SEOPF *Tissue Banking Newsletter*

Official Publication of the South-Eastern Organ Procurement Foundation

Volume 3, Number 1 | January - April 1993 | Richmond, Virginia

Current Usage, Trends and Research in Skin Grafts

Steven T. Boyce, Ph.D.
Department of Surgery, University of Cincinnati and Shriners Burns Institute
Cincinnati, Ohio

Uninjured skin provides a wide variety of protective, perceptive and regulatory functions for the human body. Protective functions result from epidermal barrier in the stratum corneum, pigment distribution at the dermal-epidermal junction, and from immune effector cells of the epidermis (Langerhans cells) and dermis (mast cells, histiocytes). Perception derives from innervation of the skin, primarily in dermis, that detects touch, temperature and pain. Other essential functions of skin are: thermoregulation by vasomotor response, evaporative cooling of perspiration, and piloerection; and excretion of salt and small organic molecules such as urea.

Deep burns destroy the physiologic functions of skin. and impose an emergent requirement for restoration of those functions. Grafting of autologous, split-thickness skin best satisfies that requirement. This procedure has greater than >90% efficacy in the hands of skilled surgeons, and accomplishes rapid wound closure. However, if burns are deep and extensive (i.e., >70% total body surface area), sufficient donor skin is not available, and wounds must be debrided and covered temporarily until autologous skin can be grafted. These requirements of massive burns have stimulated development ot skin substitutes for temporary, and/or permanent wound closure.

Temporary skin substitutes include synthetic, biosynthetic and biologic types. Synthetic skin substitutes are represented by vapor-permeable sheets of silicone rubber (Silastic™) or plastic (Op-Site™), hydrogels, or petrolatum-impregnated gauze. Bio-synthetic materials include composites of silicone, nylon mesh and collagen (BioBrane™); or collagen sponges covered with silicone. Biologic materials include tissue derivatives (collagen or fibrin), porcine xenograft, or cadaver allograft. Of these alternatives, cadaver allograft has become the temporary wound covering of choice because it adheres to the wound, vascularizes rapidly (2-3 days), provides native epidermal barrier, and is readily available. Also because of its superior physiologic properties, cadaver allograft has applications in safety testing (percutaneous absorption, cellular metabolism) of consumer products, foods and drugs. The predominant risk factor with use of cadaver allograft as a temporary skin substitute is transmission of disease and/or infection, a factor common to all allogeneic tissues.

Cadaver allograft is highly effective for temporary wound coverage, but permanent wound closure requires replacement of autologous epithelium at least, and ideally, replacement of dermis and subcutaneous tissue. In response to needs for permanent wound closure, several approaches have been taken to restore both epidermis and dermis on wounds. Epidermal substitutes include cultured epidermal keratinocytes (autologous or allogeneic), epidermal suction blisters, epidermal cell suspensions, or thin epidermal autografts. Dermal substitutes have been generated from allodermis which does not reject, collagen-basad sponges or gels populated with cultured dermal fibroblasts, or synthetic biopolymers (poly-glycolic/poly-lactic acid) populated with allogeneic fibroblasts. Although several of these models resemble skin histologically, all are avascular, and have incomplete epidermal barrier at time of grafting. To permit sufficient time for vascularization, some investigators apply dermal substitutes first, followed by grafting of epidermal substitutes 7-21 days later. This approach has accomplished wound closure, and spared donor sites, but it requires two surgical procedures to complete grafting, and more labor-intensive operative procedures. Another noteworthy approach to treatment of chronic wounds (i.e., decubitus, stasis or diabetic ulcers) is debridement and grafting with cultured allogeneic keratinocytos. Long-term healing of chronic wounds has been demonstrated by use of

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Medical Examiner's Role in Organ and Tissue Donation
The Florida Story

Joseph H. Davis, M.D.
Medical Examiner, District 11 (Miami)

Surgery is shifting gears. The "cut it off" function is being replaced by the "put it back" function. That is not to say that interest in grafting replacement tissue or organs is new, for that interest has been present long before the techniques of suitable host acceptance, and medical examiner donor source procedures, evolved. In 1912 Alexis Carrel won the Nobel Prize in medicine "for your work on vascular suture and the transplantation of organs," and "you have extended the boundaries of intervention of human surgery and proved once again that the development of an applied science of surgery follows the lessons learned from animal experimentation." (Malinin, T. L., SURGERY AND LIFE, Harcourt Brace Jovanovich, 1979, p. 52).

