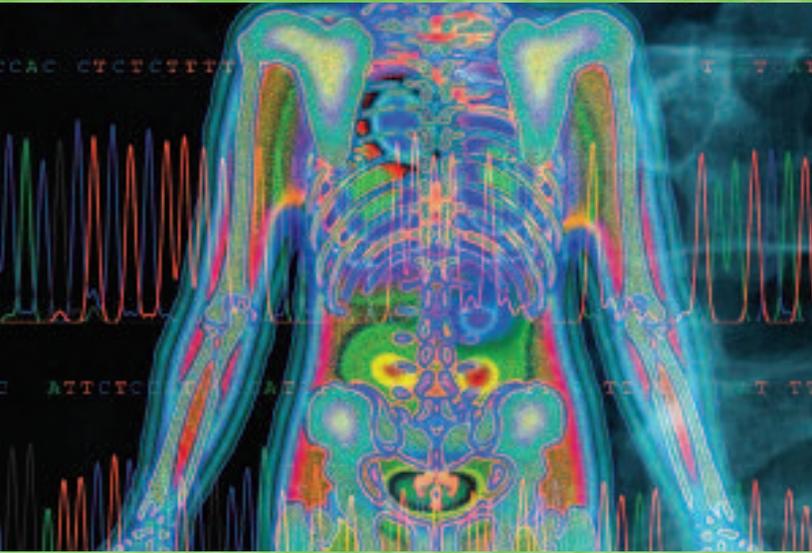


Allograft vs. Xenograft



Practical Considerations for Biologic Scaffolds

Editors: **Garth Jacobsen, MD**

Assistant Clinical Professor of Surgery,
Director, UCSD Hernia Center,
University of California, San Diego

David Easter, MD, FACS

Professor of Clinical Surgery,
University of California, San Diego

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CME INFORMATION

Course description and objectives

In the surgical setting, general surgeons must take many factors into consideration to optimize the outcomes of their procedures. It is estimated that more than 500,000 surgeries are performed annually for hernia repair alone. Surgeons must choose from a variety of materials to replace bone, cardiac valves, and abdominal walls. There are many options for appropriate surgical material among synthetics and biologics. The scientific literature on xenografts and allografts focuses on their clinical and surgical use in regenerative medicine and offers surgeons valuable information to affect positive patient outcomes. Allografts and xenografts are well described in the literature, and few head-to-head clinical evaluations comparing the two exist. This monograph reviews the characteristics of allograft and xenograft biologic scaffolds, and presents the complex factors that a clinician should know when considering available options. Choosing the appropriate material can improve patient outcomes.

At the conclusion of this learning activity, participants should be able to:

- Review the role of biologic scaffolds
- Identify the essential components of effective graft healing
- Describe the different features of xenografts and allografts
- Discuss practical considerations regarding biologic scaffolds

Statement of need

The content of this educational activity was determined by rigorous assessment of educational need and includes expert faculty assessment, literature review, medical practice, and new medical technology.

Target audience

This activity is intended for general and reconstructive surgeons and other healthcare professionals who are interested in the use of allograft and xenograft biologic scaffolds in reconstructive surgical procedures.

Accreditation statement

The University of California, San Diego School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The University of California, San Diego School of Medicine designates this educational activity for a maximum of 2.0 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Medium used

Monograph – This activity is a monograph created de novo to meet the needs of the targeted audience.

Method of participation

The estimated time to complete this activity is 2 hours. To obtain credit, participants should read the objectives and monograph, answer the 9-question multiple-choice posttest, and complete the evaluation form online at <http://cme.ucsd.edu/biologicscaffolds> to receive a certificate immediately via e-mail.

Release date: October 15, 2008

Termination date: October 14, 2009

Cultural and linguistic competency

This activity is in compliance with California Assembly Bill 1195, which requires continuing medical education activities with patient care components to include curriculum in the subjects of cultural and linguistic competency. Cultural competency is defined as a set of integrated attitudes, knowledge, and skills that enables health care professionals or organizations to care effectively for patients from diverse cultures, groups, and communities. Linguistic competency is defined as the ability of a physician or surgeon to provide patients who do not speak English, or who have limited ability to speak English, direct communication in the patient's primary language. Cultural and linguistic competency were incorporated into the planning of this activity. Additional resources on cultural and linguistic competency and information about AB1195 are available on the UCSD CME website at <http://cme.ucsd.edu>.

