



*Guidance on the Microbiological
Safety of Human Organs, Tissues and
Cells used in Transplantation*

Advisory Committee on the Microbiological
Safety of Blood and Tissues for Transplantation
MSBT

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Foreword

Transplantation of human organs, tissues and cells is now well established. In many instances the transplants save lives, in others they improve the quality of life. Transmission of infection is one of the associated risks. This guidance sets out principles and procedures to reduce that risk to a minimum.

Although there is generally a shortage of donations, we believe that organs tissues and cells must be donated freely and without reward, and should go to the patients with the greatest need. It is not acceptable to attach any conditions (not just those of a racist kind) to a donation. A donation cannot be accepted if donors or their relatives insist on such conditions.

Tests and technologies are developing all the time. These are being kept under review by the Committee on the Microbiological Safety of Blood and Tissues for Transplantation. The Committee intends to issue amendments when there is good evidence to support revision of this current guidance.

I am grateful to members of the working group for producing such a carefully considered document.

Dr Pat Troop
MSBT Chairman
Deputy Chief Medical Officer

Preface

This guidance updates and replaces the 'Guidance on the Microbiological Safety of Human Tissues and Organs used in Transplantation' issued in 1996 by the Committee on the Microbiological Safety of Blood and Tissues for Transplantation (MSBT). The role of MSBT is to reduce to a minimum the risk of transmission of infection through transplantation. The guidance has been written by a working group (members of which are listed in annex 6) after extensive consultation.

The underlying principle running through the guidance is that the risk of infection being passed on through transplanted organs, tissues and cells should be kept to a minimum, taking account of the balance of risk and benefit for the person receiving the transplant. In urgent life-saving situations a higher risk of infection may be acceptable; stricter controls are needed in non-urgent situations and for transplants aimed at improving a patient's quality of life rather than saving it.

The main recommendations covering organs, tissues and cells from an infected (or potentially infected) donor are contained in tables 3, 4 and 5. The information requirements for assessing a donor's risk of infection are set out in annex 2. Where appropriate, this guidance follows the recommendations for testing blood donors. However, there are some situations (particularly in urgent organ donation), where the testing of potential donors will be different. These situations, and the testing that will need to be carried out, are set out in this guidance.

This is a developing area and the guidance reflects best practice in accordance with available evidence, supplemented by expert opinion where published evidence is lacking. This guidance acknowledges those areas that are contentious and recognises that further work and debate are needed. The recommendations in this guidance need to be regularly reviewed, for example around the introduction of nucleic acid testing and the present uncertainties about the transmissible spongiform encephalopathies.

This guidance challenges those involved in transplantation to turn the recommendations into working clinical tools.

Introduction

Transplantation has been one of the great success stories in health care over the last thirty years. However, there have been numerous reports of transmissions of viruses, bacteria, fungi and protozoa following transplantation of organs, tissues and cells. These transmissions can be problematic as the people receiving transplants of organs, cells and some tissues are immunosuppressed, and this makes them more susceptible to infection.

People from a range of specialist fields are involved in the selection of donors and in collecting, testing, processing, storing and transporting organs, tissues and cells. They include surgeons, physicians, clinical microbiologists and transplant co-ordinators, as well as laboratory staff and specialists working in tissue banks. Good transplantation programmes rely on team work. This guidance is provided for everybody involved in transplantation.

Transplants have many benefits, whether life-saving (such as heart or bone marrow transplants) or aimed at improving the quality of life (such as bone grafts). The risk of infection from a particular donor may be an absolute contraindication to accepting a bone donation but a relatively minor contra-indication for liver donation where the potential recipient would otherwise die from liver failure. For this reason, the criteria used to choose a tissue donor can and should be stricter than those for organ donors. However in all cases where unusual or extra risks of infection are identified, these should be discussed in detail with the person who would receive the organs or their family where appropriate.

Infection may also result from transplant material becoming contaminated from organisms in the environment. This contamination may occur while processed tissue grafts are being collected, processed, packed, tested and transplanted. Standard procedures for all these activities should include a microbiological risk assessment as part of a wide-ranging quality assurance programme.

The risk of infection during the whole process of transplantation can never be completely removed. This guidance sets out precautions that should help to keep the risk as low as possible.

Underlying principles

The highest standards should be maintained when choosing donors and when collecting, testing, processing, storing, transporting and actually transplanting organs, tissues or cells. Introducing and maintaining a recognised quality management programme (for example ISO9001) will contribute significantly to the safety and quality of all types of graft used in transplantation.

Scope of the Report

This document updates and replaces the previous paper ‘Guidance on the Microbiological Safety of Human Tissues and Organs used in Transplantation’ published in March 1996. Other publications on this subject were taken into consideration during the preparation of this document. Separate guidance is available on the transfusion of blood and blood products. Supporting literature is listed in annex 5 at the end of the document.

This guidance looks specifically at microbiological disease. Avoiding the transmission of malignant cells in transplanted organs, tissues and cells is also essential but is not covered by this guidance. The Council of Europe have recently produced a publication on this subject (see supporting literature). Other medical issues which do not relate to microbiological risks are also not covered.

Table 1 contains an incomplete list of the organs, tissues and cells covered by this guidance. The donation of embryonic cells, fetal cells, and gametes are not specifically considered here, but the principles set out in this document apply to them in many ways. The broad principles also apply to human cells cultured in a laboratory before transplantation and to manufactured products or services that use human cells or tissues.

Because of the known risk of transmitting Creutzfeldt-Jakob Disease (CJD), human dura mater should no longer be banked or transplanted.

Table 1 Examples of human material covered by this guidance

Organs	Tissues	Cells
Bowel	Bone	Bone marrow
Heart	Cartilage	Ocular stem cells
Kidney	Cornea/sclera	Peripheral blood stem cells
Liver	Heart valves	Placental and umbilical cord blood
Lung	Larynx	Pancreatic islet cells
Pancreas	Limbs	T-cells (for adoptive immunotherapy)
	Neural tissue	
	Skin	
	Tendons	
	Other vascular tissue	

Steps in the Transplantation Process

Opportunities and responsibilities for reducing risk

Tissues and organs may come from living or dead donors. Cells can come from living donors or from umbilical cord blood at the time a baby is born. The precise circumstances of collecting transplant material, and also whether or not it can be stored or cultured in a laboratory, will determine which steps are necessary to reduce the risk of infection from the donor and the environment.

The risk of infection depends on the actions of various people involved in the process leading to transplantation. **Everyone involved in the process should have clear responsibilities so that the appropriate procedures are carried out at each stage.** Annex 1 sets out a summary of responsibilities.

Identifying and choosing donors

The time available for assessing a potential donor depends on the type of donor and the type of donation. Table 2 sets out the classification of donors used in this guidance. In common usage the term cadaver refers to any dead person. However within this guidance we specify three types of dead donor to take account of circumstances and the interval between death and the donation of their organs, tissues or cells.

Before choosing a living donor, that person (or, if they are incapable, the most relevant family member or life partner) should be interviewed. The main purpose of this interview is to seek consent for the donation and to assess donor risk factors. It is also an opportunity to explain the consequences of making a donation, including testing and possible results.

Table 2 Type of donor

Type of donor		Circumstances surrounding the donation
Dead	Heart beating	Donation taken from donor certified as dead by brain stem testing while on respiratory and circulatory support
	Non-heart beating	Donation taken within approximately 1 hour of circulatory arrest
	Cadaveric tissue	Donation taken within the 48 hours after circulatory arrest
Living		Autologous Altruistic: Organ (e.g. kidney, liver, lung) Bone donation (e.g. hip replacement) Heart valves (after heart transplant) Cells (e.g. bone marrow)

In the case of dead donors, the most relevant life partner or close family member should be interviewed. The main purpose of the interview is to make sure that the deceased did not object to organ donation carried out under the Human Tissue Act 1961. The partner or family member also needs to know the consequences of agreeing to donation, including the tests carried out and the need for traceability. However the person interviewed may not be the most relevant to provide medical, behavioural, travel and residence history. The referring clinician should be able to provide information, as should the general practitioner of the deceased if initial assessment suggests that further details are required. Annex 2 sets out the information requirements for assessing infection risks from donors.

