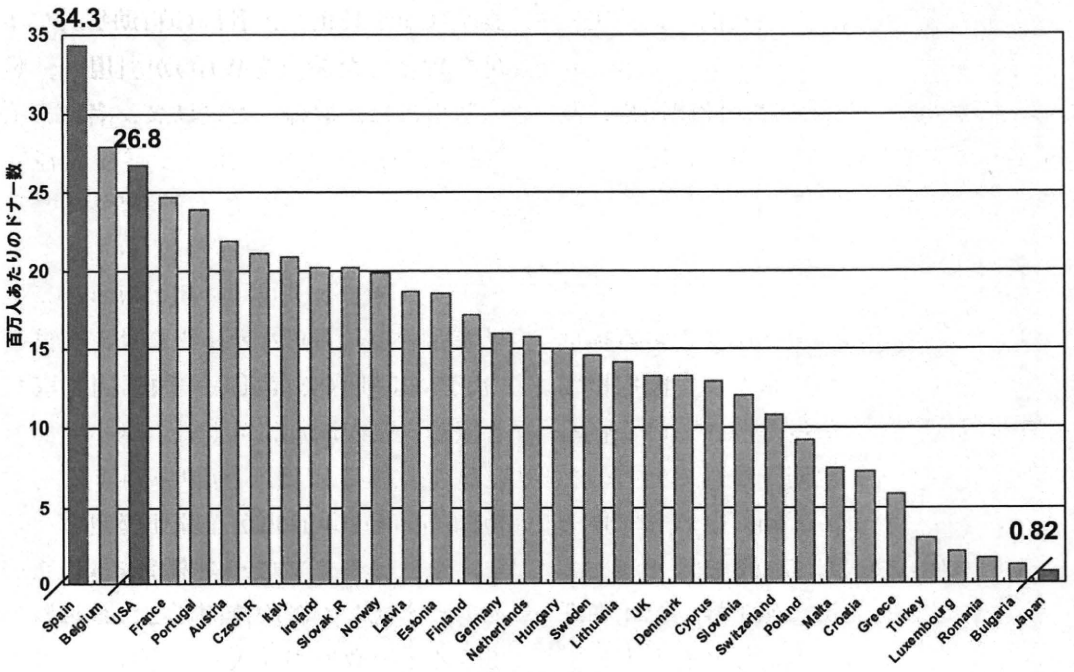


図3　世界の臓器提供者数.

2007年の人口百万人当たり数（PMP（per million of population）数）.

医療現場での社会基盤整備と共に，社会教育による死生観，脳死，臓器提供，並びに臓器移植に関する文化構築を平行して行わなければならず，これらを連携して実施しない限り，その効果は大きく無い事が推察される。

スペインのTPMは，90年代に入り政府もその有効性を認めざるを得ない状況となり，政府関連機関としてONTを設置し，臓器提供が行われた際の費用配分において，これらの機関が医療機関内で実施した活動の効果が現れた際に財政的支援が行われる制度等が体系化された。さらに，イタリアを含む欧州やアジアでもTPMの教育を導入するに至り世界中で確固たる位置を占めるようになっている。

TPMは臓器提供プロセスを再分化し，下記の如くの教育プログラムを実施している。

1）Donor Detection：ポテンシャルドナーの選別が救急現場で実施できるための知識と方法，並びに院内体制整備に向けた活動方法

2）Brain Death：脳死判定に関する医学的な教育

3）Family Care：家族の精神面でのケアや，救急搬送，治療時における家族支援方法

4）Donor Management：脳死下での医学的臓器保存方法

5）Organ Retrieval：臓器摘出，搬送方法

これらの項目を，経験と理論により構築された，体系的教育として実施した上で，臓器あっせんのための機関を，架空の地域で作成させて効果的なリソースの利用方法や，移植コーディネーターの配備，医療機関の教育方法等のプログラム作成等が，マネージメントの概念で作成，評価されるセッションなど，詳細な設計となっている。また，データ収集も科学的に行われている。現在，厚生科学研究事業「臓器移植の社会的基盤に関する研究」でも，DAP（ドナーアクション・プログラム）のデータベースを使用し，TPM教育に医師，移植コーディネーターを派遣し，国内展開モデル事業を実施してるが，これらの手法を理解して，