EDITORS

Garth Jacobsen, MD
Assistant Clinical Professor of Surgery
Director, UCSD Hernia Center
UCSD Medical Center
San Diego, California

Garth R. Jacobsen, M.D. received his medical degree from University of Washington School of Medicine in Seattle. He performed his surgical training at University of Illinois, Chicago and then pursued fellowship training in laparoscopy at the University of California, San Diego. He serves as the UCSD Hernia Center Director with a special commitment in the repair of complex hernias. Dr. Jacobsen also is interested in the treatment of obesity, and is an active bariatric surgeon in the Center for Treatment of Obesity. Dr. Jacobsen is board certified by the American Board of Surgery and his general surgery practice focuses on minimally invasive surgery.

David Easter, MD, FACS
Professor of Clinical Surgery
Department of General Surgery
UCSD Medical Center
San Diego, California

As a recent Director of the Clinical Oncology Programs for the Rebecca and John Moores UCSD Cancer Center, Dr. Easter has organized the Cancer Center's clinical and research efforts to provide the finest possible care for cancer patients. At the Cancer Center, he has created specialized clinical teams to care for patients who have specific types of cancer, such as breast cancer. He recently passed the leadership of the Cancer Clinics to another physician so he can concentrate on medical education and safety for patients in the surgical care setting.

Dr. Easter serves as the Program Director for General Surgery on the Graduate Medical Education Committee. He also participates on the Patient Care Committee and a number of other groups that influence patient care at UCSD. Recently, UCSD honored Dr. Easter as the first UCSD recipient of the Vice Chancellor's Excellence in Clinical Care award. At UCSD and in national surgical organizations, Dr. Easter is a leader in developing new methods to ensure that medical students and surgical residents receive excellent training in the increasingly complex world of surgery.

Dr. Easter conducts clinical and basic science research in many areas, including techniques and results of laparoscopic surgery procedures, the causes and treatment of gastrointestinal reflux disease, approaches to surgical training, and empathy in the doctor-patient communication. One of his recent studies addressed ways for physicians to improve their ability to help cancer patients understand and discuss their fears during a clinic visit. Dr. Easter conducts patient clinics and performs surgeries at UCSD's medical center in Hillcrest.

Faculty disclosure

The University of California, San Diego Continuing Medical Education (UCSD CME) requires that the content of CME activities and related materials provide balance, independence, objectivity, and scientific rigor. Planning must be free of the influence or control of a commercial entity and promote improvements or quality in healthcare. Faculty participating in UCSD-sponsored CME programs are expected to disclose to the activity participants any conflict(s) of interest that may have a direct bearing on the subject matter in their role as planners or presenters. This pertains to relationships with pharmaceutical companies, biomedical device manufacturers, or other corporations whose products or services are related to the course content. UCSD CME has the following mechanisms in place to resolve conflicts of interest: 1) altering the financial relationship with the commercial interest, 2) altering the individual's control over CME content about the products or services of the commercial interest, and/or 3) validating the activity content through independent peer review. UCSD CME will resolve all conflicts of interest prior to an educational activity being delivered to learners. Participants will be asked to evaluate whether the speaker's outside interests reflect a possible bias in the planning or presentation of the activity. This information is used to plan future activities.

Dr. Jacobsen disclosed the following relevant financial relationships: Speaker for USGI Medical; Consultant for LifeCell.

Dr. Easter has no relevant financial relationships to disclose.

Off-label disclosure: This educational activity may contain discussion of unlabeled and/or investigational uses of agents that are not approved by the FDA. Please consult the prescribing information for each product.

Allograft vs. Xenograft

Practical Considerations for Biologic Scaffolds

INTRODUCTION

The utilization of biologic scaffolds is increasing at a rapid pace. Such scaffolds can be employed in a wide range of surgical procedures. While historically synthetic materials have been broadly used in these settings, they have demonstrated limited biocompatibility and can trigger the induction of vigorous inflammatory responses. This monograph reviews biologic scaffolds as an alternative to synthetic scaffolds. It is intended to provide practical and clinical knowledge of the healing process with biological scaffolds and to highlight important considerations involved in choosing material that offers both surgeon and patient the best possible outcome regardless of the specific clinical setting.

WHAT ARE BIOLOGIC SCAFFOLDS?