The medical and behavioural assessment will be similar for all donors. The microbiological assessment will vary for different donors. Tables 3, 4 and 5 set out the recommendations for testing. The results of the assessments will inform the risk-benefit analysis in deciding whether a donor is suitable in a particular transplant situation.

The risk assessment will consider different factors depending on;

- The type of donor (see table 2);
- Whether organs, tissues or cells are being donated;
- Whether the transplant is for life-saving or life-enhancing purposes;
and
- Whether the material must be transplanted immediately;
- Whether the material can be stored or cultured in a laboratory.

Referral for donation

Heart beating donors

All clinicians responsible for the care of those who, following brain stem testing have been declared dead while on respiratory and circulatory support, should consider that patient's potential for donating organs and tissues. Not all infections present in donors prevent transplantation. Any clinician who is not sure whether a potential donor is suitable for organ or tissue donation should discuss this with the donor co-ordinator from the local transplant team or tissue bank. The clinician should have up-to-date microbiological results on the donor. The risk arising from infected donors should be discussed with a consultant microbiologist when circumstances are unusual as advice from a specialist centre may be required. Tables 3, 4 and 5 summarise the recommendations of this guidance.

Non-heartbeating donors

Because of a shortage of organs for transplant, in some circumstances non-heartbeating donors may be used. There may be very tight time limits for gathering the necessary information but, wherever possible, a risk assessment should be carried out as for heart beating donors. Non-heartbeating donors may also donate tissue, in which case full screening should be carried out as for cadaveric tissue donors (see below).

Cadaveric tissue donors

In circumstances where circulatory arrest has occurred, tissues that are not rapidly degraded (such as corneas, bone, heart valves, tendons and skin) may still be used for transplantation even though the donor is not suitable for the donation of organs. In the case of these potential donors, accident and emergency departments and many non-clinical professional groups (including the police) may refer potential donors and their families to tissue banks or donor co-ordinators. The donor's family (or most relevant life partner) should be interviewed and relevant health professionals (such as the donor's GP) contacted. Any necessary blood tests will usually be arranged by the tissue bank. The donor co-ordinator or trained tissue bank staff should record the fact that the appropriate questions have been asked and procedures have been followed. Everyone involved in this procedure should take into account that tissue banking has a lower benefit-to-risk ratio than organ transplantation.

Living donors

Circumstances for living donations differ. Some people want to donate an organ to a relative or other person they are close to. Others may agree to donate surplus tissue (for example, donating heart valves from the diseased heart after heart transplantation, donating bone following hip-replacement surgery, or donating cells to a cord blood bank). The information needed to assess any risk should be gathered from the potential donor or, in the case of children too young to understand the issues, from the adult with parental responsibility for that child (as specified by the Human Organ Transplants Act 1989).

Information requirements for donor assessment

For organ transplants, the transplant surgeon must be able to assess correctly the risk of the potential donor having an infection. In the case of donated tissues and cells, the medical director of the cord blood bank, tissue bank or bone marrow registry is responsible for making sure the risk of infection is assessed correctly. The relevant information should be collected by the donor co-ordinator or trained tissue bank staff as soon as possible.

Collection of donor information is currently not standardised between different centres: tissue banks have developed their own forms and a core organ donor data form has been made available by UK Transplant. Annex 2 sets out the information requirements that enable donor infection risk to be adequately assessed. There is need for collaborative work between relevant professional groups to incorporate the information requirements into a useful clinical tool.

The information needed for the risk assessment should be gathered from the donor's medical records (in consultation with the referring clinician and the donor's GP) and through discussions with the donor's family or most relevant life partner.

Detailed information is needed on the following.

- Any treatment received before donation (including the choice, duration and dose of antimicrobial and other drug therapy), as this may influence the suitability of the donation.
- Any immunosuppression (by disease or drugs) or previous organ or tissue donation, as this may affect the interpretation of test results or the donor's suitability.
- All intravenous infusions (including colloids, crystalloid and blood) the donor received in the 48 hours before death or the taking of a blood sample. This is particularly important in patients who have had multiple transfusions as donor plasma dilution may affect the reliability of the microbiological test results.
- Blood sampling history as a pre-infusion blood sample, where available, may assist microbiological testing.

A brief examination of the potential donor may indicate extra risks of infection. For example needle marks made by the patient could indicate possible risk behaviour and should be taken into account when assessing the donor suitability.

Results of any other recent microbiological tests should be reviewed. For organ donation, all the information gathered should be kept in the donor's records and the records of the person receiving the transplant. In the case of tissue donations, all of this information should be in the donor's record at the tissue bank.

Requirements for microbiological testing of donors

The clinical information set out in annex 2 should be gathered by donor co-ordinators.

Table 3 sets out the requirements for microbiological testing of all potential donors, and recommends action to be taken when a positive result is found.

Table 4 summarises the circumstances when further testing may be necessary.

Table 5 sets out clinical conditions in which specialist microbiological advice is needed on the advisability of taking organs, tissues and cells for transplantation. A risk assessment should be carried out where necessary. Microbiological testing is not usually needed to reach a decision.

The recommendations in all the tables are more stringent where the transplant is used to improve the quality of life rather than to save a life.

Table 3 Requirements for microbiological testing of all donors

Infection	Test (1)	Organs: action on an initial reactive result (2)	Tissues: action on a positive result	Cells: action on a positive result
HIV 1 and 2	HIV 1 and 2 antibody	Contraindication to donation	Contraindication to donation	Contraindication to donation
Hepatitis B	HBsAg (3)(4)	Contraindication to donation. Consider only in life-saving situations (after discussing all implications with organ recipient or those close to the patient) if the patient is already infected with or immune to Hepatitis B	Contraindication to donation	Contraindication to donation (5) (6) except for autologous transplants and related recipients where individual risk assessment suggests chemoprophylaxis and immunisation may be acceptable to cover HBsAg positive donation
Hepatitis C	HCV antibody	Contraindication to donation. Consider only in life-saving situations (after discussing all implications with organ recipient or those close to the patient) if the patient is already infected with Hepatitis C	Contraindication to donation	Contraindication to donation (5) (6) except for autologous transplants and cord blood donation to related recipient where mother is HCV positive – consider each case individually
Syphilis (7)	Treponemal specific antibody	Donation acceptable	Contraindication to donation of tissues for banking. Donation of cornea/sclera acceptable	Donation acceptable

Notes to table 3

- (1) We anticipate that for cadaveric tissue donors, nucleic acid tests may be used as well as serological markers when tests are validated.
- (2) An initial test is described as reactive when the result is beyond the cut-off level defined by the manufacturer of the assay.
- (3) Routine anti-HBc testing is not advocated except for liver donation (including multi-organ donations involving the liver). For organ transplants other than the liver, where the anti-HBc status is known, donations positive for anti-HBc may be used as long as HBsAg is negative (see table 4).
- (4) In viral screening tests for HBsAg undertaken on cadaveric blood samples, high rates of non-specific reactivity are recognised. Where confirmatory tests (antigen neutralisation on the initial test plus a second EIA test of equal or greater sensitivity) clearly indicate the absence of infection, material derived from donors whose blood samples are repeat reactive in HBsAg screening tests may be used.
- (5) For adult related bone marrow donors where no alternative HLA compatible donors are available, donation may be acceptable after risk assessment informed by expert microbiological advice.
- (6) Although patients infected with blood borne viruses may have a poor prognosis, this should not preclude autologous transplantation of cells.
- (7) Testing transplant donors for syphilis has been maintained due to recent UK outbreaks. Testing of donor sera should be carried out for treponemal specific antibody but transplantation may proceed prior to the availability of the test result. Reactive tests require confirmatory testing. Antibiotic prophylaxis should be given to recipients of confirmed syphilis antibody positive donors. Recipients of material from donors with repeat reactive samples should be treated for syphilis and live donors assessed by a genitourinary physician.

