BASIC AWARENESS

The use of musculoskeletal allograft tissue in reconstructive orthopaedic procedures has markedly increased over the last decade. (Figure 1)

Surgeon knowledge of tissue bank practices in donor gifting and screening, serology testing and processing is important when making the decision to use these allograft tissues.

The orthopaedic surgeon also has the responsibility to inform the patient about the risks and benefits of using allograft tissue.

This handout provides an overview of some of these issues.

What are Commonly Used Allografts in Orthopaedic Procedures?

**Bone**
- Demineralized bone products (osteoinductive)
- Cortical/cancellous – powder, chips, wedges, dowels, crest, pegs and screws
- Structural – segments, shafts, long bones, pelvis, acetabulum
- Osteochondral long bone (cryopreservation cartilage)
- Ribs, mandible, calvarium, ear ossicles

**Soft Tissue**
- Patellar and Achilles tendon (bone block), rotator cuff, other tendons
- Fascia lata

**Cartilage**
- Menisci, osteoarticular segments, costal cartilage

*Figure 1: Musculoskeletal allograft usage. Source: U.S. Census Bureau, Statistical Abstracts of US 2001.*
What are the Milestones in Tissue Banking?

1881  First human bone transplant under aseptic conditions
1925  Lexer: First reported large series of bone transplants (50% success rate)
1950  U.S. Navy Tissue Bank established in Bethesda, Maryland
1955  Low temperature preservation of bone (reduction of antigenicity)
1960s Early reports of successful use of tissue implants
1972  Ottolenghi: Long bone/osteoarticular allografts series
1973  Parrish: Long bone allograft replacement series
1983  Mankin: Two hundred large bone allograft series
1984  First Standards for Tissue Banking published by the American Association of Tissue Banks (AATB)
1985  AATB Inspection/Accreditation Program initiated 1983
1989  AATB Training and Certification Program for Tissue Bank Specialists (CTBS)
1993  FDA: Interim Rule on Tissue Transplantation (FDA Auditing initiated)
1994  AATB Inspection/Accreditation Program using trained former FDA compliance officers
1997  FDA: Final Rule on Tissue Transplantation
2001  Establishment of Registration and Product Listing
  Proposed Good Tissue Practices; Inspection and Enforcement
  More than 800,000 tissue transplants annually in the U.S.
2002  72 AATB Accredited Tissue Banks (Consult AATB Web Site at www.aatb.org)

Figure 5: First depicted allograft transplantation. 12th Century painting of Saints Cosmos and Damian.
Figure 6: AATB Standards.
Figure 7: Femoral strut.
What Practical Steps are Taken in Tissue Banking in Assessment and Processing?

Detailed inquiry into donor’s medical, social and sexual history (including autopsy if accomplished)

**Donor Screening: History**

At Time of Donation, **No** History of:

- Recent active infection or sepsis
- Systemic viral illness (Hepatitis, HIV, West Nile, etc.)
- Untreated syphilis, active tuberculosis, leprosy
- Autoimmune disease
- Ingestion toxic substances
- Rheumatoid arthritis, systemic lupus, polyarteritis nodosa, sarcoidosis, myasthenia gravis
- Clinically significant metabolic bone disease
- Clinically significant malignancy
- Dementia, dura mater transplant or use of human derived pituitary growth factor (Spongiform Disease, CJD)
- Risk factors for HIV (as listed by US Public Health Service)

*Figure 8: HIV virus - led to improved donor screening.*
Donor Screening: Physical Examination
Physical Examination of Potential Donors Includes No Evidence of:
- Active infection: viral, bacterial or fungal
- Physical evidence of risk for sexually transmitted diseases such as genital ulcers, herpes simplex, syphilis, chancroid
- Needle tracts (nonmedical); recent tattoos (12 months)
- Lymph node enlargement (disseminated)
- Jaundice, icterus, hepatomegaly
- Blue/purple spots consistent with Kaposi’s sarcoma
- Evidence anal intercourse (perianal condyloma)
- Oral thrush
- Open local wounds
- Clinically significant skin lesions

Serologic Testing
Tests Required by FDA; performed by CLIA - approved laboratories:
- HIV 1/HIV 2 Antibody (residual risk 1:689,655)
- HTLV I/HTLV II Antibody
- HBsAg (residual risk 1:77,220)
- HCV Antibody (residual risk 1:19,850)
- Syphilis
- HB Core Antibody (FDA: For living donors) (general New York State requirement)
  Residual Risk Source: GAO/HEHS-98-205 Blood Plasma Safety