忠実に再現できている地域，医療機関では確実にドナー数が増加し，また，一旦，上昇しても，システム化が行えなかった場所では，欧州同様に減少に転じると言う結果が得られてきている。

これまでの臓器提供では，移植医が積極的にドナー発生の可能性が高い医療現場に働きかけ，また，平成９年の臓器移植法制定以降は，移植コーディネーターの仲介による医療機関での臓器提供シミュレーション等が行われて来たが，医療機関での教育，並びに，個々の医療機関における臓器提供プロセスの阻害要因の解明，排除のためのアクションプラン作成，実施，評価，というプロセスでの学問体系は作られてこなかった。その上，医学教育を含む国民教育での，死生観，脳死の理解，臓器不全患者のニーズ等の情報共有も十分ではなかった。上記，研究班では都道府県単位でのアクションや，医療機関単位でのプログラム等，いくつかの手法で検証を加え，適切な人材が行えば確実に臓器提供，臓器移植が欧州の手法でも増加する事を検証してきた。しかし，現時点はスペインのようにこれらのプロフェッショナルを体系的に教育する人材も，場面も少なく，研究班で年間１～２名をスペインに派遣してTPMを受講させ，これらの人材に研究協力者になってもらい実施するという手法をとっている。

３．臓器移植をめぐる世界の動き

臓器移植患者数の増加は，生体間移植の増加や臓器売買を引き起こした。前述の1991年WHO移植ガイドラインの制定後もそのトレンドは変わらず，遂に2010年に改正ガイドラインの制定に至った。この改正での特記すべきポイントは，１）臓器のガイドラインから，細胞・組織・臓器に関するガイドラインと明記，２）生体ドナーも含む，提供，移植のすべてのトレーサビリティーを確保する，３）臓器売買，渡航移植のモニターリングのための国際コード化，などである。その中でも，国際移植学会（TTS）のイスタンブール宣言を受けたWHOガイドラインの部分に，世界共通コード化が上げられる。基本姿勢として臓器売買，渡航移植を禁止し，各国の自助努力による自給自足を旨とした論点をWHOが引用し，臓器売買等の防止には，取締りと同時に，各国政府による臓器提供の推進活動を促すと言う内容になっている。すなわちスペインモデルをWHO加盟各国政府に推奨すると言う形が取られた。

イタリアでは，自国の臓器移植の取り組みの効果が顕著に見られなかったため，公式にスペインのTPMに教育を委託し，数年間の取り組みにより臓器提供が増加に転じた。スペインモデルで特に目を見張る点は，DAPを利用した医療機関でのDonor Detectionから脳死判定率，呼吸器装着率，家族へのアプローチ率，家族拒否率等をすべてデータ化して医療機関ごと，地域特性等が分析できる上，政府が介入し，それらの改善プランを設計し，実行，検証すると言うPDCAサイクルによる事業を実施している点である。

例えば，バルセロナを中心とする臓器提供の認定病院119（全体の78%）のデータでは，６年間のICUでの死亡は94,000名余，そのうち脳死と診断されたものは11,000名である。その11,000名の脳死と診断された患者様の中で臓器提供された方は5,827名であった。スペイン政府機関であるONTは，51%しか臓器提供に至らない理由の調査を国費で実施している。その結果からreferralされていなかった症例が138例，medical contraindicationが27%と出て，スペイン政府からこの項目について各々の指令が出された。これらの指令には目標設定があり，例えばunreffered donor 1.2%は，全体数から見ると11,000のうちのわずか138例であるが，「138例を０」にするにはどうしたら良いのか」ということで，国のスタディーグループが形成され，原因究明ばかりかその改善プランの設計も行われた。また，家族拒否による臓器提供拒否例が，全体の15.2%，移植コーディネーターが面談したご家族の中で22%であるが，全体の10%まで落とす，同時に面談したご家族の拒否率の22%を，15%にするプロジェクトが指導されている。日本であれば，家族の拒否は自由意志である，と，筆者自身，勝手に思い込んで