An allograft or xenograft is a biologic scaffold, which is a mammalian extracellular matrix (ECM) composed of laminin, fibrinectin, elastin, and collagen. An allograft is tissue transplanted between genetically nonidentical individuals of the same species.¹ A xenograft is tissue transferred from one species to another species. Key differences between allografts and xenografts are tissue source, species of origin, and methods of processing.^{2,3}

Biologic scaffolds have been developed for use as supportive material in the surgical setting in an effort to overcome the problems associated with synthetic materials. Synthetic mesh materials for significant abdominal wall repair are notable in their ability to achieve tension-free repair. However, the incidences of seroma/hematoma, fistula formation, skin erosion, infection, and pain in patients with synthetic materials seem to outnumber those with allograft material.^{4,5}

OPTIONS IN BIOLOGIC SCAFFOLDS

There are many types of biologic scaffolds available that can be used for indications that include, but are not limited to, abdominal wall reconstruction, hernia repair, breast reconstruction, cranial/facial defects, musculoskeletal and tendon repair and replacement, and gynecological reconstruction. As we learn

more, options continue to grow. Tissue sources from which biologic scaffolds are chosen include:

Allografts

- Human donor

Xenografts

- Porcine (small intestine, dermis)
- Bovine (pericardium, fetal, dermis)
- Equine

CHARACTERISTICS OF AN IDEAL BIOLOGIC SCAFFOLD

Regardless of clinical application, material for biologic scaffolds must be chosen based on the ability to protect the patient and support the healing process. This is most likely achievable with grafts that are well tolerated, resist infection, and are rapidly vascularized.

For abdominal wall reconstruction, the ideal graft achieves rapid vascularization and infiltration of host cells with minimal scarring. Cellular infiltration of a dermal substitute material has been shown to be essential in achieving effective wound closure, thereby minimizing wound contraction and hypertrophic scarring.⁶

ESSENTIAL COMPONENTS FOR EFFECTIVE WOUND HEALING

Repair and healing of wounds involves a series of complex biochemical events that take place in a sequential manner, although they overlap in time. These biochemical events—the inflammatory, proliferative, and maturation or remodeling phase—are integral to effective healing. An effective biologic scaffold supports fibroblast penetration, degradation, and remodeling of surrounding tissue, while avoiding host response to surface antigens.

Inflammatory phase and fibroblast infiltration

Following the initial inflammatory response in which clot formation, platelets, macrophages, and polymorphonuclear macrophages play a role, proliferation of fibroblasts occurs.

In this phase of wound healing, fibroblasts must penetrate the collagen matrix within the biologic scaffold to begin the degradation and remodeling process. Fibroblasts migrate into acute wounds within two days and comprise the majority of granulation tissue postoperatively.⁷ Fibroblast infiltration is essential to host acceptance of biologic scaffolds.

Controlled remodeling

Fibroblast outgrowth must be supported by the biologic scaffold in a way that leads to long-term host acceptance. This is best accomplished when controlled remodeling occurs with predictable outcomes. The fibroblasts secrete proteolytic enzymes that allow for subsequent collagen degradation and remodeling as well as cellular reorganization around the graft. Grafts composed of collagen are beneficial because they support natural cell interactions such as proliferation and migration.

A key issue related to effective controlled remodeling is whether the biologic scaffold has been chemically or mechanically cross-linked, and what effect this has on the long-term stability of the graft.^{8,9}

Biologic scaffolds or grafts can be intentionally cross-linked through chemicals or irradiation to enhance mechanical stability. Some processing techniques may also result in unintentional cross-linking. While chemically cross-linked grafts may enhance the long-term mechanical strength of the scaffold, they may also stimulate resistance to degradation and fibroblast penetration.^{8,9} Non-cross-linked scaffolds are replaced more readily by host neoconnective tissue, although at varying rates depending on the site of implantation and the thickness of the materials.¹⁰ Further research is necessary to investigate the clinical impact and long-term performance of cross-linked and non-cross-linked biologic scaffolds.

Host response

Host immunologic response is the degree to which the host responds to surface antigens on biologic grafts. Surface antigens may include the Gal epitope and DNA.² These antigens may be removed by processing methods such as decellularization. However, processing methodologies have not been the focus of systemic study in the clinical community.

TYPES OF HOST RESPONSE

Host responses include incorporation, encapsulation, resorption, and mixed response.¹⁰ Incorporation is the ability of the graft to allow for cellular infiltration, neovascularization, and collagen deposition. Encapsulation occurs, but may not result, when the graft is surrounded by connective tissue. Resorption occurs as non-cross-linked grafts are replaced by connective tissue at varying rates. A mixed response occurs in grafts perforated to allow for incorporation through the graft openings, combined with encapsulation around the remaining material.