Table 4 Additional microbiological tests for specific indications

Infection	Indication	Test	Organs: recommended action on an initial reactive result	Tissues: recommended action on a positive result	Cells: recommended action on a positive result
CMV	For solid organ and allogeneic bone marrow donors	CMV antibody (1)	Consideration should be given to risk of CMV positive donation to CMV negative recipients. Where high risk of CMV disease is identified, monitoring for pre-emptive therapy or provision of prophylaxis should be considered	Test not usually required as recipients not normally immunosuppressed EXCEPT in donation to babies <1500g for whom only CMV negative viable tissues should be used	Consideration should be given to risk of CMV positive donation to CMV negative recipients. Where high risk of CMV disease is identified, monitoring for pre-emptive therapy or provision of prophylaxis should be considered For cord blood donors where mother CMV antibody positive confirm infant's infection status
Hepatitis B	Liver donors	AntiHBc (2)	Contraindication to donation. Consider only in life-saving situations (after discussing all implications with organ recipient or those close to the patient) or where the patient is already infected by or immune to Hepatitis B	Test not required	No action required
Toxoplasma	Heart, liver and bone marrow donors (for patients not receiving cotrimoxazole prophylaxis after transplant)	Toxoplasma antibody	Give cotrimoxazole prophylaxis for at least 6 weeks to toxoplasma antibody negative recipients of positive donors	Risk assessment required for fresh tissues given to immunocompromised patients	Test donor if recipient toxoplasma antibody negative – prophylaxis for recipients of positive donors

Notes to table 4:

- (1) Where possible two assays should be used and a consensus achieved.
- (2) It is highly desirable to have antiHBc results for liver donation (including multi-organ donations including the liver). However the test currently has a high false positive rate. Based on current knowledge, donations positive for HBc antibody alone may not represent a significant risk for organ donations other than liver donations. Organs other than the liver may be used as long as HBsAg is negative (see table 3). This is being kept under review and further guidance may be required in the future.

Table 5 Clinical conditions affecting eligibility of the donation

Infection	Clinical context	Organs	Tissues	Cells (1)
Bacterial meningitis	No visible damage or local infection in organ at retrieval	Donation acceptable with appropriate recipient antibiotic prophylaxis covering donor organism	Donation acceptable where adequate donor antimicrobial chemotherapy. Expert advice may be required	Related donations acceptable with appropriate recipient antibiotic prophylaxis covering donor organism
Viral meningo-encephalitis (2)	Herpes simplex or Varicella zoster infection diagnosed	Contraindication to donation unless HSV/VZV treated for 7+ days. If treated less than 7 days, recipient should have anti-viral prophylaxis	Contraindication to donation	Contraindication to donation
	Other aetiology, donor not abroad recently	Careful expert case by case assessment required	Contraindication to donation	Contraindication to donation
	Other aetiology, donor abroad recently	Contraindication to donation	Contraindication to donation	Contraindication to donation
Tuberculosis	Donor with active disease, or Donor within the first six months of treatment and either no M. tuberculosis detected on culture or an isolate shows resistance	Contraindication to donation unless recipient receives appropriate drug treatment if the donor has not completed a course of chemotherapy	Contraindication to donation	Contraindication to donation
	Past tuberculosis at the site of donation	Donation of other organs acceptable	Donation acceptable provided donor completed curative course of chemotherapy	Donation acceptable provided donor completed curative course of chemotherapy
Bacteraemia	Occurring in preceding 5 days. No visible damage or local infection in organ at retrieval	Donation acceptable with appropriate recipient antibiotic prophylaxis covering donor organism	Contraindication to donation and banking	Donation acceptable with appropriate recipient antibiotic prophylaxis covering donor organism, except bone marrow for banking which remains contraindicated. For cord blood review on a case by case basis (3)
Abscess	Occurring in preceding 5 days and at a distance from material to be retrieved (4)	Donation acceptable with appropriate recipient antibiotic prophylaxis covering donor organism	Contraindication to donation	Contraindication to donation
Colonisation with resistant bacteria (e.g. MRSA)	At any time	Donation acceptable. Specific prophylaxis may be required where donation site in continuity with colonised site (5)	Donation acceptable except skin	Donation acceptable

Infection	Clinical context	Organs	Tissues	Cells (1)
Viruses	Causing severe systemic infection in immuno-compromised patients (eg Adenovirus in paediatric recipients, active Varicella zoster)	Seek expert microbiological advice	Seek expert microbiological advice	Seek expert microbiological advice
HTLV 1 and 2	Known infected donors	Case by case risk assessment	Contraindication to donation	Contraindication to donation
Fungal infection	Mucosal thrush or skin infection	Donation acceptable	Donation acceptable	Donation acceptable
	Candidaemia, candidal abscess	Donation acceptable with appropriate recipient antibiotic prophylaxis covering donor organism	Contraindication to donation	Contraindication to donation
	Aspergillosis or other systemic infection	Contraindication to donation except following risk assessment and antifungal prophylaxis for recipient	Contraindication to donation	Contraindication to donation
Malaria (6)	Known active infection and no curative chemotherapy	Contraindication to donation	Contraindication to donation	Contraindication to donation (7)
Unusual bacterial / fungal / protozoal infections	Unusual infections in the past, including those acquired outside Western Europe (see annex 2)	Seek expert microbiological advice	Seek expert microbiological advice	Seek expert microbiological advice
	Infections common in immunocompromised patients (e.g. Listeriosis, Nocardiosis)	Seek expert microbiological advice	Seek expert microbiological advice	Seek expert microbiological advice
	Infections which lie dormant or are difficult to eradicate (e.g. Brucellosis, Lyme disease, Typhoid)	Seek expert microbiological advice	Seek expert microbiological advice	Seek expert microbiological advice
Transmissible spongiform encephalopathies (8)(9)	Definite diagnosis or high suspicion of any TSE	Contraindication to donation	Contraindication to donation	Contraindication to donation
	Identified risk factors for classic CJD (see annex 2)	Contraindication to donation except in life saving situations after full discussion with organ recipient or those close to the patient	Contraindication to donation	Contraindication to donation except in life saving situations after full discussion with bone marrow recipient or those close to the patient

Notes to table 5:

- (1) In most circumstances, cells will not be retrieved from an unwell donor.
- (2) The aetiology of fatal viral encephalitis is often difficult to establish. Herpes encephalitis can be treated and the likelihood of disseminated infection in the donor is small. If there is any possibility of acquisition of infection abroad the donation is contraindicated as rabies or other exotic infections cannot be ruled out.
- (3) Positive aerobic or anaerobic cultures of cord blood are generally due to bacterial contamination rather than bacteraemia in the donor infant. Culture and sensitivity to antibiotics should be provided to the transplant centre at the time of selection of the cord blood for transplantation.
- (4) An abscess caused by local spread may have no impact at all on a specific distant organ and in these circumstances the recipient will not require antibiotics specifically for this. Transmission of infection is unlikely after drainage of the abscess and adequate antimicrobial chemotherapy in the donor. However abscesses caused by certain organisms such as staphylococci and streptococci are more likely to spread to distant organs where they may cause infection if these are transplanted.
- (5) Colonisation with resistant bacteria is only of concern if the bacteria are resistant to any antibiotic prophylaxis used in the recipient. Colonisation at sites distant to the organs or tissues transplanted is not normally a risk.
- (6) Afebrile patients with a travel history to a malarious area can be accepted as donors. Febrile patients with a travel history require a malarial film to be taken before donation. If the donor was born or lived in a malarious area for more than 3 months at any time of life, a validated anti-malarial antibody test should be carried out. Donation may proceed pending the results; if the results are positive the recipient will require anti-malarial treatment.
- (7) In very special circumstances, eg the donor is the only match for a bone marrow transplant, expert advice should be sought to inform a risk assessment. Clinicians caring for recipients should be advised of the potential risk of contracting malaria and consider the diagnosis if the recipient subsequently becomes ill with pyrexia.
- (8) See Health Service Circular 1999/178 on Variant Creutzfeldt-Jakob Disease (vCJD): minimising the risk of transmission. Currently there are no agreed means for identifying risk factors for variant CJD and the population prevalence is unknown. There is currently no effective screening test. For this reason donors with neurological disease of unknown aetiology cannot be accepted. For life saving

organ and bone marrow transplantation only, donor exposure to risk factors for classic CJD (see annex 2) should be taken into account in the risk assessment but does not preclude donation.

