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A paradigm for a skin graft substitute*

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ABSTRACT

Skin grafts have remained relatively unchanged since their introduction as a medical treatment for burns/wounds. This paper seeks to open an academic discussion as to whether their use-by date has now been passed. A skin graft substitute is described in a paradigm using fine leaf gelatine sheets which inherently possess several distinct advantages including, discarding the harvest of autologous tissue from patient donor sites. A clinical study will be needed to determine its suitability taken together with the understanding that experimental animal studies may not provide unequivocal answers to its *in situ* modus operandi.

Keywords: Skin Grafts; Guided Tissue Regeneration; Autologous Cell Spraying

1. INTRODUCTION

Skin grafts were introduced in 1869 by Reverdin [1] and improved upon by Blair and Brown, 1929 [2] with the introduction of split-thickness skin grafting [3]. Their shortcomings are well documented and whether they work as intended, that is "take" or not, the healing of painful donor sites still needs to be addressed. Standard clinical practice dictates that all burns/wounds should be covered to prevent the advent of infection. In modern times, the introduction of cultured skin substitutes and cultured epithelial autografts/allografts (CEAs) has sought to alleviate the need for skin grafts especially in patients whose total surface body area (TSBA) is so wholly affected by their injuries that the garnering of an autologous skin graft whether full- or split-thickness is not a viable clinical proposition.

This paper seeks to kick start a reconsideration of skin grafts and introduces a new paradigm which it is hoped will be recognized on its merits for offering a readily available, off-the-shelf, graft substitute which is easy to use, is cheap, and can be re-applied by both medical and nursing staff as treatment gets underway. Also, it expands on the principles described in the author's previous report on guided tissue regeneration of the human epidermis [4].

2. THE PARADIGM

It is well known there is a clinical precedent for using gelatin sponges to staunch bleeding. Using that fact as a springboard leads to the thought of using *fine leaf gelatine sheets* as a skin graft substitute. At this juncture, the required thickness of the individual sheet is uncertain. It might need to be slightly thicker than the sheets found in the baking goods aisle of supermarkets being sold under commercial brand names, e.g. Dr Oetker™ *fine leaf gelatine sheets*. A sheet weighs approximately 2.5 grams (Silver grade/160 Bloom) and is Type A gelatin derived from pork skin (See www.modernistpantry.com/gelatin-sheets-silver.html [5]). Individual sheets can be manufactured with fine perforations embedded in each sheet to allow for an air flow over the damaged tissue. On deploying, each flexible sheet (can be cut with a pair of surgical scissors for any required size) will be laid on a sterile dental wax plate and subjected to:

1) A fine spray of a suitable mixture of lightweight antibiotics to both sides which will provide a measure of wettability to allow,

2) Thorough dusting (and subsequent adherence) of pure, sterile, corn starch granules on the total surface area of both sides of the sheet; any excess of which will be gently shaken off.

3) Application to the recipient area of the wound/burn site insuring that additional sheets will overlap half the width of the preceding sheet. It is expected that a lightweight gauze dressing will be gently overlaid with no pressure applied and their ends secured with surgical

*Disclosure: This paradigm was not developed on any University premises or with the involvement of any University staff. The addition of a spray-on percentage of oil of cloves solution to provide, hopefully, a measure of pain relief is not described herein but is included in UK and USA patent applications in the author's name.

staples.

4) It is to be hoped that any seepage will be absorbed by the overlapping fine leaf gelatine sheets as well as the corn starch granules and the gauze dressing. Furthermore, with the passage of time and continuous natural airflow, these covering fine leaf gelatine sheets should naturally shrivel and be subject to easy removal.

5) New sheets, prepared as described in 1) and 2) above, will be applied to the wound/burn site. These will have larger perforations at spaced intervals to permit the cell spraying of an autologous mixture of papillary and reticular fibroblasts followed by the spraying on of autologous epidermal brown rosettes [4], provided a postage stamp size of the patient's own skin tissue can be utilized in the tissue culture laboratory.

6) All fine leaf gelatine sheets used in this paradigm may also be embedded with suitable visible markers for bacterial and other contaminants allowing medical/nursing staff to see at first glance whether a wound/burn bed has become infected during treatment.

3. DISCUSSION

At the outset, it must be emphasized that these are a set of proposals, bolstered by an underlay of proven scientific principles, being put forward for consideration by the medical community. It is also envisaged that this framework will be improved upon. Certain matters are of necessity, simplified in the absence of a definitive clinical study.