ALLOGRAFT AND XENOGRAFT: A CLINICAL COMPARISON

While there are limited studies directly comparing allografts and xenografts, clinical experience reveals advantages and disadvantages for both. Allografts are advantageous for their biocompatibility and host acceptance, but they may have limited availability. Xenografts are available in greater supply and larger sizes; however, consideration must be given to the risk of cross-contamination with bovine spongiform encephalopathy or porcine endogenous retroviruses. There is no way to adequately screen xenografts for these viruses to determine their presence. Therefore, they may develop even in acellularized xenografts.

Allografts and xenografts differ not only in tissue source, but in three additional key areas: the degree to which the graft allows for fibroblast penetration, the manner in which remodeling occurs, and the immunogenic (host) response.

Fibroblast penetration

A recent study compared human acellularized dermal matrix with acellularized porcine dermal matrix as a scaffold for human fibroblasts. Fibroblast infiltration, necessary for effective graft healing, was supported in a significantly greater number of samples of human acellularized dermal matrix than porcine dermal matrix (83%, n = 24; p<0.05 compared with 31%, n = 49).

The porcine matrices became more tightly packed than human matrices after four weeks, suggesting a possible delay in fibroblast infiltration. In addition, in each sample, a significantly greater number of cells were observed below the surface in human acellularized dermal matrix than in the porcine acellularized dermal matrix ($P < 0.05$, Wilcoxin test) at four weeks (Fig 1).⁶

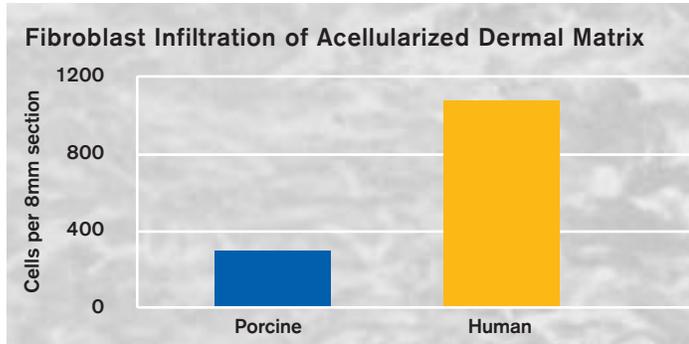


Figure 1. $P < .05$, Wilcoxin test. Fibroblast infiltration of porcine and human acellularized dermal matrix at four weeks, determined by automated cell counting.⁸

Remodeling

The manner in which remodeling occurs may differ between allograft and xenograft transplants. Remodeling occurs following equalization of fibroblast proliferation, collagen production, and degradation, when fibers are aligned along different tension lines. If the remodeling phase does not progress in a manner that contributes to overall tensile strength and host acceptance, the resultant disorganized rearrangement of tissue may lead to poor healing with chronic inflammation, scarring, or host rejection.

Host-tissue morphologic responses to five commercially available biologic scaffolds (one human and four porcine and/or bovine derived) were recently studied using rodent tissue.⁹

For the study, a musculoskeletal defect in the abdominal wall was created and repaired using the biologic scaffolds. It was then examined for degree of cellular infiltration, multinucleated giant cell presence, vascularity, and organization of the replacement connective tissue at various time points post surgery up to 112 days. The acute host response was uniformly characterized by an intense mononuclear cell infiltration, but the long-term remodeling response varied from chronic inflammation, fibrosis, scarring, and encapsulation to the formation of organized, site-appropriate tissue remodeling.

While two control groups using autologous tissue showed typical scar formation, the host tissue response to the five

biologic scaffolds was distinctly different depending on the degree to which the material was degraded and resorbed. The allograft host response showed remodeling with moderately dense organized collagenous connective tissue.³ Xenografts, composed of fetal bovine and/or porcine dermis, elicited a low-grade chronic inflammation, demonstrating the presence of foreign body giant cells.

The importance of the degradation process in relation to remodeling has only recently been recognized and has yet to be fully studied. Ideally, the rate of remodeling should be balanced with the rate of degradation to maximize the overall strength of the newly formed tissue. Earlier researchers believed that chemical cross-linking a porcine xenograft protected it from biodegradation and preserved its permanence.¹¹ More recent studies suggest that chemical cross-linking employed with xenografts make them less porous, thus preventing the cascade of events necessary for effective wound healing: sufficient fibroblast infiltration, adequate degradation, and complete resorption to avoid a chronic inflammatory response.^{3, 6, 12} Theoretically, this could lead to weaker bonding with adjacent host tissue.

