Published online: 2019-11-27

Review Article

Skin substitutes: An Indian perspective

A. K. Singh, Y. R. Shenoy[1]

Department of Plastic and Reconstructive surgery, CSMMU, Lucknow, [1]Plastic Surgery, NRS Medical College, Kolkata, India

Address for correspondence: Dr. Singh AK, Department of Plastic Surgery, CSMMU, Chowk, Lucknow – 226 003, Uttar Pradesh, India.
E-mail: singhkarun@hotmail.com

ABSTRACT

There have been numerous alternatives developed to replace skin. These can either be permanent substitutes or temporary substitutes, which need to be replaced later by autologous grafts. These have been tried in recent times as an attempt to reduce the need or in the case of permanent substitutes ,altogether replace autologous skin grafts. However till date no ideal skin substitute has been developed. Various factors have to be considered while choosing one of these substitutes. In a developing country like India awareness and availability of these skin substitutes is not adequate considering the volume of cases that require this modality of treatment. Also there are skin substitutes developed in our country that need to be highlighted. This article is an attempt to review the vast array of skin substitutes that have been developed and consider their utility and feasibility for developing countries.

KEY WORDS

India; permanent substitutes; skin substitutes; temporary substitute

INTRODUCTION

Skin is the largest organ of the human body, it is composed of two specialized tissue layers, i.e the epidermis and the dermis. Although structurally it is a simple organ as compared to other complex organs it remains a reconstructive challenge when substantially compromised. Many alternatives to replace skin have been tried in recent times in an attempt to reduce the need for autologous skin grafts. These skin substitutes are numerous and varied, and a head-to-head comparison of the same is not possible. This article is an attempt to review the available skin substitutes with a special emphasis on their utility in patients in a developing country like India.

Access this article online

Quick Response Code:

Website: www.ijps.org

DOI: 10.4103/0970-0358.101322

The choice of skin substitute depends on many factors including the normal skin anatomy, the patient's condition, medical and surgical comorbidities, the amount of skin requiring replacement and the level of contamination of the wound. Other factors that are of importance are the visibility of the area to be covered, contour abnormalities, vascularity of the wound bed, ability to immobilize the patient postoperatively and aesthetics.[1] In a developing and varied country like India certain other factors too creep in like the therapy are cost of the skin substitute, its availability, its ease of storage, the number of operative interventions required and certain religious considerations for use of a particular substitute. After all these clinical and social factors have been adequately considered a strategy has to be formulated with the goals of early wound healing, prevention of infection, stable skin coverage, minimal or no donor site morbidities and early return to day to day function.

Until a layer of tissue mechanically similar to the integument is placed over a reconstruction site, the reconstruction is incomplete and prone to failure. In addition, primary genetic diseases of the skin present further challenges to reconstruction, making bioengineered skin substitutes a solution that has received much attention lately.

Skin substitutes are a heterogeneous group of substances that aid in the temporary or permanent closure of many types of wounds, depending on wound coverage that vary based on wound and product characteristics. Although these products are not substitutes for adequate surgical debridement or standard surgical therapies such as flap coverage, they offer alternatives when standard therapies are not desirable. Skin substitutes provide reconstructive solutions that may be superior to other available methods because they may require a less vascularised wound bed, increase the dermal component of the healed wound, reduce or remove inhibitory factors, reduce the inflammatory response and provide rapid and safe coverage.[2] Also these avoid donor site morbidity like pain and hypertrophic scar formation. These skin substitutes are very important in cases of massive burns where autografts are insufficient to provide adequate skin cover. They also allow flexibility within the reconstructive ladder, enabling practitioners to use an approach more analogous to a reconstructive elevator, rather than a ladder. The practitioner can advance up and down the reconstructive ladder from extremes of coverage options, skipping in-between steps if desired.