Cadaver tissues have been utilized for much more than autopsy determination of cause of death or the study of disease. Such material is a valuable resource in assessment of the body burden of subclinical environmental contamination by naturally occurring metals and industrial chemicals or pesticides (Stanley, J.S. PCDDs and PCDFs CHEMOSPHERE, 15, Nos. 9-12, pp. 1605-1612, 1986). The National Human Adipose Tissue Survey (NHATS) is an ongoing chemical epidemiological investigation which depends upon age and sex stratified tissue samples derived from participating strategically chosen medical examiner systems. This is an outgrowth of previous studies of pesticide effects and earlier cadaver tissue studies of trace metal variations and radioactive burdens. It is a logical conclusion that medical examiner case material would likewise be a rich source of donor material for therapeutic purposes.

Such has been the case starting with the mark of the National Pituitary Foundation whose extracts of human growth hormone were the only source for many years. Only in the past few years have chemists been able to develop a synthetic hormone suitable for therapeutic use. This was none too soon. Jakob-Kreutzfeldt virus contamination has been found in some human derived hormone preparations.

The National Pituitary Foundation, now the Growth Foundation, helped to pioneer the concept of specialized legislation to authorize the retention of pituitary tissue from medicolegal autopsies for such a worthy treatment and research function.

Concomitant with this has been the Lions Club International interest in blindness. From this national effort has arisen the political legislative and legal acceptance of corneal donations from medicolegal autopsy material.

Following along has been the concept of bone, fascial and dural tissue from cadaver to patient. Again, it is medical examiner derived tissues which constitute the main source.

The glamour stock of transplantation has been kidney, then heart, liver and now lung, which injects the question of "brain dead yet organ alive" into the harvesting procedures. Concomitant legal and ethical problems were and are the expected result of such advances in medical science a half century after Alexis Carrel won the Nobel Prize.

Why Use Medical Examiner Cases as a Resource?

Voluntary donations have not met the need for several reasons. One reason is that hospital based deaths are usually unsuitable due to disease or other contamination. The only source of potentially uncontaminated tissue is to be found in the sudden violent death population which comprises the major investigative component of a medical examiner system. The motorcycle has become the "donorcycle."

Another is the fact that medical examiners are already authorized by law to carry out the ultimate in postmortem mutilation, the autopsy, as compared with many donor procedures which involve only limited areas of the body.

Yet another are enabling acts which provide statutory authority for the medical examiner to authorize harvest of certain tissues normally removed in the course of autopsy as well as other specified tissue.

Despite the fact that medical examiners perform thousands of autopsies annually, 10 percent of a total of 137,122 deaths in Florida for the year 1991, there is still a serious nationwide shortage of donor material. Over 20,000 people await kidney transplants. About 5,000 people are waiting for a suitable cornea. Nearly 2,000 pediatric livers are needed each year (UNOS, 1992 March). The author has a granddaughter who needs a double lung transplant.

A major advance was made in Florida by the creation of the Florida Statewide Organ and Tissue Donor Consortium and the Organ Donor Coordinator's office of the Department of Health and Rehabilitative Services. There existed a spirit of

Volume 3, Number 1, January - April 1993
SEOPF *Tissue Banking Newsletter*
is published tri-annually by the
South-Eastern Organ Procurement Foundation
5004 Monument Avenue, Suite 101
Richmond, Virginia 23230

Executive Director .....Tom Armata
Editor and Circulation .....Hazel Graham
Contributors.....Steven T. Boyce, Ph.D.
Joseph H. Davis, M.D.