いた節もあり，かなり反省させられた。家族の拒否は，文化的問題，教育的問題，あるいは承諾時の病院の中の雰囲気や移植コーディネーターの問題等の解析を行わなければ，その改善策は作成できない。このように臓器提供プロセスに関するデータを解析し，日本での患者様のプロファイルがどうなっているのか，ということを解析するために，厚生労働省厚生科学研究補助金事業の「臓器移植に関する社会的基盤に関する研究」では，DAPのデータベース，並びにTPMの教育ツールのライセンスを受けて実施している。

システム上の問題として，米国の規制当局であるFDAと並列に，臓器移植のプロモーションを行うHRSAがある。わが国のJOTNWに該当するUNOS及びOPOの予算配分はHRSAから充当される。当然，これらは財団であるため，総事業費の何パーセント以上の寄付を得なければならないという縛りはあるが，実質的な予算執行と，年次計画の立案から評価までを，外部の評価が可能な形で実施する事で，透明性の確保ばかりか，効果的，効率的な方法へのインセンティブが発生する。臓器提供，臓器移植推進のためのアクセル役がいわばHRSAであり，そこに規制をかけるブレーキ役がFDAというふうに別れている。欧州の場合でも，例えはドイツを例にあげると，DSOがドイツ国内の臓器提供の責務を持っており，国内での一般啓発教育や，各ドナー病院の医療従事者教育も実施している。欧州の国をまたぐあっせんに関しては，Euro-transplantが実施するという二重構造になっておりそれぞれが機能的に活動している。

また，院内のシステムに関しては，救急体制の中でのドナーディテクションに注目した。各国の医療現場に則した制度が配備されることが絶対条件となる。ERとICUが一括管理されている場合には，これらを統括する部署での教育，人員配備に重点を置くとスペインのTPMモデルのような，ドナー選択，ドナー管理の教育を受けた救急医，麻酔科医等を公的に補充する事で，救急現場の助けになる上，ポテンシャルドナー発生時には，提供側のコーディネーターとして専従できるため，医療機関としてドナー病院の指定を受ける事が，大きなインセンティブとなる。米国は，医療機関側の人材（医師，看護師）に自ら教育を受けさせ，更に医療機関への資金が臓器提供の際に比較的高額に入るというモデルである。医療文化として，救急医らが医療機関の収入になるというインセンティブで臓器提供が増加するという仕組みには，わが国の医師の概念として，違和感を感じざるを得ない。従って医療文化の類似する欧州で成功した，ドナー家族精神ケアの教育まで受けた医師を救急の現場に派遣して，ドナーディテクションを行える体制整備を行う形態がわが国には適していると考えられる。

北米以外では，ドナーディテクション，ドナー管理において，外部からの移植コーディネーターが，救急現場でリーダーシップを発揮できる状況の受け入れは，患者サイドからも容易であるとは思えない。従って救急現場への医療支援的，救急医，脳外科医，麻酔科医等の派遣の形態が整うことが，患者家族へのケアも含めて有用であると考えられる。特に2010年の法改正後の，小児臓器提供が発生した際には，ご家族への支援はこれまで以上に重要な医療機関側の責務となるが，これらの分野にも専門家が必要となり，その教育機関を含めて，社会基盤の整備を救急体制整備の観点から実践する必要がある。