Immunogenic (host) response

Immunogenic responses to biologic scaffolds can occur despite thorough cleaning, lysis to remove remnant cells, and utilization of sterilization methods. The occurrence, however, is far less extensive than with synthetic materials which are nonresorbable and are capable of eliciting a strong inflammatory reaction. Investigators have shown that grafts made from porcine small intestine submucosa (SIS) elicit a local and systemic inflammatory response beyond the initial postoperative period.¹² Immunogenicity of xenografts may be caused by surface antigens. A humoral response and evidence of inflammation was observed in arterial xenografts, but not in allografts, despite similar treatment to remove antigenic cells. Porcine DNA was reported in a study of SIS-based implants for tendon reconstruction despite the fact that the scaffolds were labeled “acellular.”¹³ The possibility of immunogenic responses should be considered when evaluating differences between allograft and xenograft scaffolds.

The effect of host response (incorporation, encapsulation, and resorption) on the subsequent strength of graft repair of hernias was recently measured using commercially available xenograft and synthetic biologic scaffolds. However, no direct comparisons of allograft and xenografts have been published.

EVALUATING BIOLOGIC SCAFFOLDS

The list of scaffolds available to surgeons for use in regenerative medicine for the repair and augmentation of tissue defects is extensive. It is imperative to compare the critical factors when evaluating both allografts and xenografts. Apart from product-to-product commercial comparisons, practical considerations relate to tissue supplier, tissue screening and recovery, donor and animal standards, processing and sterility methods, packaging and storage requirements, sizing and availability, and economic considerations [Table 1].

Table 1. Critical Questions in Evaluating Biologic Scaffolds

Tissue supplier

- Who is the supplier providing the tissue to the hospital? Is the same organization procuring and processing human and/or animal tissue?
- Is the supplier following all the requirements and recommendations for tissue as set forth by the respective governing bodies (FDA/CBER/USDHHS, AATB)?*
- What is the safety record of the supplier?
- Is the supplier a nonprofit or profit-centered organization?

Tissue sourcing

- What is the source of the tissue and how is it regulated? Does the tissue supplier meet or exceed donor/animal source and recovery recommendations?
- Are the tissue donors recovered from the United States or internationally?
- Are the animal tissues derived from the United States or international herds?
- How is the tissue recovered?

Donor standards

- What are the minimum standards for donor/animal criteria as set forth by the tissue supplier? Do they meet or exceed government requirements?
- Who sets and reviews the policy and criteria for donor and animal tissue within the tissue supplier's organization?

Processing/sterilization methods

- What are the requirements with regard to processing and sterilization of tissue?
- Is terminal sterilization used? If so, at what levels?
- How do processing/sterilization methods affect clinical outcomes?

Risk management

- Who is responsible for evaluating which company's product would be the safest?

Packaging and storage requirements

- What is the shelf life of the material?
- Are special temperature controls needed?
- Are there special handling requirements prior to surgery?

Sizing and availability

- Is the chosen tissue available in the sizes necessary to meet patient needs?

Economics

- Does evaluation of tissue cost considerations include the economic impact of potential complications and less than expected clinical outcomes?

*FDA: Federal Drug Administration; CBER: Center for Biologics Evaluation & Research; USDHHS: United States Department of Health & Human Services; AATB: American Association of Tissue Banks.

Status of tissue suppliers

It is important for the surgeon to know the supplier used by the hospital, and whether it is a nonprofit or profit-centered organization. Sometimes the same organization may procure and process the tissue. Human tissue products and tissue banks that supply allografts are regulated by the FDA. In addition, some tissue banks are voluntarily accredited by the American Association of Tissue Banks (AATB). The AATB recommends certain industry standards with regard to retrieval, processing, storage, and/or distribution. Specific FDA regulations for allografts can be found at www.fda.gov/cber/tiss.htm and information about the AATB can be found at www.aatb.org.

