

Tissue Donor Screening

I CETEBIO Meeting Technical Studies in Multi-tissue Banks Fundação HEMOMINAS

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Introduction

Successful tissue donor screening involves the diligent collection of relevant information that's used to evaluate a potential donor's risk for transmitting disease and to assess the donor's history for conditions that could affect tissue quality and ultimately the outcome when used for transplantation. Donor eligibility screening is performed by review of past and current medical history, evaluation of risk associated with behavior, travel, and findings at physical examination of the potential donor. An analogy can be made to detective work performed by police investigators because it may be difficult when searching for resolution to suspicions encountered during assessment of risk and quality. It is our professional obligation to properly identify the potential tissue donor and to seek relevant information to sufficiently protect future allograft recipients as well as tissue bank staff who will handle the recovered tissues. In addition to preventing transmission of viral, bacterial, malignant, or prion-associated diseases, provision of tissue that possesses a quality that will be beneficial to recipients is also important and steps can be taken that offer controls. As information is gathered and created during donor screening, physical assessment, infectious disease testing, tissue recovery, and even processing, steps taken must be clearly documented in a donor record you create. This collection becomes the donor's "relevant medical records" for tissue donation. This set of records is ultimately reviewed by a responsible person (or persons) who determines the donor's suitability. This is additionally used with the technical review of processing and storage parameters that leads to assessing tissue allografts for suitability for release and distribution for transplantation. The donor screening process is extensive and necessary for the provision of safe tissues for transplant. Requirements regarding cell and tissue donor eligibility criteria may vary by country but should be used to establish a significant layer of safety. This document only considers donor screening recommendations for deceased tissue donation. Additional criteria specific to ocular donation is not specifically addressed but can be added.

Obtaining legal consent or authorization for tissue donation is not addressed in this document. Refer to your local laws or regulations for requirements. Pursuit of consent or authorization can occur before taking steps to screen the donor for eligibility, or consent/authorization can be pursued after initial screening steps have been taken and the donation generally appears acceptable. There are advantages and disadvantages when selecting either approach.

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Donor Referral and Initial Screening

The notification to a tissue bank that a death has occurred, or the “referral,” is often made by a telephone call, and this initiates the first step in donor screening. Basic information is collected to properly identify the deceased as well as the location of the body, and to obtain contact information for the person who is responsible for the body. To qualify the donor, specific information must be collected and this includes initial, useful information such as:

- Given name, family name, age, and sex
- Cause of death
- Known risk factors for disease (malignancy, HIV, viral hepatitis, etc.)
- Clinical information (from hospital or other records)
- Location of body “now” and the plan for moving the body
- Contact information, such as the telephone number for:
 - Family member(s) - also obtain their address (& mobile phone number)
 - Person in charge of body (hospital personnel or Funeral Home Director)

This information should be from a reliable source and can be collected by telephone or in person. A form created by the tissue bank’s management should require all this information be gathered and documented to show that a proper initial evaluation was performed. To accommodate the screening process, the tissue bank management must establish donor eligibility criteria in written policies and, beginning at this referral step, persons screening potential tissue donors must reference and use this information. Personnel handling referrals should be properly trained and competent so they collect pertinent, available information.

Current Clinical Information

As soon as possible, available records should be obtained, reviewed, and evaluated. Death can occur in a hospital or outside of the hospital setting, so the types of available records can vary. There may be few records or many records.