No perfect or ideal skin substitute exists. There are many skin substitutes in the market, which claim to be better than the other, their claims and closeness to an ideal skin substitute characteristics are not easily quantified in individual products. Each type of product has applications, strengths and disadvantages that vary depending on the clinical scenario. The variety is so great that a true head-to-head comparison of all products is not feasible. Hence what we have attempted here is to summarise the skin substitutes in use with their advantages/disadvantages and scenarios where they may best be used.

Characteristics of an ideal skin substitute[3]

- Ability to resist infection
- Ability to withstand wound hypoxia
- Cost efficient
- Easy to prepare
- Easy to store
- Easy to use
- No antigenicity
- Long-term wound stability
- Lpidermal and dermal components
- Ability to resist shearing forces
- Widely available
- Easy to store and use

There are various ways to classify the skin substitutes. A classification was proposed based on composition as follows:[1,4]

Temporary impervious dressing materials

(a) Single layer materials
- Naturally occurring or biological dressing substitute, e.g. amniotic membrane, potato peel
- Synthetic dressing substitute, e.g. synthetic polymer sheet (Tegaderm® , Opsite®), polymer foam or spray

(b) Bi-layered tissue engineered materials, e.g. TransCyte®

Single layer durable skin substitutes

(a) Epidermal substitutes
- Cultured epithelial autograft (CEA)

(b) Dermal substitutes
- Bovine collagen sheet, e.g. Kollagen®
- Porcine collagen sheet
- Bovine dermal matrix, e.g. Matriderm®
- Human dermal matrix, e.g. Alloderm®

Composite skin substitutes

(a) Skin graft
- Xenograft
- Allograft
- Autograft

(b) Tissue engineered skin
- Apligraft®
- Dermal regeneration template, e.g. Integra®
- Biobrane®

Single layer biologic material

Human amniotic membrane

Human amniotic membrane has been used since 1910 to provide epidermal barrier function. These have now been replaced world over by porcine allografts due to the better longevity of allografts, but it is still occasionally used at present.[2]

Its advantages are that the epithelium in human amniotic membrane provides good protection from evaporative loss, as well as barrier function, whereas the fibronectin

and collagen matrix provide some dermal function. It is transparent, which offers good wound surveillance capabilities, and is minimally adherent, which facilitates dressing changes every 2 days.[5]

However the disadvantages with regards to the use of amnion are that it is difficult to obtain, prepare, and store; it must be changed frequently; and it has more significant potential for infectious disease transmission than other products.[5]

Conventionally, Amniotic Membrane is preserved wet by freezing (cryopreservation) and therefore requires dedicated storage facilities normally only found in specialist treatment centres, and which cannot easily be supported. However recently dried amniotic membrane has been developed, which solves most problems of storage and supply.[6]

Amnion is primarily used for covering partial-thickness burns until complete healing. It is particularly useful for superficial partial-thickness facial burns.

A prospective comparative study of amniotic membrane dressing versus normal saline dressing in non-healing lower limb ulcers was done in Mangalore which concluded that amnion is a good substitute for skin for treatment of non-healing ulcers.[7]

Potato peels

These have been used as temporary dressings for burn patients but are not technically skin substitutes. Potato peels and banana leaves are organic materials that are locally available in far flung rural areas and help in limiting moisture loss from burns involving large parts of the body and thus help in limiting fluid and electrolyte losses. These have to be changed regularly and run the risk of leading to infections in these patients.[8]

Studies show the suitability of potato peel as a burn wound dressing in developing countries. Clinical trials have demonstrated that epithelial growth occurs under the potato peel dressing in superficial partial thickness skin loss burns. In deep partial, full skin thickness burns and in the late granulating burn wound the results are not so favourable and other substitutes must be used.[8]

The use of these agents is limited only to patients or centres with no access to other suitable skin substitutes. Also in the Indian scenario these substances are sometimes the only substitutes available at no or very low cost.