(9) Donor deferral and CJD

Issues around the potential for passing on transmissible spongiform encephalopathies and the deferral of donors are complex. For classic CJD, transmission by corneal grafts, dura mater grafts and human pituitary-derived growth hormone and gonadotrophin is well documented and a donor's exposure to these should be taken into account when assessing their suitability for donation. There is no good evidence of transmission by organs or tissues other than those of the central nervous system. There are to date no reports of variant CJD being transmitted by any form of transplant. There is currently no agreed means of identifying risk factors or testing potential donors to exclude those at risk of developing variant CJD. This situation is being kept under review and further expert guidance may be expected (see annex 2).

Retrieval of material for testing

Heart beating donors and non-heartbeating donors

Blood samples are taken in the normal way as for living donors.

Cadaveric tissue donors

Cadaver blood sampling and tissue retrieval many hours post circulatory arrest should be undertaken by trained staff in order to maximise the quality of the material retrieved. Where ante-mortem blood samples taken for other purposes exist, these samples (taken up to seven days preceding death) are usually preferable to post mortem samples for testing.

Appropriate systems should be in place to make sure samples can be identified and stored in optimum conditions. Where no ante-mortem sample is available, a post mortem sample can be used, provided samples for testing are taken as soon as possible and preferably within 24 hours of circulatory arrest. The sample should be inspected before testing to assess the degree of haemolysis. The site from which the sample was obtained and the time of sampling should be documented in the donor's file. Preferred sites for taking samples include cardiac or subclavian puncture and femoral vessel puncture. It is essential to avoid sites close to intravenous lines.

Living donors

A sample taken up to 30 days before donation, or up to 7 days after donation, is considered to meet the requirements for testing as long as the donor's risk status has not changed in the time between the sample being taken and the donation of tissues or cells.

Donors under 18 months or breastfed children

When assessing infection status in a dead donor less than 18 months of age, and older children who have been breastfed within 12 months of donation, nucleic acid testing should be carried out on the infant's specimen, as well as an antibody assessment. This will avoid the need for a blood sample from the mother. However, any behavioural risk of the mother should still be assessed.

Validity of samples for testing

Validating testing

The principles for finding out the infection status of donors of organs, tissues and cells are based on the principles that have been established for donated blood. The tests used should meet the same standards of accuracy and timeliness as the screening of blood donors. Full quality assurance procedures should be in place for all tests in routine use. All blood samples taken for testing must be accurately identified and labelled, with records kept so there is always a link between a donor and the sample.

Nucleic acid tests are becoming more widely available but need to be validated and quality assured for use in transplantation.

Testing blood from cadaveric tissue and non-heartbeating donors

As time passes after a donor's heart stops beating it becomes more difficult to test samples taken from that donor, as the blood has often deteriorated. These samples may give false positive reactions in serological tests. Inhibitors to nucleic acid tests may also be present in cadaver samples, giving false negative results. So blood samples should be taken as close as possible to the donor's death and preferably within 24 hours following circulatory arrest. When tests have been validated for use with cadaver blood samples these should be used, provided they are of acceptable sensitivity as well as specificity.

Plasma dilution

If a donor is known to have had significant blood loss and received blood, colloids or crystalloid, a sample taken before the transfusion or infusion (and up to 7 days before the donation) should be tested in parallel where available. A calculation of plasma dilution can be made as part of the risk assessment. The US Food and Drug Administration has published detailed guidelines (see supporting literature). An algorithm that may be used is given in annex 3. However, further research is needed in this area to assess the significance for microbiological testing in the light of the sensitivity of current tests.

Interpreting test results

The test result finally issued by a laboratory should be positive or negative. Reactivity in the initial test should only be reported as positive after interpretation, for which further tests may need to be carried out.

Initial reactive results

When an initial test is reactive, if there is time, a repeat test should be carried out on the same sample before the results are released. An alternative test of equal or greater sensitivity should also be carried out. Tables 3 and 4 in this guidance set out recommended action when an initial reactive result is reported for urgent organ transplantation. Although the time available for testing organ donors is always limited, all testing laboratories should make provision for urgent confirmatory tests as well as urgent initial tests.

Repeat reactive test results

A repeat reactive test result may not exclude a donated organ or cells for a life-saving transplant. In the case of tissues, a repeat reactive test should normally exclude the use of the material.

For every sample which is weakly reactive at the initial test, a repeat test should be carried out on the same sample using the same kit, as well as a second test of equal or greater sensitivity than the first. The best possible history should also be gathered about the donor. If only weak reactivity from one testing kit is present, no risk factors have been identified, and the other kit test is negative, the donation could still be used, providing expert microbiological advice and an assessment of the risks of not giving the transplant make the donation the best option for that patient.

Where organs, tissues or cells from one donor have been sent to other banks or centres, these banks or centres should be told about repeat reactive results. This is to prevent unsuitable tissues being transplanted, as it often takes a considerable time to get confirmed results.

Positive results

Positive results should be notified urgently to the source bank, donor co-ordinator or supplier of the organ, tissue or cells so that clinicians in all centres that have received organs, tissues or cells from the same donor can be informed and take appropriate action. Clinicians at a local level can also consider the need to speak to close contacts of the donor. However, passing on any positive result of this kind to contacts of the donor is a breach of confidence and the decision to give this information can only be made by the transplanting physician or surgeon or tissue bank physician, taking into account the relevance to the health of those contacts (see supporting literature).

Divergent results

Donors' specimens have often been tested for microbiological markers at more than one centre, and by more than one test, by the time the decision on their suitability has to be made. If the results differ the matter must be resolved in discussion with the consultant microbiologists concerned, with a final decision being taken by the transplanting surgeon, or the medical director of the tissue bank. While it may be cautious to accept the worst result and reject the donation, false positive results may occur due to a poor quality sample and an earlier sample may have given a more accurate (and negative) result.

Accreditation of testing laboratories

Microbiological tests for donation and transplantation should be carried out only in laboratories accredited by Clinical Pathology Accreditation (UK) Ltd (or equivalent) for performing those tests.

Acceptance of donation

Organs, tissues and cells must be donated freely and without reward and should go to the patients with the greatest need. It is not acceptable to attach any conditions (not just those of a racist kind) to a donation. Organs, tissues and cells cannot be accepted if donors or their relatives insist on such conditions.

Organs

The retrieving surgeon should review the suitability of the donor and be satisfied that all donation criteria are met. That surgeon should review the risk of infection (in consultation with a consultant microbiologist when circumstances are unusual). This will involve reviewing the donor's medical notes and, if necessary, discussing the matter with the donor co-ordinator if there are any areas of difficulty. If further contact with the donor's family is necessary this contact should be made through the donor co-ordinator as he or she will usually have interviewed the family before. If further details about the donor are needed, the GP or the clinician caring for the donor immediately before the donation should be contacted.