If the death occurred in a hospital or other healthcare facility, the following records may have been produced and, if so, should be obtained and reviewed:

- Admission date/time
 - Emergency room records; admission physical examination; emergency medical transport (ambulance) records, if applicable
- Progress notes
 - Physician’s orders/notes and nursing observations
- Laboratory testing
 - Results from testing performed by the following departments: microbiology, chemistry, hematology, virology, urinalysis, toxicology, or pathology.
- Miscellaneous records
 - Transfusion and infusion information

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- Collect information regarding product type, and dates/times administered (requires evaluation of blood sample to be used for infectious disease testing to ensure there is not sufficient plasma dilution that may affect test results - i.e., produce false negative test results) - refer to section on *Plasma Dilution Evaluation*
- X-rays (chest/thoracic, abdominal, limbs)
- Surgical
 - Look for additional transfusions and infusions if recent/relevant
 - Potential for biopsy to have been taken to evaluate suspicion of a disease
- Consultations
 - Psychiatry
 - Infectious disease
 - Neurological
 - Orthopedic
 - Oncology
 - Rheumatology
- Discharge/death record
 - See *Cause of Death* below
 - Look for evidence that an autopsy is planned (or not)

Direct communication with the potential donor's attending physician, or the medical staff caring for the patient, is encouraged and often proves valuable. Specific inquiries regarding their concern for the patient having an active infection or communicable disease should be made. An extensive hospital stay can increase risk for acquiring a serious infection during hospitalization. Patients experiencing prolonged ventilator assisted respiration should be evaluated for possible infection associated with that therapy and potential connection to the death event.

If the death occurred outside of a hospital or other healthcare facility, these records may have been produced and, if so, should be made available to you and be reviewed:

- Police records (drug abuse information?)
- Medical examiner or coroner records (drug abuse information, infection/malignancy concerns)
- Extended care facility (assisted living facility, retirement home, nursing home) records - contact caregivers, Director (infection/malignancy concerns)
- Funeral home records - contact Director

A thorough review of all available records is expected. If records are known to exist but are not readily available, they should, ideally, be found before tissue recovery begins but must be located and reviewed prior to release of tissue for transplantation.

All records of the donor that you review should be photocopied for inclusion in your tissue donor record. If this is not possible, relevant information from the records must be transferred and documented on forms that you create. Your forms must accurately and completely reflect relevant information you have gained from review of these records and from discussions with medical or other personnel. Transferring information from one

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form to another carries the risk of transcription or interpretation errors. These steps must be performed by well-trained, competent staff members from the tissue bank.

Cause of Death

The potential donor's cause of death (COD) is important and can indicate the donor has, or there is a suspicion of having, a transmissible disease or can point to other concerns regarding tissue quality or overwhelming contamination. If the COD is unknown, this is not acceptable for tissue donation because death may have been due to an active infection that could be transmissible. If the COD is related to an active systemic infection such as bacteremia, viremia, or sepsis, the patient cannot be accepted for tissue donation. If the clinical history leading up to the COD includes meningitis or encephalitis, the etiology must be determined and is unacceptable if due to an infectious agent. If the etiology cannot be established, the donor is not suitable. Communication with the physician or medical staff caring for the patient is desired if you have any questions regarding the patient's clinical history (the events leading to death).

You should consider the risk that may be associated with certain causes of death. For example, if the patient overdosed on non-prescribed drugs, this can increase risk for an infectious disease due to associated behavior. However, this risk should be evaluated on a case-by-case basis and can be resolved with good information. If ingestion or exposure to toxic substances caused death, or if death was due to a high voltage electrocution, these circumstances can affect the quality of some tissue types and may cause harm to recipients if used for transplant. The COD also may indicate that massive trauma is present that may preclude recovery of tissue. For example, crushing injuries to the abdomen or limbs, a fall from a great height, or massive internal and/or external trauma from being struck by a vehicle may preclude the ability to provide safe tissues due to overwhelming contamination. A death due to drowning requires scrutiny (type of water, how long submerged, was it witnessed, time of year/temperature) due to high potential for contamination by water-borne microorganisms. Visual examination of the body by tissue bank staff may be necessary during initial screening if adequate information regarding the condition of the body cannot be obtained verbally.