Next Issue: May - August 1993

Send typed copy to:
SEOPF Tissue Banking Newsletter, c/o Hazel Graham, South-Eastern Organ Procurement Foundation, 5004 Monument Avenue, Suite 101, Richmond, VA 23230

interagency cooperation to achieve supportive favorable legal decisions and medical examiner participation. Subsequently based on reports from the Consortium and a task force, legislation was enacted pertaining to a licensing system for Florida. Legislative refinements are anticipated. Current legislation clearly protects the authority of the medical examiner.

In southeast Florida, the Lions Eye Bank obtained 1,652 corneas from medical examiners, 1,060 from Dade and 592 from Broward counties respectively. Other sources contributed 1,292.

Medical examiner tissue acceptable for surgery was 92 percent. Only 20 percent of corneas from non-medical examiner sources were deemed suitable! The average age of medical examiner donor subjects was 40 years and that of the recipients was 65 years. Almost 2,009 patients received corneas from this University of Miami based eye bank, 71 percent of them in Florida.

During 1991 the University of Miami Bone and Tissue Bank collected bone from 126 cadavers of which 42 were also organ donor subjects. About 7,000 bone specimens for transplantation were distributed last year. Most of this donor material comes from the Dade and Broward Medical Examiner facilities with sources also from other counties. Medical examiner support is crucial to such an effort. According to the Department of Health and Rehabilitative Services (HRS), 10,857 allografts were made from the total cadavers harvested by the bone and tissue banks of Florida.

In Dade County the new 89,000 square feet medical examiner facility houses the Thomas L. Wolfe Memorial sterile autopsy room for the express purpose of harvest utilizing the ultimate in sterile technique. The Miami Rotary Club raised the funds to equip this facility.

Statewide over 286 viable cadaver tissues were collected in 1991 including 114 hearts, 479 kidneys, 160 livers, 36 pancreatic tissues and so forth (Association of Organ Procurement Organizations).

Problems on the Horizon – Their Prevention

Florida medical examiners can be proud of their compliance with these worthy programs. However, suitable cases may be missed due to:

1. Lack of complete integration of harvesting personnel with medical examiner case flow. However, this has improved steadily.
2. Inability to determine or track next-of-kin in a timely manner in many cases.
3. Lack of public education leading to lack of acceptance of the concept. There is pronounced variation of donation permission amongst different ethnic groups. Some high use groups are low in donor permits.
4. Lack of critical legislation in some areas such as standards on imported tissue.
5. Not yet complete harmony in the professions occasioned by turf competition.
6. And, variations in medical examiner concurrence in some types of cases.

Medical examiners should be extremely critical of any program if there appears any taint or suspicion of unethical practice. This is one reason that the Medical Examiners Commission of Florida is represented on the HRS Task Force. The Attorney General also sits on the Medical Examiners Commission which provides a useful opportunity for oversight.

Excellent standards of quality control for harvest procedures and specimen preparation must not be subverted for price advantage. There is much to be said for sterile autopsy harvest procedures and little to be said for unsterile techniques other than price. This is especially so when Jakob-Kreutzfeldt disease, rabies and other contagious diseases have been transmitted due to questionable harvest and processing procedures. The ubiquitous HIV infections, common to certain subsets of medical examiner case material, are a very serious consideration. The harvesting protocol must include a meticulous medical examiner autopsy and serological study in addition to the donor tissue processing component.

Accordingly, it behooves medical examiners to become familiar with the various techniques of harvest, the processing of tissues, and the distribution systems in order that medical examiners be assured that the cooperation they display in the transplant programs is followed by the highest possible level of ethical and quality standards.

Human cadaver tissue transplantation must always remain a public trust, never a business.