The retrieving surgeon is responsible for making sure all information that could possibly rule out the use of organs is passed to the surgeon performing the transplant. The retrieving surgeon will sign the relevant donation form to confirm absence of contra-indications to donation.

Tissues and cells

For tissue and cell donations, all clinical information relevant to the donation and the suitability of the donor should be reviewed by the medical director of the tissue bank, cord blood bank, bone marrow registry or cell culture facility. Acceptance may be provisional pending further testing of the donor.

For banked tissues, there needs to be a distinct clearance procedure which allows tissue to be moved from quarantine to a separate freezer from which material can be issued when a set of criteria has been met. These criteria relate not only to the donor, but also to the various microbiological and quality assurance checks that have taken place since the donation was released for processing.

Responsibilities for minimising transmission of infection before transplantation

Under arrangements for clinical governance and risk management, chief executives of hospital trusts are responsible for ensuring systems are in place to confirm the quality and safety of organ, tissue and cell donations and transplants. Chief executives need to make sure there are appropriately trained and experienced staff responsible for the safety and quality of any tissue and cell bank activities within their organisation (including the availability of appropriate microbiological advice). As organ donor testing is often out-of-hours, there should be an adequate level of staff and equipment for testing, and secure protocols for recording results given by phone.

Organs

The surgeon performing the transplant should make sure the patient receiving the organ (or the person with parental responsibility for the patient) knows about any special risk of infection involved in the particular transplant procedure and gives their valid consent to the operation.

The surgeon performing the transplant should review the relevant donor form and, if necessary, contact the donor co-ordinator to obtain any further information and test results, in line with the recommendations in tables 3, 4 and 5 of this guidance and annex 2. **The surgeon performing the transplant is ultimately responsible for deciding on the quality of the transplanted organ and its suitability for a particular patient.**

The surgeon performing the transplant should consider the following when assessing microbiological suitability in the light of the risk of infection, seeking specialist microbiological advice if there is any uncertainty.

- The risk of the donor having an infection, based on the history and microbiological testing.
- The risk of infection being passed on in the transplanted organ.
- The incubation period and likely severity of the infection.
- The ease of treating an infection if the organ were transplanted, taking account of the level of immunosuppression the transplant patient would receive.
- The risk that the transplant patient would suffer significant disease or death if the transplant were not performed.

Tissues

The following activities should be carried out in line with written procedures approved by a consultant microbiologist.

- Making sure the donor did not object to donation (or getting valid consent in the case of living donors).
- Screening donor selection information (including donor history) and maintaining donor records.
- Collecting and testing blood samples.
- Collecting tissue.
- Transferring the tissue to the tissue bank or transplant centre in a secure and microbiologically safe way.
- Making quarantine arrangements.
- Processing, storing and releasing tissues.
- Maintaining archives of blood samples for microbiological testing.

The medical director of the tissue bank (taking appropriate microbiological advice) is ultimately responsible for the microbiological safety of the tissues in the tissue bank. Once the tissue has left the bank, the surgeon performing the transplant must be satisfied that the tissue is microbiologically safe.

Cells

The clinician caring for the patient receiving transplanted cells from a related donor should make sure procedures are in place to protect the health and safety of the patient. For related donors of cells, responsibility for assessing the fitness and safety to donate rests with a clinician not responsible for the care of the patient receiving the transplant. For unrelated donors, the medical director of the cord blood bank, tissue bank or bone-marrow registry is responsible for the donor's health and safety.

Special considerations

Organ recipients as simultaneous donors of organs

Domino donors are patients who receive a heart-lung transplant and then donate their heart to another patient. An assessment of any infection risk needs to be carried out and, whenever possible, domino donors should be tested in the same way as other donors. If this is not possible, those patients awaiting transplantation who are likely to be domino donors should be re-tested at least every 3 months so a valid assessment of any risk can be carried out at the time of the transplantation.

Organ recipients as non-simultaneous donors of organs

Some people who have received an organ transplant in the past may want to become an organ donor after their death. In this situation there are concerns about the validity of HCV antibody tests due to immunosuppression of the donor at the time they acquired their infection, as 60% of such patients do not produce antibody. These donors, if antibody negative, should undergo nucleic acid testing or the recently described HCV antigen test. Careful attention should be paid to the risk assessment for transmitting infection.

Organ recipients as donors of tissues

Patients who have received an organ transplant may be suitable as tissue donors as long as a nucleic acid test (or the recently described HCV antigen test) confirms their Hepatitis C status is negative. Organ transplant patients who die in the period immediately after the operation may still have valid microbiological markers but may not be suitable for donation because of significant plasma dilution at the time of the organ transplant.

If a patient receiving a heart or heart-lung transplant donates heart valves from their own heart and is alive after 180 days, they should be re-tested for the relevant organisms (see table 3). The heart valves from these donors should be quarantined until the results of the re-test are available. However, as the donor's immune responses will be suppressed at the time of re-sampling, nucleic acid tests for Hepatitis C virus (or the recently described HCV antigen test) should supplement antibody tests. Nucleic acid tests should also be considered for Hepatitis B and HIV. Expert advice should be sought when interpreting results.

Tissue and cell recipients as donors of organs/tissues

Patients who have received tissue and cell transplants can act as donors as long as they are not immunosuppressed. The exceptions to this are patients who have received dura mater or ocular tissue (cornea, sclera, stem cells), in which cases donation is **never** allowed. Where allowed, donation may be considered from 180 days after the transplant.

Autologous transplants

If the material to be transplanted has been stored or cultured in a laboratory, the patient should undergo tests as for an allogeneic donor. This is to rule out any risk of infection arising from contamination during culture or storage or identification error on issue. **If materials are used immediately after being taken and are not stored, there is no need for testing.**

Others

Cases where patients receive novel therapies (such as gene therapy which uses viral vectors) will need to be considered individually, taking account of expert advice. Patients who have received gene therapy are not suitable as donors for at least 3 months following completion of therapy.

Donations sent between countries

Organs, tissues and cells donated abroad should be transplanted according to the principles set out in this document. Centres receiving transplant material should have a designated person responsible for making sure this guidance is followed.

Organ donations from abroad may be accompanied by information about screening tests already carried out on the donors. Sometimes they are accompanied by a blood sample. Repeat screening tests may be needed if time and circumstances allows this, especially if any accompanying records are poor or they are not consistent with UK standards. However the quality of the accompanying blood samples, and whether there has been plasma dilution, may not be known. By the same token, donations sent abroad should be accompanied by good records and by samples that would allow further screening tests to be done. The surgeon performing the transplant should get expert microbiological advice where appropriate to make sure that a risk assessment on the quality of the donation, and the quality of the information available on that donation, is carried out.

In the case of tissues from abroad, the tissue bank accepting the donation must make sure this guidance has been followed by the tissue bank that sent the tissue to the UK. To do this, the medical director of the tissue bank in the UK, together with the manager responsible for quality, should review information on the policies and procedures in place at the other tissue bank. For imported tissues that do not pass through a UK tissue bank (for example corneas), the surgeon performing the transplant is responsible for making sure this guidance has been followed.

Cell grafts from abroad may have the necessary samples taken before the actual donation arrives, or the appropriate tests may be asked for before the graft is selected. In these circumstances only the appropriate documents need to accompany the graft. However, the graft needs to be handled appropriately by airport authorities. To make sure this happens, the graft should be accompanied by a trained person or handled by a specialist company. The physician performing the transplant should assess the safety of any cell graft from abroad.

Environmental safety in gathering and processing material for transplanting

Organs should be removed in a sterile setting as for any operative procedure. Professional guidelines are available (see supporting literature). Standard operating procedures, drawn up with appropriate expert microbiological advice, are needed to cover these processes.