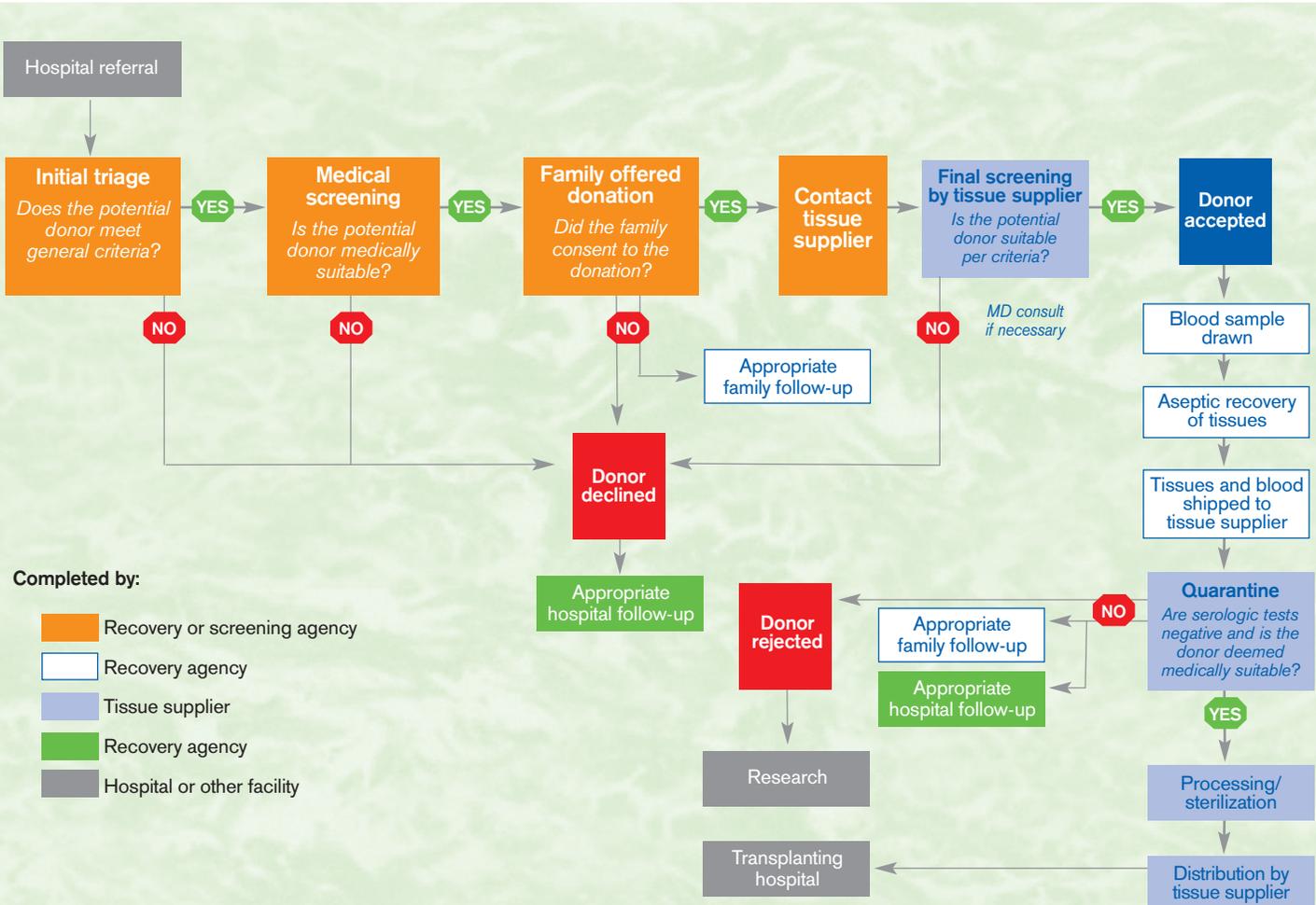
Tissue suppliers that distribute xenografts are also regulated by the FDA and these scaffolds are regulated as medical devices. Therefore, manufacturers are required to show equivalence to mesh scaffolds for their specific applications. Specific guidelines in the use of animal tissues for xenotransplantation are found at www.fda.gov/cber/gdlns/clinxeno.htm.

Tissue sourcing

Knowing the source of the tissue and how it is regulated is also important. Allografts are procured from human donors whose families have consented to tissue donation. These donors are prescreened by the tissue bank and tissue recovery must take place in hospital operating rooms or other settings such as medical examiner offices, morgues, or funeral homes that have been registered by the FDA. Environments for recovery are defined by the standard practices of the particular tissue recovery organization and tissue supplier requirements. Tissue recovery should follow written policies and procedures to reduce bioburden (microbial contamination).

The process outlined in Figure 2 for donation of allograft tissue follows the FDA requirements and AATB recommendations. It is a multiphased process with a system of checks and balances from donor screening and acceptance through recovery, processing, and distribution. This system is designed to provide the utmost level of safety by preventing the transplantation of contaminated tissue.