Additional Testing Usually Done:
- HIV Antigen
- HIV PCR Testing
- CMV
- Possible use of NAT testing as used in blood (present blood banking NAT testing for living donor serum since 2000 U.S. residual risk HIV 1:2,000,000; HCV 1:2,000,000 and HBV 1:250,000: Transfusion 42: 966-972, 2002)

Tissue Processing
- Audited or accredited facility following Good Tissue Practice guidelines
- Validated Quality Control/Quality Assurance Program
- Elimination or reduction of debris and cells to reduce disease transmission
- Bacteriologic and virucidal washes
- Evaluation bacteriologic bioburden (preprocessing cultures to evaluate contamination)
- Possible use of gamma radiation 1.5 Mrads (15 kilogray) or more (pre- or post-processing)
- Final product testing for bacteriologic contamination (swabs vs. tissue piece)
- Potential discard of tissue or donor lot based on certain types of early bacteriologic contamination
- Final review by tissue bank medical director of screening/serology/processing prior to release of tissue for transplantation

Sterilization (Selected Tissues)
- Gamma radiation 1.5 - 2.0 Mrads [15 - 20 kilogray] (these amounts or higher may raise concern for integrity of tissues especially soft tissues)
- Ethylene Oxide (concern for residual toxicity and penetration depth)

<table>
<thead>
<tr>
<th>Virus</th>
<th>HIV</th>
<th>HCV</th>
<th>HBV</th>
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<tbody>
<tr>
<td>Window Period using FDA Licensed Tests</td>
<td>22 days (anti HIV)</td>
<td>70 days (anti HCV)</td>
<td>56 days (HBsAg)</td>
</tr>
<tr>
<td>Window Period using NAT* Testing</td>
<td>7-12 days**</td>
<td>10-29 days</td>
<td>41-50 days</td>
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*Nucleic Acid Test
** p24 testing between 12 and 22 days

Window Period
Period between infection and time virus is detectable by screening tests.
What are the Episodes of Documented Disease Transmission?

Over past decade more than 5 million musculoskeletal allografts have been safely transplanted. Relatively few incidents of disease transmission have been reported:

**Bacterial:**
- Tuberculosis - One case (four recipients): *James et al, JBJS 35B:578, 1953*
- Infections - One case: *Tomford et al, JBJS 63A:244-248, 1981*
  - Three cases: *Lord et al, JBJS 70A:369-376, 1988*
  - Cases under investigation by CDC: *MMWR 50(48), December 7, 2001* and *MMWR 51(10), March 15, 2002*

  
  **Situation One**
  - Death November 2001 Clostridium sordellii
    - Osteochondral femoral allograft segment in 23 y/o male

  **Situation Two:** Tissue from same donor - tissues irradiated
  - Patient A bone-tendon-bone Pseudomonas aeruginosa, staph aureus, enterococcus
  - Patient B bone-tendon-bone Pseudomonas aeruginosa

  **Situation Three:** Tissue from same donor - tissues were to have been irradiated but not accomplished
  - Patient A bone-tendon-bone Citrobacter werkmanii youngae; group B streptococci
  - Patient B bone-tendon-bone Klebsiella oxytoca/Hafnia alvei

  Total of 26 cases under review as of March 2002: 13 of 26 were infected with clostridium with 85% of these positive clostridial associated infections coming from a single non-AATB accredited tissue bank. These reports and other allograft “associated” infection reports are under review by CDC. A number of these reports are not allograft “caused” infections.

**Viral:**
- Hepatitis B - One case: *Shutkin, JBJS 36A:160-162, 1954*
- Hepatitis C - One case: *Eggen and Nordbo, NEJM 326:411, 1992*
  - Two cases: *Conrad et al, JBJS 77A:214-224, 1995*
  - One case: 2002 bone-tendon-bone (possible 3 other tissues); under review

  **HIV** - One case: *MMWR 37:397-99, 1983* (Pre-HIV antibody testing)

What is the Message?

- More than 800,000 musculoskeletal allografts distributed in US in 2002.
- Disease transmission is very rare.
- Conventional sterilization techniques used for metallic implants may adversely affect functional, biological and mechanical properties of most allografts.
- No reports of disease transmission using demineralized bone products.
- Some grafts can be treated with 1.5 Mrads (15 kilogram) or more to reduce contamination. This may affect properties of the allograft.
- Inherent safety of the graft is based upon Good Tissue Practices:
  - Donor screening and physical examination
  - Serologic testing
  - Careful processing techniques
  - Attention to quality control/quality assurance
- Need for centralized reporting of adverse episodes by surgeons with subsequent investigation and documentation.
- Outcome studies to improve safety and efficacy.
- Orthopaedic surgeon needs to know “the tissue banker”.
- Surgeon/patient interaction regarding the risks and benefit of using allograft tissue in their procedure is requisite.