It is worth recalling Turing's words in 1950 [6] that "no engineer or chemist claims to be able to produce a material which is indistinguishable from human skin" …. *in spite of modern efforts* (author's italics). Present day skin cell constructs do not reproduce the epidermal brown rosettes *in vitro* and no skin patches were formulated with that intra-epidermal micro pattern in mind. Both CEAs and cultured skin substitutes are expensive to produce and have their drawbacks e.g. incurring hypertrophic scarring and pigmentation problems in treatment of burns [7].

Describing her stay (as a Surgical Fellow at Queen Victoria Hospital, East Grinstead, England) in a published report [8], an illustration of the use of a dermatome to obtain a skin graft from a patient's thigh was pictured (her Figures 1 and 2 on pages 8, 10). This raises the following question: "Why are the empirical surgical lines of the human body namely, Langer's lines, being so totally disregarded?" (See [9], Viewpoint 4; Figure 3(a): page 562; also see [10] and references therein).

Most trauma surgeons will be hard pressed to answer the question: "What is the precise weight, in grams, of the skin graft you are about to deploy?" It has not been considered that the weight of skin grafts in whatever shape or size, plus the application of dressings, might be leading to the "mechanical loading" of damaged tissue. The proposed covering sheets are too lightweight for this consideration to be advanced any further.

Secondly, there is total dependence on plasmatic imbibition for nutritional maintenance of the applied skin graft. The sheets with their cornstarch content will provide an additional carbohydrate source of nutrition for the natural regeneration of the underlying tissue as well as allowing for a measure of absorbance of wound seepage and drainage.

The dermis is not rebuilt as a consequence of skin graft overlay probably because the uppermost layer of the dermis, the papillary dermis layer of the graft is left relatively intact in both full- and split-thickness skin grafts (STSGs). There is therefore, no intercellular interaction or participation of this cellular layer in the subcutaneous architectural rebuild of damaged tissue.

As a result of the successful regeneration of the human epidermis [4], considerations arose as to (a) whether the cornstarch granule layer(s) was/were providing an actual *physical partition* between the remnants of the epidermis and the damaged dermis, possibly fooling the leading edge of wound epithelium into adopting a normal, tissue regenerative mode of conduct via cell signaling and other intrinsic mechanisms as if there were in existence an *in situ* dermal-epidermal junction (where none exists) and/or (b) whether their presence (the cornstarch granules) were hijacking the normal cascade of wound healing phases by providing a go-ahead for the impedance and/or period shortening of the tissue inflammation phase of wound healing. It is doubtful whether animal studies would provide fulsome answers to these speculations. Trials on soft tissue, *chronic non-healing wounds* using this paradigm as a clinical procedure would be of particular interest.

It is to be hoped that the similar sort of service as that previously seen in the tissue repair of human epidermis [4] will be provided by the cornstarch layer(s) on the applied sheets leading to the guided tissue regeneration of the wounded/burnt skin tissue without undue scarring and pigmentation problems. The exact steps need to be worked out as to when the stoppage of applied sheets (as in step (3 previously) should occur, to be replaced by step 5) and cell spraying of both autologous dermal and epidermal cells, respectively.

In summary, a biodegradable nutritional source/cell scaffold and lightweight antibiotics are being applied to the wound/burn site via appropriate flexible sheets of *fine leaf gelatine*. These sheets have been used in the preparation of culinary desserts and to provide the gel coating of prescription drug capsules for decades without any contraindications. If manufactured from bone gelatin or from pig skin, official committees have ruled that there is very little chance of transmission of animal diseases to

wound beds [11,12]. Hence, this denatured collagen material is also being manufactured as sponges and used clinically to staunch bleeding. It is expected that the cornstarch granules will adhere to the moist wound/burn site. Later on, as clinically required, cell spraying of an autologous mixture of dermal fibroblasts followed by autologous epidermal brown rosettes will be executed. It is paramount that the dressings used are lightweight and not weighing down on the recipient wound/burn site.

It is fervently longed that no future photograph of a healed, burnt buttock would ever again display a rather prominent meshed pattern, a wholly disagreeable cosmetic outcome, as can be seen on the website [13] www.avitamedical.com under the 2010 heading, "*Using Re-cell™ kit to treat flame burn in combination with wide mesh graft*". It should be noted that any *whole skin tissue* (*with the possible exception of neonatal foreskin*) processed by this kit does *not* take into account the fact that the basal layer of the epidermis may contain *the beginnings of a basal cell lesion* (prior to it manifesting itself on the outer skin surface); see Figure 3, [4]. There is therefore a definite chance of unknowingly inserting carcinogenic vectors into the patient's wound bed.

Well-padded dressings, immobilization periods, clinical worry about shear forces on the skin graft, meshing machines may all be confined to historical medical archives if this paradigm were to prove its worth.

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