Tissues and cells may have to be recovered in less satisfactory conditions. There is clear guidance about the environmental conditions needed for processing or culture of material for transplantation (see supporting literature). Staff should be trained to maximise the quantity and quality of the material removed using sterile techniques, equipment and instruments and cleansing the skin of donors. For cadaveric tissues, bacterial decontamination after the material is gathered is desirable.

If any processing is carried out on organs (including bench surgery, perfusion or preparation for transplantation without further decontamination) it is important that the risk of contamination from processing agents or the environment is minimised.

Expert microbiological advice should be sought for environmental monitoring, tissue processing and process control of any tissue or cell bank.

Transport, processing, preservation and storage

Organs

Organs are normally kept cold in sterile conditions while being transported to the transplant patient. The organ container must be sturdy and protect any packing materials used. Non-disposable packaging (such as organ boxes) should be appropriately cleaned. Packaging should allow sterile handling by transplanting staff, which usually means double wrapping with a sterile inner container or bag. This packaging should not be disturbed until the organ has reached its destination and can be opened in an operating theatre.

Tissues

There are general guidelines covering the gathering, processing, preservation and storage of tissues (see supporting literature). The evidence base for standards in this area should be reviewed.

Cells

Standards for processing, collecting and transplanting cells from blood and bone marrow have been published (see supporting literature). Good practice includes:

- Testing all donations;
- Removing units from donors who test positive as soon as the results are available;
- Maintaining a list of units, with clear identification and location details;
- Cleaning tanks after removing contaminated units and removing and replacing the outer bags of remaining units.

Wherever possible, the results of microbiological testing should be known before the units are frozen. Any donations that are stored should be securely double bagged.

Material from autologous donors should be stored in a separate tank if any test has had a positive result. In some circumstances test results may not be available before the cells are cryopreserved and stored. In these cases the material should be quarantined in a separate storage tank until test results are available, at which time the material may be transferred to the main store (as long as test results are negative).

Quarantine

If tissue has been taken from a living donor and is to be banked, the material should be quarantined and the donor re-tested for the required markers after 180 days. This is in line with current UK and European guidance.

Two samples from each living donor must be tested. The first sample should be collected as close to the donation as possible, and no more than 30 days before or 7 days after the donation. The second sample is taken at least 180 days after the donation.

In exceptional circumstances where no sample from the time of donation is available from a living donor, the 180 day sample can be tested and the donation used if the result is negative for antiHBc and the required microbiological markers (table 3). A first sample is still desirable to avoid the storage of infected material.

When a donation is gathered from a living donor and the 180 day sample cannot be taken, nucleic acid tests may be used on the first sample. The tissue can be used if all other criteria for accepting the donation are met. Before any approach to abandon quarantine can be considered, further work is needed to check the validity of one stage nucleic acid testing.

Archives for testing

Appropriate archives of serum and other material should be maintained for microbiological testing. Reasons for this approach include the emergence of new pathogens, the development of new tests and changes in donor selection criteria. Maintaining the potential for retesting will prevent donated tissue and cells being discarded because the risk of infection would not otherwise be able to be reassessed.

In the case of cord blood banks, there should be a written policy for retesting the relevant microbiological markers before issuing a cord blood unit. This should be done by resampling the mother at least 180 days after delivery or by performing nucleic acid testing on the mother's original sample and the cord blood unit. Further testing for extra infections, for example HTLV, may be carried out at that time (depending upon the special needs of the transplant centre).

Review prior to release

There should be a clearly defined procedure for approving release from the tissue bank or cord blood bank. Only those materials gathered, processed and stored in line with acceptable standards and validated standard operating procedures should be assessed as being safe to use. That assessment must include a review of all donor records, processing and storage records and post-processing quality control test results. The acceptance of a bone marrow donor for cell retrieval should also have all the donor's records reviewed by the donor centre or the physician carrying out the medical assessment of the donor.

Discard policy

There should be written procedures for discarding organs, tissues and cells unsuitable for clinical use. Records should include the date and method of discard and the reason for it. Material to be discarded should be handled appropriately and disposed of in a dignified way which takes account of any wishes of the donor or their relatives, but is also consistent with guidelines for the disposal of clinical waste (see supporting literature). The discarded material can only be made available for research if there is appropriate prior consent.

If the discarded material is believed to be infected an appropriate risk assessment should be made for staff working with the material. Appropriate arrangements should be made for immunising the staff or giving them prophylactic treatment where appropriate.

Recipient risk assessment

Although transplant patients should ideally be free from infection at the time of their transplant, it may be impossible to eradicate infection before the operation. Examples include infection in a potential bone marrow transplant patient and sepsis confined to the organ (such as a lung or liver) to be removed. Chronic infection may be the cause of the organ failure and it may be impossible to eradicate these infections (for example Hepatitis C). This may alter the risk assessment for a particular combination of donor and transplant patient. Any known infection in the transplant patient should be recorded. In such cases the clinician caring for the patient is responsible for making sure that placing them on the active transplant list is in their best interests. Where a clinician decides to use an organ which may pose a risk to the patient, the decision and reasons for the decision should be clearly recorded.

Acceptance for transplant

With organs, the surgeon performing the transplant has final responsibility for making sure the minimum amount of risk is attached to the transplantation process. It is their responsibility to check that all the necessary tests have been performed and to address any problems that are identified, by arranging for tests to be performed before the transplant.

For banked tissues or cord blood the responsibility for ensuring safety lies with the designated registered medical practitioner at the bank. But the clinician performing the transplant is responsible for making sure tissues that have not passed through a tissue bank are microbiologically safe. That clinician should have sufficient evidence to be satisfied that all appropriate tests and checks have been carried out. The clinician performing the transplant carries ultimate responsibility for ensuring the least risk is attached to the transplant process.

In the case of unrelated bone marrow transplants or unrelated cord blood transplants the responsibility rests with the clinician performing the transplant.

Recipient follow-up: information needed to trace patients and manage poor outcomes