Time of Death, Body Cooling, and Limits for Tissue Recovery

If there is any question regarding when (date and time) the prospective donor died, this must be evaluated for acceptability. Policies must be established that describe determination of "asystole" that offers guidelines for expectations and limitations regarding how long after death is an acceptable time frame for tissue recovery to occur. Time limits may be based on the type of tissue, how the tissue will be used (its utility), and maintenance of cell viability or other claims or expectations related to tissue preservation. Imposing time limitations can also be related to a desire that funeral arrangements or religious activities should not be delayed. Many factors can affect decomposition of the body after death (putrefaction), and this may be slowed by placing the body in a cool or refrigerated environment. Contamination can spread post mortem between body cavities (e.g., normal flora from the gut, or respiratory flora) via blood

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vessels or due to trauma. Cooling of the body soon after death is recommended to slow this proliferation. Time limits imposed for recovery of tissue may include specific parameters for length of time the body is cooled or time to body cooling after death.

To determine if time limits will be exceeded, the time of pronouncement of death is used as “asystole” unless the death was not witnessed or there were no obvious recent signs of life at the time pronouncement was made (official pronouncement can be significantly delayed). An un-witnessed death can include death by suicide or when the person is alone for any reason and death occurred. In these cases, the time of death (asystole) should be considered as a worst-case scenario. The last time the donor was last seen or known to be alive should be used and, if too much time has elapsed, tissue donation/recovery may not be appropriate. Consideration regarding when and how long the body was cooled after death, or how much time has passed since the last time known alive, should be scrutinized. In cases such as this, a visual assessment of the deceased’s body may show indications of advanced putrefaction (skin sloughing, body bloating), which increases the potential for contamination with microorganisms and this can also adversely affect tissue quality.

In general, published guidelines establish requirements that the body must be cooled within 12 hours after death (or last time known alive), and tissue recovery must begin within 24 hours of death (or last time known alive). If the body is not cooled after death, the limit for tissue recovery may be restricted to within 15 hours of death.

Relevant Medical Records

Inquiry regarding the potential donor’s relevant history takes place by collecting information from various sources. These can include:

- available, relevant medical records;
 - hospital records
 - clinic records
 - records from a physician specialist
- personal physician or medical staff caring for the patient;
- donor risk assessment interview with someone knowledgeable regarding the donor’s health history, travel history, medication/drug history, and sexual/social behaviors; and a
- physical examination/assessment of the donor.

Important information should also be sought from medical records so these documents must be pursued (refer to *Current Clinical Information* above). Communicating with hospital officials or the management at a clinic may be necessary to gain access to the medical records of the potential donor. She/he may have a medical specialist that offered treatment for a specific, relevant condition and these records should also be obtained and reviewed. Relevant information may be scattered and found in different medical facilities.

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If the donor died while in a hospital, you are encouraged to communicate with the patient's attending physician, personal physician, or the medical staff caring for the patient to gather useful information. These professionals should know the status of the patient during the hospital course up to the time of death. These healthcare providers may know if there was a suspicion of sepsis or another infectious disease at the time of death and this may not be well documented in the records. Of particular concern for infectious risk is evidence of patient symptoms that may include persistent fever, a rash, significant weight loss recently (loss of >10% of normal body weight without cause), enlarged lymph nodes, or recent oral or genital ulcers. Abnormal, unexpected, or unusual results from testing performed such as from microbiological cultures, biopsy results from pathology, or hematological evaluations such as very low or abnormally high white blood cell counts, and a cell differential evaluation that describes the morphology of white blood cells and red blood cells should be scrutinized. Certain cells and cell counts can indicate active infection. If a series of CBCs (Complete Blood Counts) are available, they should be reviewed for trends and changes.