Figure 2. Sample Overview of Dermal Donation Process



With regard to xenografts, the FDA has set forth specific guidelines for source animal husbandry and screening, source animal facilities, procurement, and screening of xenotransplantation materials. FDA guidelines have recently been revised to emphasize risk minimization precautions appropriate to xenografts. For example, animals are procured from closed herds or colonies raised in facilities that have appropriate barriers to effectively preclude the introduction or spread of infectious agents. Samples from all xenografts are screened by direct culture for bacteria, fungi, and mycoplasma.

Donor and animal standards

Potential allograft donors should be relatively healthy individuals screened for HIV-1, HIV-2, Hepatitis B and C, exposure to toxic substances, high risk behavior, and any conditions that could compromise graft safety. Minimum requirements for donor screening and allograft processing are provided by the FDA (www.fda.gov/cber/gdlns/cadbid.htm) and are included in the current Good Tissue Practices.¹⁴ The AATB also has recommendations for donor screening/tissue processing. However, individual tissue banks are responsible for setting the minimum standards for donors and validating the process and procedures they employ.

In 2002, the Centers for Disease Control and Prevention (CDC) investigated the potential for transmission of viral and bacterial disease and found that 13 of 26 reports were caused by a single species, clostridium, and that 11 of 13 clostridium cases were sourced to a single tissue bank.¹⁵ This underscores the importance of FDA requirements and AATB recommendations with regard to donor screening and subsequent handling of tissue samples.

Animal sources for xenografts from any country or region where transmissible spongiform encephalopathy is known to be present are prohibited. The FDA guidelines were revised regarding the screening for xenografts in response to concerns raised by the public and a number of professional, scientific, medical, and advocacy groups over the risk of transmission of viral and bacterial diseases. The FDA guidelines now describe exactly how animals qualify for consideration as a tissue source. [FDA Guidelines for Industry: Source Animal, Product, Preclinical, Clinical Issues Concerning the Use of Xenotransplantation, www.fda.gov/cber/gdlns/clinxeno.htm.]

Processing and sterilization methods

Allograft and xenograft tissues should be recovered, processed, and handled under carefully controlled conditions. It is best to process biologic scaffolds in a tightly controlled clean room that observes a series of procedures designed to ensure quality control. Appropriate chemical agents should be used to clean and disinfect the tissue to inactivate the common microorganisms found on the body and skin.

Allograft scaffolds are processed using proprietary procedures where the donor skin is decellularized, removing the epidermal layer and cells. This process leaves behind an acellular dermis that is then disinfected and packaged. In addition, some allografts may undergo freeze-drying and/or a final terminal sterilization step. All tissue banks are required to design and validate their individual processing methods in accordance with the FDA current Good Tissue Practices. Nonetheless, packaging and storage requirements may vary depending on the donor standards and processing procedures that are used.

Xenografts also undergo proprietary processing techniques, which may include decellurization, cross-linking of the scaffold, and terminal sterilization. The xenografts are packaged and must meet FDA requirements for a medical device.

According to the FDA, the distinction between disinfection and sterilization is that disinfection destroys pathogenic and other types of microorganisms by thermal or chemical means, while sterilization is a process intended to remove or destroy all viable forms of microbial life, including bacterial spores, in order to achieve an acceptable level of sterilization.¹⁶

Recognized methods of sterilization include dry heat, moist heat (autoclave), ethylene oxide, ionizing radiation, and liquid chemical sterilants. Dry and moist heat sterilization methods change the structure and function of biologic materials and are therefore unsuitable for sterilization of biologic materials. Sterilization methods for biologic scaffolds include the use of ethylene oxide, gamma or e-beam radiation, and liquid chemical sterilants. Each of the methodologies used for sterilization has a different mechanism of action.

While xenografts are regulated as medical devices, most allograft tissue is classified as a Human Cell & Tissue/Product (HCT/P) by the FDA and not as a medical device. The FDA does not require a specific sterilization technique or Sterility Assurance Level (SAL) for allografts.

The effects of sterilization on the long-term strength of biologic scaffolds has not been fully examined. Therefore, questions still remain regarding how best to balance processing and sterilization of the tissue and protecting the integrity of the graft.

Packaging and storage requirements

Packaging and storage requirements of biologic scaffolds are set by the individual manufacturing company and may depend on the processing technique used. Biologic scaffolds can be freeze-dried, frozen, refrigerated, or available as ready-to-use. Freeze-dried materials need to be rehydrated before use, and this may extend time in the operating room. Some biologic scaffolds, including allografts, have been developed as ready-to-use, which adds to their convenience.