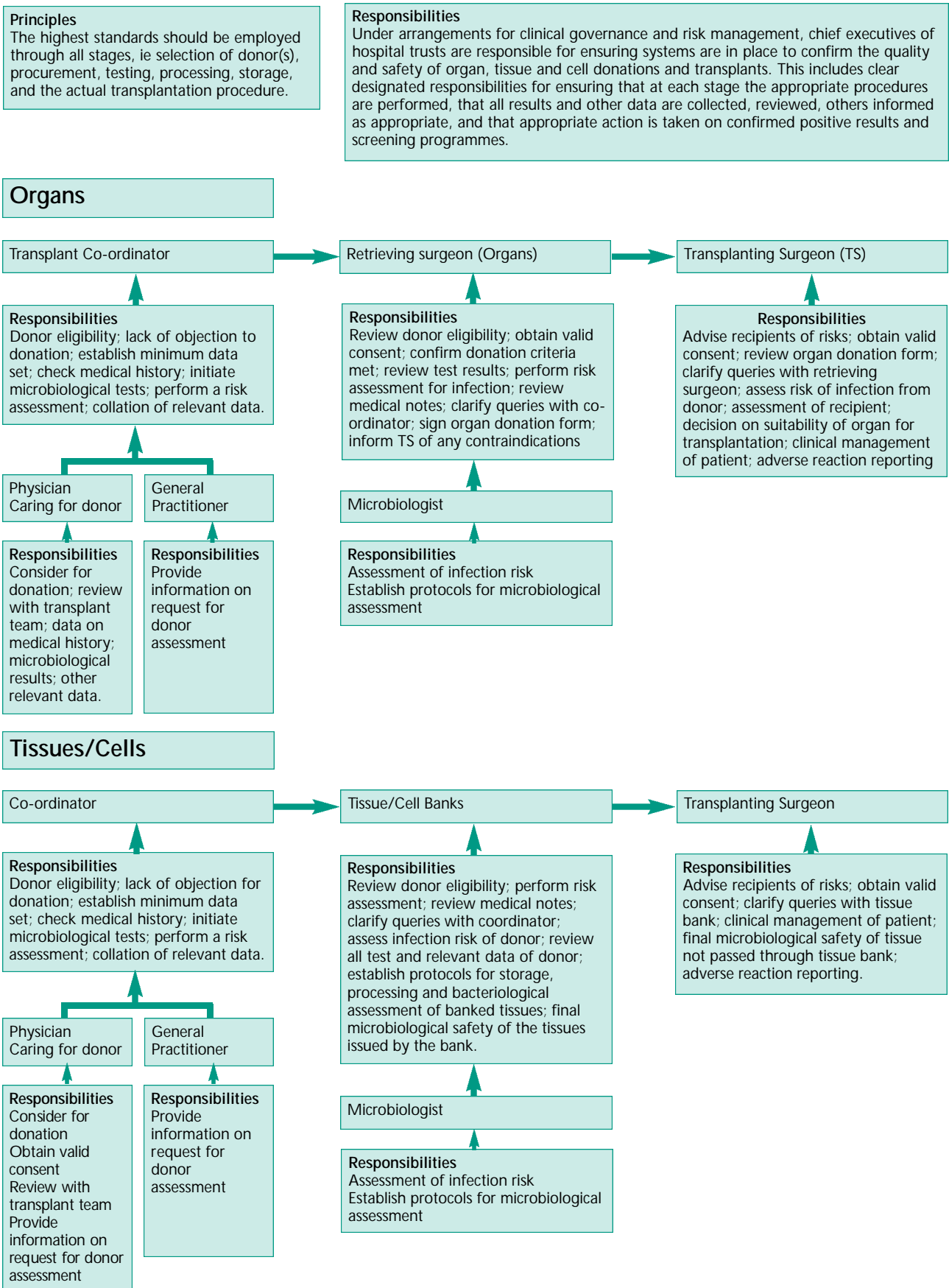
Procedures should be in place to maintain a link between transplant patients and donors, so that, in the event of an adverse reaction, any patient who received the organs, tissues or cells from the same donor can be identified. This is also relevant to late reports of information on donors, where tissues have been issued or transplanted before a risk has been identified. **Clinicians should give appropriate information to transplant patients if this is relevant to their health or wellbeing.**

In respect of certain organs (kidney, heart, lung, pancreas, liver) the surgeons retrieving and transplanting those organs must send detailed notification forms to UK Transplant.

Department of Health guidance states that donor records should be kept for at least 11 years after any transplant. The equivalent Scottish guidance gives a minimum retention period of 6 years from the date of the last recorded entry, or three years after death (see supporting literature).

Any infection which may have come from a donor or been transmitted at the time of a transplant should be reported to the donor co-ordinator or tissue bank. The donor co-ordinator should tell UK Transplant about untoward events in transplant patients. UK Transplant is responsible for informing medical staff in charge of patients receiving all other organs. For tissues and cells, relevant information should be passed by the medical director of the tissue bank, cord blood bank or bone marrow registry to the clinicians responsible for the patients receiving any other organs, tissues or cells from the same donor. They should also inform any tissue bank still holding tissues from the donor and, where appropriate, relatives or close contacts of the donor. Records of the source of a donation, but no details which would identify the donor, should also be kept in the transplant patients hospital notes.

ANNEX 1 Key responsibilities from procurement to transplantation



ANNEX 2 Information requirements for assessing donor infection risks

This data set is recommended as the basis for developing a nationally standardised donor assessment questionnaire. Further work (outside the remit of this guidance) will need to be carried out. This work should involve microbiologists, donor co-ordinators, transplant medical staff and tissue bank directors.

Recommended data set	Reason for asking the question – further information required
Did the donor have a current acute infection (bacterial or otherwise)?	
Was there a clinical, diagnosis of infection in the donor, whether or not supported by microbiology?	Some infections (for example partially treated meningococcal sepsis) may not be supported by culture data. Any microbiological culture may have been from a distant site (for example faecal culture for <i>Salmonella typhi</i>). Successful antibiotic treatment may make donation acceptable. Focal residual infection (for example after ventilator support) may be acceptable for tissue donation.
Was an organism detected in the last 7 days, from blood, cerebro-spinal fluid or a local site related to transplant (for example urine for kidney, airways for lung)? If so, when and what antibiotics were effective against it?	The person receiving the transplant may need antibiotic prophylaxis to take account of this. Specific information about the organism may be relevant to specific donations (for example, active herpes simplex in lung donors), although most bacterial colonisation and infection (for example MRSA) can be covered by appropriate changes in antibiotic prophylaxis and do not prevent donation if expert advice is taken.
What antibiotics had the donor received (dose and from when to when)?	Was treatment adequate or should recipient prophylaxis be modified?
Did the donor have an incubating infection which might transmit to the recipient in a window period before serological tests are positive?	
Is there any history of recent behaviour that might increase the risk of HIV infection, syphilis, or blood borne viruses (Hepatitis B, Hepatitis C) within the last six months?	<p>Most tattoo artists and ear or body piercers work to high standards, but not all do. Tattoos or any piercing do not make a donor unacceptable if they were present more than six months before the donation. Signs of scarification, branding or self-mutilation may indicate a risk of virus transmission.</p> <p>A history of hepatitis or jaundice in childhood is usually caused by Hepatitis A, and jaundice at any age can have other non-infectious causes. If there is an alternative diagnosis or jaundice occurred more than six months ago donation is possible as long as tests for Hepatitis B and Hepatitis C are negative.</p>

Recommended data set	Reason for asking the question – further information required
	<p>The following information should be gained from living donors or, for dead donors or living donors not capable of discussing these matters, from their most relevant life partner or close family member.</p> <ul style="list-style-type: none"> - Is the donor or their partner known to have HIV, Hepatitis B or Hepatitis C ? - For men, has the donor ever had sex with another man? - Has the donor ever received money or drugs in payment for sex? - Has the donor ever injected or snorted drugs, even once? <p>In the last 12 months, has the donor had sex with:</p> <ul style="list-style-type: none"> - someone who is, or may be, HIV positive? - a man who has had sex with another man (if the donor is female)? - a person who receives money or drugs in payment for sex? - anyone who has ever injected or snorted drugs? - anyone who has been sexually active in parts of the world where the main route of HIV infection is heterosexual sex? (This currently applies to all countries in Africa except Morocco, Algeria, Tunisia, Libya and Egypt.)
<p>Could the donor have been at risk of incubating a transmissible infection (for example transmissible spongiform encephalopathy) for which there is no microbiological test or serological test?</p>	
<p>Is there any family history of CJD, vCJD or Gerstmann-Straussler-Schienker disease?</p>	<p>15% of CJD cases have a genetic link to family members. Donations cannot be accepted if there is a family history.</p>
<p>Is there any history of the donor receiving human pituitary-derived growth hormone or gonadotrophin before 1989?</p>	<p>Some batches of human pituitary-derived hormone came from cadaveric pituitary glands of people who may have died of classic CJD. So potential donors who have received these hormones could transmit CJD.</p>
<p>Has the potential donor received an ocular tissue transplant (cornea, sclera, ocular stem cells)?</p>	<p>There is an increased risk of disease being passed from a donor who received a corneal transplant, with documented cases of CJD being transmitted. A donor who has received an ocular tissue graft cannot donate ocular tissue.</p>