4．臓器提供，臓器移植に関する国民的感情

日本での世論調査の結果を見ると，国民意識の移植医療に対する変化が少なくなかった事が伺える。特に平成16年以降の移植医療に関する意識は急激に変化し，臓器提供をしたいという比率は，35%から43.5%に上昇し（図4）逆に，臓器提供したくないと答える国民は，33%から24.5%となった。これらの意識の改革は，欧州の世論調査とほぼ同等のレベルとなってきており，一般普及啓発において我が国のマスメディアを中心とした情報発信は，国民の理解度を高める上で良い結果を

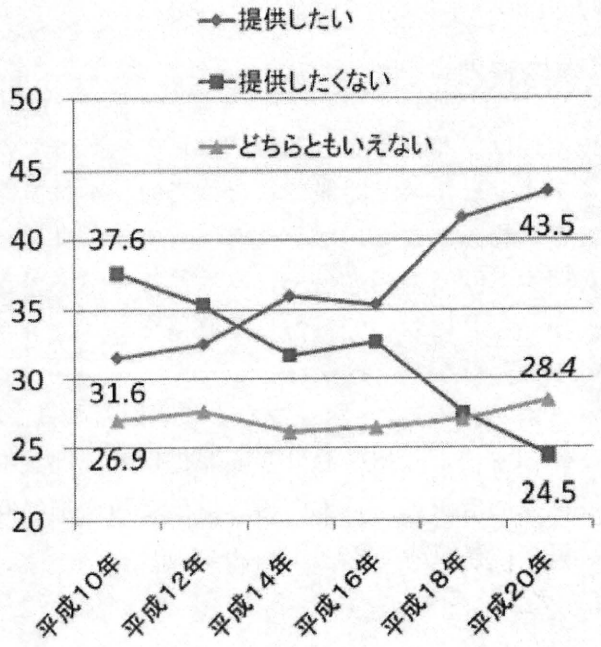


図4　脳死下での臓器提供に関する世論調査

もたらしている事が示唆される。さらに正確な情報である事が重要であり，その観点からも単なる臓器提供，臓器移植という情報発信でなく，死生観，脳死と植物状態の差，臓器不全等，多角的な情報を国民に提示できる手段を講じる必要があり，米国のHRSAが実施しているような教育や啓発を専門的に行える体制，財政基盤が不可欠であると考える。

また，臓器提供の教育は，一般的な概念の普及による文化構築と同時に，家族が脳死に陥ったという緊急時に決断できる状況，並びに，医療機関側からの臓器提供に関してのオプション提示が無ければならない。家族の緊急時に，救命を切望する家族が臓器提供を考える事は，まず，不可能であり，そのような事態の中での医療従事者からのリマインドが，訓練された形で，医療従事者側の負担無く行える環境整備が無ければならない。このためにも，1）臓器あっせん機関（わが国ではJOTNW）以外の，医療機関への教育・移植コーディネーター派遣機関，及び，2）国家的普及啓発機関：学校教育，医学教育を含む一般啓発活動を恒常的に実施する機関，の設立が必要である。これらの機関を国がすべて負担して設立するのか，或いは，NGO等の形態で行うのかは議論が必要である。規制当局である厚生労働省が一つの部局（臓器移植対策室等）が，片輪で規制をかけながら，もう一方で移植推進事業を行うと言うのは，物理的，倫理的にも問題があり，米国政府の様に別個の機関が行う事で利益相反の無い健全な体系がもたらされるであろう。

筆者の所属する東京歯科大学市川総合病院では，4年前から，全ての死亡退院患者の情報を主治医がアイバンクに連絡すると言う，海外のRoutine Referralを実施している。昨年，米国で発表した際に実施した3年間のデータでは，1,230例の死亡退院症例中，主治医より連絡を頂けたのは991例，80%であった。平成21年に限定すると，95%を超えている。医学的禁忌等を排除した中で，移植コーディネーターがインフォームドコンセントを得られた456症例の中で82ドナー，161眼の角膜の提供を受けた。つまり，承諾率が18%であった。海外でも同様のシステムを運用しているが，全適応ドナー中，承諾率は11～12%程度であり，我々のデータからもわが国の国民が，臓器提供や献眼に対して，文化的に否定的であるという見解は誤っている。