A donor risk assessment interview questionnaire is a relevant medical record and must be developed and referenced in the tissue bank's policy and procedures manual (see *Donor Risk Assessment Interview: Medical History, Behavioral Risk Assessment, & Travel History* that follows). It must cover all relevant risks associated with medical history as well as behavioral history. A knowledgeable historian for the deceased person is identified and interviewed. This interview, which is comprised of multiple questions covering risk for infectious diseases and indicators that can affect tissue quality, is administered soon after the potential donor's death during a highly emotional and unstable time for the person(s) supplying the information (historian). Care must be taken during this interview to consider their emotional state but this should not override the need to properly screen the donor for relevant risks. Answers from this interview can reveal information not found in available medical records. The interview is expected to be a dialogue between the interviewer and the historian(s). The donor's historian(s) should be informed that they can ask questions when they do not understand the risk information being sought or when they perceive a risk exists for something you may or may not have asked. The interviewer representing the tissue bank should have adequate training and resources available to be able to properly answer any questions the historian(s) may have. The historian(s) you select should be instructed to answer the questions to the best of their knowledge and should know the donor well to be considered acceptable. The historian should not simply be a person that is most readily available to you. Although a family member may seem appropriate, another individual may be able to provide better information, such as the donor's: current sexual partner, girlfriend, boyfriend, fiancé; a current housemate; a caretaker; or, a close friend. It may be important to assess whether the historian you have selected has known the donor for a recent period of time of significant length. For example, although not required, it's best if they have known the donor for at least the past five years. Selecting a historian that currently lives with the potential donor is preferred. A historian that meets these criteria may be able to offer the best current, relevant risk information and this can be used as a guideline when selecting a historian. An important expectation of the interviewer is that they are capable of deciding whether the historian is knowledgeable and when to seek another historian.

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The interview should be conducted using questions that are easily understood by the general public. Avoid using medical terms when possible and short direct questions are best for comprehension. If your region is affected by risk associated with specific diseases, questions that assess this risk should be included in your questionnaire. These regional risks can change: dengue fever, yellow fever, malaria, Chagas Disease, tuberculosis (TB), plague, chikungunya virus, West Nile Virus (WNV), Q fever, etc. All relevant medical, behavioral, and travel risk associated with transmissible disease must be covered by questions as well as assessment of health risks associated with adverse affects on tissue quality. The questionnaire format should be standardized and documentation clearly readable.

Donor Physical Assessment

A thorough physical examination of the body of the potential tissue donor is a critical safety step. Observations made that indicate risk for transmissible disease results in a determination that the donor is not eligible. Tissue recovery personnel must perform a complete examination of the donor's body prior to beginning the procurement of tissue and must clearly document these steps. Proper training of personnel is required so they can be aware of findings on and in the body that can be an indication of high-risk behavior or an increased risk for infectious disease. Tissue recovery technicians should expect the unexpected when performing physical assessment of the tissue donor. Risks to look for include the following:

- Systemic disease
 - active malignancy (suspicious skin lesions)
 - malnutrition, deformities
 - jaundice, icterus, hepatomegaly
- Signs of bacterial or viral infection
 - recent receipt of a live vaccination (vaccination site infection, scabs, lesions)
 - recent receipt of a tattoo, body piercing, or acupuncture when non-sterile instruments were used (shaved area, redness, swelling, scabbing - may require further investigation to assess risk)
 - skin lesions such as a rash, petechiae, skin ulcers, blue/purple or gray/black lesions, shingles
 - oral lesions such as ulcers or thrush
 - an enlarged lymph node (or nodes)
 - jaundice, icterus, hepatomegaly
- High-risk behavior (related to infection with HIV or viral hepatitis)
 - injection drug use (non-medical injection sites)
 - inspection of tattoos (for hiding injection sites, also assess content & location of the tattoo)
 - genital or skin lesions or trauma suspicious of a sexually transmitted disease
 - evidence of anal intercourse (male) - insertion trauma, perianal lesions
 - genital warts, herpetic lesions, syphilitic chancres and other lesions
- Trauma
 - fractures, avulsions, lacerations, or abrasions that may affect (contaminate, compromise integrity) tissue to be recovered