SEOPF Tissue Banking Workshop a Great Success

The SEOPF Tissue Banking Workshop, "Current Issues in Tissue Banking: A Users Perspective" was a bone smashing success in Lake Buena Vista, Florida on January 13, 1993. Approximately 60 attendees enjoyed a review of current usage of tissue bank grafts in various clinical arenas organized by the Bone and Tissue Committee and moderated by Dr. Mitchell Goldman of University of Tennessee, Knoxville.

Dr. Hugh Morris of Florida Hospital reviewed current therapy of replacement of the hip and the use of a variety of bone grafts for that purpose. Steven Boyce of the Shriner's Burn Institute in Cincinnati, Ohio, reviewed the broad area of ongoing research in skin grafting and the use of various skin grafts in burn therapy. David Butler, PhD of the University of Cincinnati introduced some new concepts in the effects of irradiation on bone. Dr. William Angel of St Joseph's Heart Institute in Tampa, Florida, reviewed the indications, preparation, and implantation of allograft cardiac valves. He gave the meeting some tips on how best to prepare the grafts and predicted that the usage of cardiac allografts would increase.

Bone grafts in spinal surgery was the topic discussed by Mark Brown, MD, PhD, of the University of Miami School of Medicine. He gave a comprehensive review of how bone grafts are utilized in the repair of various spinal defects. Gary Friedlander of Yale University gave an update on the biology of bone grafts. Of note was the discussion by Hans Burchart, PhD, on whether or not tissue banking was safe. Concern for infection and transmission of disease was obviously the foremost aspect of this discussion. After that, Dr. Burchart talked about profit vs. nonprofit. He briefly discussed the nuances which make "not for profit" organizations seem to edge closely to the "for profit" arena.

All in all, it was a very interesting meeting and the subsequent reviews were excellent with special thanks to Dr. Malinin, Ed Robb and to CryoLife for their support.

Skin Grafts . . .

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cultured epidermal allografts, but it is also understood that allogeneic cells do not persist on wounds longer than 2-3 months. Therefore, the mechanisam of action of cultured epidermal allografts is believed to be paracrine delivery of keratinocyte cytokines and attachment factors that condition the wound to allow resurfacing of by autologous epidermis from the wound perimeter.

Banking of skin substitutes by cryopreservation is well established for cadaver allograft. This technique, and others (i.e., freeze-drying, short-term refrigeration) are directly applicable to most experimental skin substitutes. If skin substitutes containing cultured cells are proven effective, it may be expected that cell and tissue culture will be integrated into tissue banking as standard methods. Separate and combined use of allodermis and keratinocytos may also be expected to continue in the future, because these materials have the greatest biologic homology with uninjured, native skin. As alternative materials are demonstrated to be safe, efficacious and advantageous over split-thickness skin grafting, tissue banking of skin substitutes will expand and diversify in response to demand for cultured cells and tissue derivatives for treatment of acute and chronic skin wounds. However, establishment of new therapeutic standards for skin wound healing will require regulatory guidelines that assure the public health and welfare are maintained. These guidelines will include: a) protection against disease transmission from the donor to the recipient (pathogen testing), and to universal precautions (i.e., protective clothing, sterile procurement) for the tissue bank staff; b) evaluation of cost effectiveness; and c) determination of reduced mortality or long-term morbidity to patients. Although rigorous safety guidelines exist for tissue banking, evaluations of cost-effectiveness and medical benefits will depend on specific protocols being studied. With completion of comprehensive multicenter studies that satisfy regulatory requirements, advances in treatment of skin wounds are virtually certain to influence the practices of skin and tissue banking. Procurement of cadaver skin by contemporary standards and procedures provides a foundation for innovations that will redefine wound care in the future.

SOUTH-EASTERN ORGAN PROCUREMENT FOUNDATION
5004 Monument Avenue, Suite 101
Richmond, Virginia 23230