わが国で臓器提供を適切に推進して行くには，様々な工夫が必要である。その中でも，特に教育に関する部分は重要であると考える。特にスペインモデルに代表されるTPMは，もはやWHOが推奨するまでに至り，その運営方法や各国の文化，医療制度にどのようにマッチさせるのかが問われている。費用面からも，保険医療制度の中だけの運用で，これら全ての経費が負担できるものではなく，国家的な枠組みや，経営的発想が無ければこれらの機関の設立は容易ではない。

5．おわりに

平成22年7月には，いよいよ改正臓器移植法が施行され，家族による承諾での臓器提供が開始される。グローバル・スタンダードの法律下での移植医療の推進は，特に救急現場への負担増が懸念

される。また，20数名の移植コーディネーターしか所属していない日本臓器移植ネットワークで，全国の移植事例へのあっせん対応，医療機関の教育，ドナー家族の対応等がまかなえるはずも無く，これらの社会基盤整備を早急に実施する事は急務である。その中でも，統計的に評価のできるシステムを構築する事が現代の社会には重要であり，この概念からも世界的に通用するシステムとして評価されるのは，ドナーアクションデータベースを使用した，TPM教育である。

教育の水準や，教育者の質も評価されるので，当初は抵抗がある事は理解できるが，医療はすべて「患者様のため」である事を再認識し，国民に取って後悔の無い移植医療を提供する体制整備が急がれる。

参考資料

1) 本稿は，2008年11月23日に東京の六本木アカデミーヒルズで開催された第35回日本臓器保存生物医学会シンポジウム「ドネーションに関する欧米の相違――日本はどこを学ぶべきか――」において報告した原稿をもとに書き下ろしたものである。

2) 日本ドナーアクションプログラム運営委員会. 特別寄稿　欧州における臓器提供の現況と推進への取組み－日本の臓器提供者数増加に向けて. 移植39（2）；145-162, 2004

Key words
WHO Guiding Principle
イスタンブール宣言
小児救急医療体制
小児ドナー家族ケア

特集 わが国の小児臓器移植医療をいかに発展させるか 8

円滑な小児臓器移植医療の推進に向けて

篠崎 尚史（しのざき なおし）*

要旨

2009年7月に，参議院で臓器の移植に関する法律の一部改正案が可決成立し，2010年7月から施行される．世界的な標準である家族による承諾で，提供者本人の書面による意思表示が必要なくなり，また，15歳未満の小児の臓器提供が可能となる．この流れが世界的にみてどのようなものであったか．また，本特集の中から浮かび上がる施行に向けた問題点について言及する．

はじめに

1950年代に開始された臓器移植が，免疫抑制薬の発達に伴い技術的にも手術のみならず，術後管理の充実とともに，臨床成績も向上してきた．1980年代に入り，先進国での生活習慣病などによる腎不全を中心とする患者急増の影で臓器売買が横行し，1987年のWHO総会（WHA）にて，臓器移植のガイドラインを作成すべきとの決議が採択された．4年間の議論を経て，1991年にWHO移植ガイドライン“Guiding Principles on Transplantation”（WHA42.5）が作成された．

この議論の間にも多くの国々で「臓器移植法」が成立し（**表1**），わが国でも1997年に「臓器の移植に関する法律」（法律第104号）が国会で可決成立し，翌年施行されたことは，世界的な動向からみれば妥当であったと思われる．しかしながら，脳死下での臓器提供には，本人の書面による意思表示が義務化され，さらに15歳未満の書面による意思表示が，遺言書での有効年齢が15歳以上であるとの法的引用により認めないとする，国際的にも稀有な法律となった．そのために臓器提供者は非常に少数で，当然の結果として海外に移植を求める患者も後を絶たず，また，小児患者では現行法施行の1997年以降，100名を超える渡航移植が実施された．その間にも，臓器不全となったほとんどの小児は，国内でその短い命を絶つこととなった．