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- internal trauma that can cause agonal/cross-contamination between cavities
 - o injury to the bowel, penetrating or crushing injuries
- Cleanliness of body
 - the state in which the body is found (can relate to increased risk for contamination/cross-contamination)

The eyes should be inspected to assess for signs of systemic disease (e.g., lymphoma) or infection (e.g., vaccinia keratitis, congenital syphilis). The donor's weight (morbid obesity) cannot compromise the requirement to perform a thorough physical examination. If the body cannot be properly assessed for risk, for example if the posterior aspect of the body cannot be examined, the deceased should be determined not suitable for tissue donation/recovery. Every potential donor must be thoroughly examined and screened following established protocols.

Any suspicious findings must be investigated and resolved for a proper determination to be made regarding donor suitability. No finding suggestive of possible risk should be left to speculation (unresolved). A biopsy of a suspicious external or internal lesion, or of an enlarged lymph node, can be obtained and placed in a fixative such as formalin. A gross and microscopic report can be produced that resolves suspicion. When obtaining a biopsy of a lesion, the lesion should be excised whole or a portion obtained, along with a section of normal tissue that borders it. This allows the pathologist to compare normal tissue versus the lesion. Thick lesions or nodes should be cut in half to allow fixative to reach all parts of the specimen. A digital photograph can also be taken of the lesion and/or it should be thoroughly described to allow for sufficient evaluation by a pathologist who will perform a gross and microscopic exam:

- Site where lesion or node found on body
- Color(s)
- Size - report widest dimension and height, if raised
- Surface - smooth, rough, flat, ulcerated, or finger-like
- Shape - circular, ovoid
- Borders - irregular, well-defined, raised
- Consistency - firm, soft, nodular

A standardized physical assessment form should be developed for use by, and for training of, tissue recovery personnel so all descriptions of observations are complete. See AATB Guidance Document No. 1, v2 Tissue Donor Physical Assessment Form at this link: <http://www.aatb.org/aatb/files/ccLibraryFiles/Filename/000000000082/aatbguidancedocument1v2.pdf>

Donor Risk Assessment Interview: Medical History, Behavioral Risk Assessment, & Travel History

The donor risk assessment interview (the questionnaire) described earlier provides answers that must be assessed and used for determining donor eligibility. This is utilized in conjunction with information derived from all relevant medical records that were found and the physical examination that was performed. Risk analysis includes considerations for the type of tissue to be recovered, how it will be supplied, and how it

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may be used. This risk assessment must be documented in the donor record maintained by the tissue bank that is responsible for determining the final suitability of the donor.

Medical History

Disorders to be evaluated to determine donor suitability can include histories related to:

- Malignancy
 - requires evaluation of type, course/recurrence, treatment, and affect on tissue to be recovered
- Neurological disorders or symptoms
 - degenerative or demyelinating disease/disorder of unknown etiology involving the Central Nervous System
 - diagnosis of dementia (gross & microscopic examination of brain may be required to rule out prion-associated disease)
 - suspicion of prion-associate disease (CJD, vCJD)
- Autoimmune disease
 - systemic, chronic, inflammatory disease, is etiology understood, what is affect on immune system, risk for infection associated with this disease, possible affect on tissue to be recovered (tissue quality)
- Genetic disease
 - evaluate possible affect on tissue to be recovered (tissue quality)
- Other conditions
 - increased risk for malignancy includes: cirrhosis, serious gastrointestinal disorders, previous hx of malignancy without regular follow-up after treatment
 - increased risk for infection: diabetes, leukemia, steroid therapy, malnourishment, malnutrition conditions, respiratory diseases/conditions
 - if it is known that the potential donor was excluded or deferred from donating blood by a blood collection establishment, and the specific reason for deferral cannot be discovered, the donor may be considered not eligible for tissue donation

Medication and therapies must be evaluated to determine donor suitability due to risk for the following:

- Weakened immune status
 - anti-rejection drugs: organ transplant recipient
 - corticosteroids: long term, high-dose therapy can mask a current viral infection
 - radiation and/or chemotherapy (can also weaken tissues near target area)
- Toxicity to tissue
 - treatment with heavy metals to treat disorders (e.g., gold for arthritis)
- Infection
 - recently prescribed antivirals or antibiotics, then death occurred
 - exposure to endogenous retroviruses from non-human animals

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- xenotransplantation risk - receipt, ever, of a xenotransplantation product or intimate contact with a person who has been exposed to such a product; xenotransplantation products are rare and include *live* cells, tissues, or organs from a non-human animal source, or cells/tissues exposed to such live cells (example in the US is Epicel™ used to treat severe burns); results in donor not eligible
- a past history of viral hepatitis of an unknown type can disqualify a donor, however, a remote history of cytomegalovirus (CMV), Epstein-Barr virus (EBV), or hepatitis A virus (HAV), can be acceptable if no active infection is suspected at the time of death
- Transfusion of blood or blood products
 - risk concern is raised if administration of blood or blood products occurred many years ago before adequate disease screening tests became available
 - also see consideration for *Blood Sample and Plasma Dilution Evaluation* that follows below
 - the blood supply is not considered to be a “risk” since blood donors are screened and tested using current, modern technology
- Receipt of human, pituitary-derived growth hormone or gonadotropin, or human dura mater
 - risk concern for CJD; receipt ‘ever’ means the donor is not eligible

Behavioral Risk Assessment

Behavioral risk is evaluated to determine donor suitability and should include inquiry regarding the following histories that can increase risk for transmissible disease such as HIV and viral hepatitis:

- Sexually transmitted disease - especially genital ulcerative diseases (syphilis, gonorrhea, herpes)
- Incarceration - long term, recent (may wish to consider jail, prison, and juvenile detention centers)
- Sex with high risk individuals - sex in exchange for money or drugs, sex with person from a high risk region (see HIV-1 Group O); a male who had sex with another male (includes bisexual male); sex with an injection drug user; sex with a recipient of human clotting factor concentrates; sex with someone with a positive test for HIV, HBV, or with a person with clinically active, symptomatic HCV - all these risks may be assessed based on recent history, such as in the past 5 years or the past 12 months
- Reside with someone who has HBV or clinically active, symptomatic HCV - donor may be ineligible if occurred in past 12 months
- Injection drug use (non-prescribed drugs) - donor ineligible
- Non-prescription drug use (non-injectable illegal drug abuse)
- Recent bite from an animal (past 6 months) - if animal suspected to have rabies, donor ineligible
- A blood relative of the donor was definitively diagnosed by a physician to have CJD (no ancestry limitation is intended) - donor should be ineligible

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- Occupational or other exposure to a toxic substance in amounts sufficient to affect tissues and affect transplantation outcome (e.g., ethylene glycol)
- Exposure to someone else's blood who was known to be infected with HIV, HBV, or HCV - donor should be ineligible if this occurred in past 12 months

Travel History

Risk can be associated with travel and certain travel risks may be seasonal. Effects of climate change, globalization of trade, and the ease of international travel all increase the potential for infectious diseases to spread or emerge. As humans come in close contact with animals due to population growth and the habitation of areas where forests exist(ed) and animals live(d), pathogens only known to non-human animals can jump species and infect humans, who further transmit the new disease. Travel risk can include the following and questioning the donor's historian is the most common method to obtain information about risk associated with travel:

- variant CJD (vCJD)
 - prolonged residency or visitation, or receipt of blood transfusion in certain parts of Europe and the UK during specific time periods since 1980
- HIV-1 Group O
 - involves certain countries of central or west Africa and includes risk associated with receipt of blood transfusion or sex with a native/resident (all since 1997). Note: if a test kit used to screen the donor's blood for antibodies to HIV-1 Group O, you may not be required to additionally screen for this risk history.
- Chagas Disease
 - risk may only be relevant for tissues that would be at risk for harboring viable *Trypanosoma cruzi* parasites that can survive tissue handling steps; this disease is endemic in parts of Central and South America and in areas of the southern half of the United States
- Malaria
 - risk may only be relevant for tissues that would be at risk for harboring viable malaria parasites that can survive tissue handling steps; this disease is found in equatorial regions around the world; risk related to travel may only be relevant in the past 12 months since symptoms of infection should be evident before one year after return.

Pediatric Tissue Donors

Special screening considerations are required for pediatric tissue donors. If the child is less than or equal to 18 months old, or has been breast fed in the past 12 months prior to death, the birth mother should be evaluated for risk associated with HIV, HBV, HCV, and HTLV. Other diseases that can be transmitted vertically from mother to fetus may also be relevant, such as malaria or Chagas Disease; risk, when relevant, should be considered and evaluated. Special testing considerations are described in *Blood Sample and Plasma Dilution Evaluation*. Child donors must be screened with as much diligence as adult donors. The physical assessment must not be skipped or shortened because the

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donor is a child. Although risk associated with sexual activity may not seem relevant, infectious disease risk associated with child abuse (sexual) is possible so the examination of the genital and perianal regions are expected to be performed. Because a child's immune system is developing, protective antibodies may not yet be produced placing the child donor at increased risk.

Blood Sample and Plasma Dilution Evaluation

Controls should be developed regarding the collection of the blood sample(s) to be drawn from the donor and a determination made to be sure it qualifies as a suitable sample. Collection should occur as close to the donation date as possible but not more than 7 days before recovery. In general, to avoid sample characteristics that cause false positive test results (e.g., extreme lipemia, partial hemolysis) or that can cause a sample to be rejected for testing (complete hemolysis of red blood cells), collection usually takes place no longer than 24 hours after death. Specimens must be collected using appropriate tubes that may or may not contain an anticoagulant. When a filled blood tube is centrifuged after collection, the remaining supernatant is either serum (if a plain collection tube was used that does not contain anticoagulant) or plasma (if a collection tube was used that contains an anticoagulant). To be sure what tube types to use, you must reference the package insert instructions for the test kits that will be used for infectious disease testing. Other sample handling parameters can exist, such as time limits for centrifugation and separation of serum or plasma from the red cells. Storage parameter limitation may also apply such as limits for length of time the samples are refrigerated before testing. Familiarity with which test kits will be used and the sample type and specimen handling requirements of those test kits is important.

Evaluation of the blood sample(s) used for infectious disease testing should include qualification that these samples are not significantly dilute since this could result in false negative test results. The potential for plasma dilution and hemodilution should be routinely checked. Plasma dilution is defined as a decrease in the concentration of the donor's plasma proteins and circulating antigens & antibodies resulting from the transfusion of products containing fluids such as blood, blood components (or colloid), and/or infusion of crystalloids. Hemodilution is dilution of the donor's blood volume that contributes to plasma dilution, and only components containing red cell mass are considered in evaluating hemodilution. An algorithm is a formula developed and used to detect significant dilution due to infusions & transfusions that can affect accuracy of infectious disease test results. The donor's total plasma volume (TPV) and total blood volume (TBV) are estimated by calculation based on the donor's body weight then direct comparisons are made to amounts of transfusions and infusions that were administered prior to death OR prior to collection of the blood sample, whichever occurs first. A common algorithm follows:

- Estimate TPV of donor (weight in Kg x 40 ml/Kg)
- Estimate TBV of donor (weight in Kg x 70 ml/Kg)
- Total the blood (mls) received in last 48 hrs (A)
- Total the colloids (mls) received in last 48 hrs (B)
- Total the crystalloids (mls) received in last 1 hr (C)

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- Add B + C and compare to TPV (fluid volumes are compared)
- Add A + B + C and compare to TBV (mass/fluid volumes are compared)
- Do comparisons show > 50 % dilution? If not, blood sample qualifies and can be used for infectious disease testing.

