

Dr. Chris Carr's Critical Care Notes  
Vanderbilt Regional Burn Center

## CULTURE EPIDERMAL AUTOGRAFTS (CEA)

Hello Burn Team,

JOHN DOE is getting CEA tomorrow. I was not able to attend the inservice today so please consider this information supplemental to the inservice or a repeat of it. My sources for the information are 'Total Burn Care' by Herndon, discussions with Dr. Guy, and Genzyme's literature regarding the CEA product. Genzyme is the company that cultures the skin and creates the CEA. It is very, very expensive!

The ultimate principle and goal of treating burns is to excise dead tissue and obtain wound closure. The skin is our largest organ and violation of its protective barrier has many potential complications as we experience daily in the Burn Unit. 'Wound Closure' can take many forms. Superficial burns heal primarily which is optimal for the patient. Deeper burns require removal of the burned (dead) tissue and closure with other strategies (Autograft, Allograft, Xenograft, and the use of other products such as Integra, Alloderm, Biobrane, Acticoat, etc.). Ultimately, we prefer to obtain closure of all wounds with the patient's own skin in the form of Autografting. In very large burns when there is not enough donor site to harvest for closure of excised burns, we need another strategy.

Applying CEA (Cultured Epidermal Allograft or 'Epicel') is a strategy that permits potential closure of such large burns. While it is a strategy, it is not perfect and grafting of CEA itself is associated with complications. Failure of graft take with CEA is not uncommon and the healing process occurs over a longer period of time than autografts. The CEA is prone to shearing and blistering over many months.

CEA is 2-8 cell layers thick so it is like applying tissue paper to the wound. No wonder it is prone to shear injury and that it is associated with blistering. It is also not nearly as resistant to wound infection as autograft. So the fact that Moynihan had positive cultures (indicates colonization not invasive tissue infection which is more of a clinical diagnosis) from his torso swabs is a big deal; it is also one of the reasons that Dr. Guy changed his wound care to Silver Nitrate.

Because CEA is so prone to shear injury, it is primarily used on ANTERIOR surfaces. Application to Posterior surfaces is more likely to cause injury and failed grafting of the CEA.

For patients with very large burns, the possibility of using CEA must be considered early since skin biopsies must be sent to the company for culturing of the keratinocytes which takes several weeks. The biopsies are taken from spared areas of the patient's skin that are uninvolved by burn. The company requires 2 skin biopsies measuring 2 x 6 cm which are significant in size and can be difficult to close depending on the area that is biopsied.

From a financial standpoint, it is a bit like medical gambling. The company demands a certain amount of money up front to start the process of culturing and growing the skin cells. Yet, the severely burned patient must survive for several weeks in order to benefit from the CEA product. And even if the patient 'survives', the degree of 'survival' or morbidity at the time of the CEA grafting likely influences outcome.

CEA is actually considered by the FDA as a Xenotransplantation product 'because it is

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manufactured by co-cultivation with proliferation-arrested mouse, 3T3, fibroblast feeder cells<sup>1</sup>.

CEA is authorized by Federal Law for use in patients who have deep dermal or full thickness burns comprising a TBSA of >/- 30%.

Contraindications for use of CEA include (from Genzyme information):

1. Hypersensitivity to agents used in manufacturing CEA
2. CEA is cultured in media containing Vancomycin & Amikacin; Amphotericin is included if indicated by patient history. Therefore, patients with known allergic reactions to these antimicrobial agents should not get CEA.
3. CEA should not be used in patients with known sensitivities to materials of bovine or murine origin. (I guess ya gotta work with some cows and mice to figure this one out.)
4. Contraindicated for use in Clinically Infected wounds.

Discontinuation of CEA use is indicated in patients who demonstrate allergic reactions causing anaphylaxis, hemolysis, Antigen/Antibody complex formation, or a cell-mediated/delayed immune response.

\*\*'Hibiclense (chlorhexidine gluconate) should not be used to treat wound bed infections in patients who have received, or are expected to receive, Epicel (CEA).' Hibiclense is cytotoxic to the cultured keratinocytes.

'Epicel is more susceptible to wound bed conditions and bacterial colonization than meshed split-thickness autografts.' (Genzyme literature)

It is believed, but has not been intensively studied, that the application of a dermal substitute enhances the success of CEA grafting. Just as its name implies, Cultured Epidermal Allograft, contains epidermis cells--keratinocytes--only. Genzyme quotes 'The use of a dermal substitute may improve final graft take, however the use of Epicel with dermal substitutes has not been studied'. If Cadaver allograft is used as a dermal substitute than the Epidermal layer of the cadaver allograft must be removed prior to the application of CEA. This is difficult since it would be very easy to debride the allograft dermis as well!! The technique of removal of the cadaver epidermis varies by burn center but may include strategies using the dermatome if the cadaver allograft is firmly adherent or dermabrasion.

CEA is supplied as sheets of cultured cells attached to a backing of petrolatum gauze which serves to support and protect the autograft during transport, during grafting, and during the early Post-Grafting period. Upon application, handling of the CEA is kept to a minimum and it should not be moved across the surface (=shear) of the wound once applied. Once all the grafts are applied, they are further secured with staples or sutures. After application, a single layer of sterile coarse mesh gauze is placed over the supporting petrolatum gauze of the grafts; the gauze is stapled in place and left undisturbed for 7-10 days (Genzyme literature). 4-5 layers of absorbent gauze is applied as a secondary outer dressing.

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Postoperatively, mechanical trauma and friction must be avoided = shear injury to the CEA. The outer absorbent dressing should be changed at least QD preventing accumulation of fluid and bacteria, but the underlying sterile coarse mesh gauze and CEA should not be disrupted. The outer absorbent dressings can be soaked in an antibiotic solution prior to application (this solution should not include acetic acid, clostrimazole, miconazole, or AK-Spore HC which have inhibitory effects on CEA).

'7-10 days after grafting, the coarse mesh and petrolatum gauze can normally be teased away from the wound bed. The coarse mesh and petrolatum gauze should be soaked in saline or Shurclens to facilitate removal. If the petrolatum gauze is firmly adherent, the graft should be rewrapped with the gauze left in place. Attempt to remove the petrolatum gauze again in several days.' (Genzyme instructions)

After graft take has been established, bathing with mild soaps and moisturizing with mild lotions is recommended, just as we do with burn wounds that are autografted. Pressure Garments are used beginning approximately 6 weeks post grafting--another common therapy we use in clinic during follow-up of autografted patients.

I know this is relatively detailed information about only one procedure. However, the CEA grafting tomorrow is relatively rare and the pre, intraop, and postop treatment and wound care we provide significantly determines the success of CEA grafting. We take care of so many wounds in the Burn Unit that it is easy to take for granted the importance of the wound care that is provided by every member of the team. The significance of this care needs to be magnified with CEA grafting.

Tissue engineering is a rapidly advancing field. Hopefully someday we will have tissue alternatives or 'Engineered Skin Substitutes' (?real skin with dermis & epidermis grown from each patient's own cells!!) that do not have the disadvantages of CEA.

If you can spare 8.5 minutes, go onto YouTube and search for 'Tissue Regeneration' and watch the CBS documentary on the topic. It is very, very impressive.

Have a good evening!

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