1991年のWHOガイドライン制定後も，国際的にも臓器売買が横行し，発展途上国では臓器ドナーとして小児の誘拐や，また，フィリピンのように金銭を求めた臓器提供が国際問題となり，WHAでは2003年5月に，移植ガイドラインの改正を決議した．

I WHOを中心とした国際的な流れ

2003年のWHAで，歯止めのかからない臓器売買を規制し，各国の自助努力を促すために，ガイドライン改正を行うことが決議され，同年10月6～9日に，スペイン政府とWHOとの共

* 東京歯科大学市川総合病院角膜センター
〒272-8513 千葉県市川市菅野5-11-13

表1　欧州各国の法整備状況

国名	法律名	制定年	死の定義
スペイン	Sobre extraccion y transplante de organos	1979	脳死（全脳死）
ベルギー	Wet betreffende het wegnemen en transplanteren van organen	1986	最新の科学による（法による規定はない）
ポルトガル	Portugal Transplant Law	1993	脳死（脳幹死）
フランス	Bioethics Acts	1994	脳死（全脳死）
フィンランド	Act on the removal of human organs and tissues for medical use	1985	脳死（脳幹死）
イギリス	Human Organ Transplant Act	1989	脳死（脳幹死）
ドイツ	German Transplant Law	1997	脳死（全脳死）
スイス	canton により異なる 法律のない canton もある	さまざま	脳死（脳幹死）および心臓死

（瓜生原葉子ほか：移植 2004；39：145-162 より改変）

同で「マドリッド予備会議」が開催された．厚生労働省健康局疾病対策課臓器移植対策室，日本移植学会，国立感染症研究所からの担当者とともに参加し，現状把握と問題点の抽出が行われた．この席で米国の人権擁護団体が実施した調査から，わが国をはじめ，米国，カナダの患者が，発展途上国で臓器移植を受けている事実が公表された．また，生体間移植の増加や挑戦的な異種移植による弊害なども同時に訴え，2004年1月のWHO執行理事会にitem 3.17として「マドリッドレポート」が提出され，同年5月のWHAで移植課の設置が決定された．

2009年のWHAでの決議を目標に，世界各地でさまざまな観点からの会議が開催された．WHOの各地域支部での政府担当者会議や（2007年のWPROマニラ会議等），細胞・組織の専門家による会議（2006年のオタワ会議等），さらには国際倫理を検討するBioethics，Medical Ethics会議（2006年のチューリッヒ会議等）などとともに，WHOでは適切な移植推進のための「World Day on Transplantation」（世界移植デー）を2005年にジュネーブでの第1回会議を皮切りに現在までに5回開催されている．

さらに，WHO移植課のAdvisory Panelとして，国際移植学会（TTS）が公式に参加したことが，今回の改正に関して大きな転換点となった．

Ⅱ 国際移植学会の動き

1991年のWHOガイドラインでも，臓器売買の禁止や生体間移植は死体からの移植の補助的な医療であるとの記載はあるものの，実質的にそれらの抑制にはならず，逆に増加傾向にあることが問題となった今回の改正の動きの中で，移植医療の現場に直結するTTSが，今回の改正に関して実効的な役割を示した．特筆すべきは，フィリピン政府の腎臓買取問題での政府との直接交渉により財団化を阻止した点，中国政府との交渉により死刑囚ドナーの臓器を外国人に移植することを禁止する法制化に成功した点，中東との交渉により臓器売買を阻止した点などが挙げられる．

さらに，これらの世界情勢を踏まえ，2008年4月30日～5月2日には，国際腎臓学会（ISN）とWHOの共同で，Istanbul Summit on Organ