Donor Infectious Disease Testing

To avoid the potential for infectious disease test problems, multiple controls should be in place. The test kits selected for use should be licensed, cleared or approved by the legal authority for use as donor screening tests. Tests validated for use with blood samples collected from a deceased donor should be used. The laboratory selected to perform testing should be approved by the competent authority since this also indicates that the laboratory follows test kit manufacturers' instructions and personnel performing the tests are competent. These controls, in conjunction with qualification of the blood sample and following sample handling requirements, can ensure accurate infectious disease test results. Although all of these controls can be in place, infectious disease test kits used for screening donors have limitations. There remain small periods of time (aka "window periods") for each test where detection of virus or antibody production after exposure to virus is not detectable by current test methodologies. These windows can range from about a week to a few months, depending on which test kits are used. This is why a reliance on donor test results is not sufficient to ensure safe tissue for transplant. If a donor is determined to be a risk by medical, behavioral, or travel history and "testing" is all negative, the donor is still not eligible and is ruled out for tissue donation.

Tissue Quality

As previously described, some conditions (e.g., autoimmune diseases) can affect specific tissues and, if recovered, processed and made available for transplantation, may cause an unfavorable performance outcome for recipients. This is evaluated on a case-by-case donor basis and for specific tissue types. For example, a potential donor with multiple known conditions related to a high risk for cardiovascular disease may not qualify as a suitable donor of cardiac tissues (heart valves, cardiac conduits) or vascular tissues (arteries, veins). Persons with skin diseases may not be suitable for skin donation. A person with a metabolic bone disease may not be an appropriate donor of musculoskeletal tissues and someone who has a collagen disorder should not be a donor of soft tissues or tissues comprised of that collagen type (tendons, ligaments, fascia lata, cardiovascular tissues). Donor age may play a role in decision-making as well as donor weight (minimums or maximums). Part of the Quality Management responsibilities of the tissue bank is an expectation to properly characterize the tissue allografts they provide for transplantation. The creation of minimum specifications their allografts should meet to be deemed suitable should be described in policies and procedures and this should relate to donor qualifications.

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Conclusion

Tissue banking professionals must be diligent in efforts to screen potential donors for suitability. Every person should have the right to donate tissues but not everyone qualifies as a suitable donor. These screening steps to determine donor eligibility are a critical part in the provision of safe tissues for transplantation and it is our professional duty to perform this function as best we can. We should actively pursue continuous education regarding the significance of human disease and risks for disease, as well as being cognizant regarding emerging infectious diseases. Management should provide continuous education, training, and re-training for staff, and competency assessment of staff functions should be routine. This supports continual improvement in practices and should be included in quality management goals that support the overall mission and service you provide to the public.

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Suggested References

Standards for Tissue Banking. 12th ed. Edited by Pearson K, Dock N, Brubaker S, McLean, VA, © 2008 American Association of Tissue Banks.

Guidance Document No. 1, version 2, Tissue Donor Physical Assessment Form, © 2005 American Association of Tissue Banks.
<http://www.aatb.org/Guidance-Documents>

Tissue and Cell Donation: An Essential Guide. Edited by Warwick RM, Fehily D, Brubaker SA, Eastlund T, © 2009 Blackwell Publishing, ISBN 978-14051-6322-4.

Essentials of Tissue Banking, Edited by Galea G, © 2010 Springer Publishing Company, ISBN 978-90-481-9141-3.

Guidance for Industry: Eligibility determination for donors of human cells, tissues and cellular and tissue based products (HCT/Ps), United States Food and Drug Administration, Center for Biologics Evaluation and Research, August 2007.
<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/ucm073964.htm>