Sizing and availability

Sizing and availability of biologic scaffolds are interrelated issues that directly affect ease-of-use. When considering different biologic scaffolds, it is important to keep in mind which sizes and tissue sources are available to meet your patient's needs.

Economics

Deliberation of economic considerations regarding both allografts and xenografts should include a risk/benefit analysis covering not just the product cost, but also the financial ramifications of potential complications or less-than-expected clinical outcomes.

Patient-related considerations

Patient-related considerations in choosing allograft and xenograft scaffolds include an overall assessment of pretransplant conditions that suggest the likelihood of a smooth postoperative course with viability and host acceptance of the graft. Additionally, surgeons must be aware of patient-specific consent considerations based on religious, social, or emotional issues associated with biologic tissues (Table 2).

Table 2. Patient-Related Considerations in Choosing Biologic Scaffolds

Clinical considerations

- Prior surgical history
 - Course of recovery
 - Transplantation history
- Indication

Comorbid conditions

- Cardiovascular disease, diabetes, history of chronic infection, allergies
- History of smoking or decreased collagen metabolism
- Occupation
- High-risk behavior affecting postsurgical course

Condition of the wound

- Degree of bacterial contamination
- Complexity
- Size

Patient consent

- Potential for risk of viral and bacterial disease transmission, which may not be recognized for an extended period of time
- Religious reasons to prevent transplant
- Social/emotional issues regarding type of biologic scaffold used

CONCLUSION

Surgeons who choose to use biologic materials will benefit by understanding the key differences between biologic scaffolds.^{2,3} Allograft and xenograft scaffolds are procured and processed under separate and distinct FDA regulations. Allografts and xenografts also differ clinically—in the degree of fibroblast penetration, the manner in which remodeling occurs, and the host immunogenic response. These differences may be attributed to tissue source, various processing methodologies, and the patient's response to the implant type. Long-term studies and studies directly comparing allografts and xenografts are needed before these differences can be fully understood.

It is beyond the scope of this monograph to make specific recommendations as to the appropriate material for any given procedure. However, while synthetics are widely used, knowledge of the critical differences between allograft and xenograft biologic scaffolds will aid the surgeon in the review of ongoing research and ultimately support an educated and appropriate choice of material to best benefit the patient.

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POSTTEST QUESTIONS

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1. Xenografts and allografts differ in their species of origin, methods of processing, and tissue source.
 - a. True
 - b. False
2. Common sources of xenografts include porcine small intestine (SIS), porcine dermis, equine or bovine pericardium, and fetal bovine dermis.
 - a. True
 - b. False
3. Which of the following is NOT an essential component for effective graft healing?
 - a. Controlled remodeling
 - b. Fibroblast infiltration
 - c. Complete chemical cross-linking
 - d. Type of host response
4. Which of the following is NOT a clinical difference between biologic scaffolds?
 - a. Fibroblast penetration
 - b. The manner in which remodeling occurs
 - c. Electrical charge of the material
 - d. The avoidance of immunogenic response
5. Encapsulation is a type of host response defined as:
 - a. Connective tissue is replaced at varying rates
 - b. Neovascularization is complete
 - c. The implant is surrounded by connective tissue
 - d. More than 40%-50% of collagen is redeposited into surrounding tissue
6. The FDA regulates both allografts and xenografts using the same requirements designed to prevent disease transmission and ensure minimum standards for donors and animals procured for transplantation.
 - a. True
 - b. False
7. Which of the following statements most closely describes the American Association of Tissue Banks (AATB)?
 - a. The AATB is an agency required by the FDA to oversee the processing of all allografts by tissue banks for use in transplantation
 - b. The AATB is an agency designed to provide data to the FDA to show equivalence to mesh products
 - c. The AATB is an agency that offers voluntary accreditation of tissue banks
 - d. The AATB provides requirements regarding the procurement of tissue by tissue banks
8. Which of the following does NOT reduce the risk of transmitting a viral or bacterial diseases?
 - a. Utilization of aseptic technique/aseptic processing
 - b. Increased fibroblast penetration of the scaffold
 - c. Proper donor/animal screening
 - d. Terminal sterilization
9. Which of the following is NOT a type of host response?
 - a. Encapsulation
 - b. Mixed response
 - c. Incorporation
 - d. Infiltration
 - e. Resorption

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