Recommended data set	Reason for asking the question – further information required
Has the donor had neurosurgery or operations for a tumour or cyst of the spine or implantation of dura mater, before August 1992?	Brain surgery often involves repairing the dura mater, and before August 1992 cadaveric dura mater was commonly used. This has occasionally transmitted CJD. After August 1992 this material was not used. Spinal fusion operations and drilling burr holes did not usually involve using dura mater.
Has the donor any history of neurodegenerative disease of unknown aetiology?	Donations can never be accepted from a donor with a degenerative neurological disease of unknown aetiology.
Has the donor any history of disease of unknown aetiology, for example multiple sclerosis, Parkinson's disease, sarcoidosis and Crohn's disease?	Unknown infectious agents may be involved in causing of some of these diseases.
Does the donor have any history of encephalitis which might be part of a systemic infection? If so, is there any history of travel and animal bites received overseas in the last 6 to 12 months?	<ul style="list-style-type: none"> • Rabies – apathetic rabies may be overlooked. • Herpes simplex – not usually a generalised infection except in children. • Unknown virus – further enquiry or diagnostic measures may be needed.
Did the donor have a past history of an infection which might transmit to and reactivate in the recipient?	
Has the donor travelled overseas in the last few months? If so, did he or she have malaria? Was the donor born, or did he or she live for more than 3 months, in a malaria endemic area?	Malaria can be transmitted by blood and viable organs, tissues and cells. The donor may not be symptomatic at the time of donation, but may still be infectious. Information about the donor's travel and residence history will enable the donor to be assessed.
Has the donor lived overseas, outside Western Europe, at any time and is he or she consequently at risk of any endemic infection? Was the donor known to have had an infection while overseas?	<p>Consider the following infections:</p> <ul style="list-style-type: none"> • Malaria - Africa, Asia, South America • Chagas disease, trypanosomiasis – South and Central America, Mexico • Endemic mycoses: <ul style="list-style-type: none"> - histoplasmosis, blastomycosis – Mississippi valley, South America, Africa, West Indies - coccidioidomycosis – California, Texas, Central and South America • Hepatobiliary typhoid carriage, melioidosis – SE Asia. • HTLV 1 – Japan, Caribbean
Has the donor had Lyme disease (Borrelia), brucellosis, or tuberculosis?	
Has the patient been tested for Toxoplasma gondii (toxoplasmosis)?	Check the result of any serological test
Has the patient been tested for cytomegalovirus?	Check the result of any serological test

Recommended data set	Reason for asking the question – further information required
Did the donor have a recent infection which might transmit in the convalescent period?	
<p>Has the donor had any recent viral infection or rash? If so, the rash should be described, including its distribution and nature (for example, whether there were vesicles, a slapped cheek distribution or a diffuse rash).</p>	<p>These rashes may indicate the following infections and be a reason for further investigation:</p> <ul style="list-style-type: none"> • Chickenpox or shingles (Varicella zoster) – patients with localised shingles are unlikely to transmit infection. Antiviral prophylaxis of the recipient may be considered in recovering generalised varicella. • Measles – the presence of a rash confirmed as caused by measles is normally evidence of the development of immunity to the infection. • Epstein Barr virus – causes glandular fever but can also cause infection and lymphoproliferative disorders in paediatric patients who have not previously been infected. • Human Parvovirus B19 – causes marrow hypoplasia and chronic infection in the immunosuppressed and those with sickle cell genes. • Adenovirus – causes systemic infection in the immunosuppressed • Enterovirus – causes systemic infection in the immunosuppressed

ANNEX 3 Calculation of plasma dilution

To be used in cases of significant blood loss*.

CRYSTALLOID INFUSED

INTERVAL PRIOR TO SAMPLING	VOLUME INFUSED (ml)	% RETAINED	VOLUME RETAINED (ml)
>24 Hours		0	None
2-24 Hours		25	
1-2 Hours		50	
<1 Hour		75	
TOTAL CRYSTALLOID RETAINED:			

BLOOD/COLLOID INFUSED

INTERVAL PRIOR TO SAMPLING	VOLUME INFUSED (ml)	% RETAINED	VOLUME RETAINED (ml)
24-48 Hours		100 (Blood) 50 (Colloid)	
0-24 Hours		100	
TOTAL BLOOD/COLLOID RETAINED:			

ESTIMATED TOTAL BLOOD VOLUME:	% HAEMODILUTION
70mls per kilogram of body weight*	<u>(Crystalloid retained + blood/colloid retained x 100 blood volume):</u>

ACCEPT (<50%)/REJECT (>50%)	
SIGNED:	DATE:
COMMENTS:.....	
.....	
.....	
.....	

*In patients receiving critical care, the circulating blood volume is typically 45 to 60 mls per kg body weight (compared to the normal 70 to 80 mls). The former figure should be used in such patients.

ANNEX 4 Overview of case reports of infections transmitted by transplantation

Infection	Bone	Cornea	Dura	Heart valve	Skin	Organ	Marrow
Bacteria including M. tuberculosis	+	+		+	+	+	
Hepatitis B	+	+ (2)		+	+	+	+
Hepatitis C	+				+	+	+
HIV 1	+			+	+	+	+
Herpes simplex		+				+	
CMV		+/- (1)			+	+	+
Epstein-Barr virus						+	+
Parvovirus B19							+
Rabies		+					
Toxoplasma						+	+
Malaria						+	+
Fungus		+		+		+	
CJD		+	+				

Derived from: Eastlund T. Infectious disease transmission through cell, tissue, and organ transplantation: reducing the risk through donor selection. *Cell Transplantation* 1995;4v:455-77.

(1) Holland et al. *Am J Ophthalmol* 1988; 105: 357-60.

(2) Hoft et al. *Cornea* 1997; 16: 132-7

ANNEX 5 Supporting Literature

Advisory Committee on Dangerous Pathogens, Spongiform Encephalopathy Advisory Committee (SEAC)

Transmissible spongiform encephalopathy agents: safe working and the prevention of infection

1998

British Association for Tissue Banking

- General Standards for Tissue Banking
- Technical Guidelines for Donor Selection
- Technical Guidelines for Cardiovascular Tissue Banking
- Technical Guidelines for Processing of Tissues
- Aseptically, or with Terminal Sterilization
- Technical Guidelines for Skeletal Tissue Banking
- Technical guidelines for Skin Banking

September 1999

British Transplantation Society

Towards standards for organ and tissue transplantation in the UK

November 1998

Council of Europe

- Group of Specialists on Quality Assurance for Organs, Tissues and Cells (SP-S-QA)
Safety and Quality Assurance for Organs and Tissues
May 1999
- International consensus document standardization of organ donor screening to prevent transmission of neoplastic disease.
Transplant Newsletter June 1997;2i:4-10

Department of Health

- Guidance notes on the processing, storage and issue of bone marrow and blood stem cells.
1997
- A strategic guide to clinical waste management for General Managers and Chief Executives
Estate Executive Letter EEL (94)1
- Safe disposal of clinical waste – whole hospital policy
Estates Policy Letter EPL (95)13

- A Code of Practice for the Diagnosis of Brain Stem Death
Health Service Circular HSC 1998/999
- Variant Creutzfeld-Jakob Disease (vCJD): minimising the risk of transmission
Health Service Circular HSC 1999/178
- Retention of Medical Records
Health Service Circular HSC 1999/051

Eastlund T.

Infectious disease transmission through cell, tissue, and organ transplantation: reducing the risk through donor selection.
Cell Transplantation 1995;4 no.5:455-77.

FDA guidance on calculation of plasmadilution

Federal Register Sept 30 1999 vol 64 no 189 page 52722-3

General Medical Council

- Serious Communicable Diseases
October 1997
- Seeking Patients' Consent: the Ethical Considerations
November 1998

Joint Accreditation Committee of the International Society for Hematotherapy and Graft Engineering (ISHAGE) - Europe and European Group for Bone Marrow Transplantation

Standards for blood and marrow progenitor cell processing, collection and transplantation
February 1998

Scottish Office

Management Executive Letter (1993)152
Guidance for the Retention and Destruction of Health Records

UK BTS/NIBSC

Guidelines for the blood transfusion services in the United Kingdom (Red Book).
Section 4 - Guidelines for tissue banking
Section 5 – Guidelines for HPC
2000

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