Boiled banana leaf

The use of boiled banana leaves as a temporary dressing for burns was started in 1996. The pain during dressing change, feeling of comfort and ease of handling dressing are more than the potato peel dressings.[9] These dressings are used mainly in partial thickness burns.

Banana plants can be easily grown. The leaves of banana are large, offering larger surface area to cover larger wounds than possible by potato peels. The surface is non-adherent, waxy and cool. The dressing can be prepared very easily with little training.[9] These dressings are also cheap to prepare and thus have a huge role to play in developing countries where there is a huge requirement for affordable burn site dressings.

AlloDerm

AlloDerm (LifeCell, Branchburg, NJ) is a commercially available acellular dermal allograft processed in a proprietary fashion and is used for varied applications. AlloDerm has been studied in burn patients where it was used for deep partial- and full-thickness injuries and has allowed the use of thinner STSGs. In fact, a single-stage procedure of meshed AlloDerm placement at the time of skin grafting was shown to be a successful reconstruction strategy. AlloDerm-grafted burns also showed less scarring, a property possibly related to its ability to act as an adhesion barrier. Although acellular dermal allografts were originally intended only for the treatment of skin defects, but their ability to reconstruct other fibrous tissue of the body has been used for reconstruction of other tissues like the abdominal wall in many surgical specialties.[10]

AlloDerm requires no special refrigeration or freezing for storage and has a shelf life of 2 years. Although there is a theoretical disadvantage in that it is human donor tissue and therefore bears a small risk of infectious disease transmission.[10]

Alloderm at present is available in India although availability is at present restricted to major cities and cost is restrictive.

Bi-layered substitutes

TransCyte

TransCyte® is a human fibroblast-derived temporary skin substitute consisting of a polymer membrane and neonatal human fibroblast cells cultured under aseptic conditions *in vitro* on a nylon mesh.[11]

Prior to cell growth, this nylon mesh is coated with porcine dermal collagen and bonded to a polymer membrane (silicone). This membrane provides a transparent synthetic epidermis when applied. As fibroblasts proliferate within the nylon mesh, they secrete human dermal collagen, matrix proteins and growth factors. Following freezing, no cellular metabolic activity remains; however, the tissue matrix and bound growth factors are left intact.[11]

The human fibroblast-derived temporary skin substitute provides a temporary protective barrier and needs to be replaced by autografts at a later stage.

TransCyte at present is available for use in major cities in India.

Apligraf

Apligraf (Graftskin; Organogenesis, Inc, Canton, MA) is a composite bi-layer product that uses a combination of bovine type I collagen gel and living neonatal fibroblasts as the dermal component, with a cornified epidermal layer composed of neonatal keratinocytes. It is available and ready to use and has a shelf life of 5 days. It is approved by the US FDA for chronic venous ulcers of more than 1 month's duration and diabetic lower extremity ulcers of more than 3 weeks' duration. It can also be used with meshed STSGs.[12,13]

This is not available in India at present and hence its use is not possible at present.

Composite skin substitutes

These contain both dermal and epidermal elements

Xenografts

Xenografts are tissues from one Species used as a graft on another species. It should be noted that all these xenografts are temporary grafts and the immune system of the host eventually rejects them. Hence they have to be either replaced by autografts or by other substitutes.

Xenografts have been used to provide skin coverage as early as 1500 BC.[14] Initially Frog skin was used but porcine products have now replaced this.[15,16] Xenografts used are de-epidermised and hence consists of only varying thickness of dermal tissue. Recent modifications include silver impregnation leading to longer lasting grafts to greater antimicrobial activity.[14]

These grafts are cheaper than human allografts and are more easily available. Cultural objections in the Indian Set up have prevented the use of allografts on a larger scale.

The Xenografts are useful in treatment of chronic leg ulcers, gastroschisis and omphalocoele and of course in Burn patients in whom autografts are in short supply.[15,16]

Allografts

Skin allografts have been used for ages and these can be obtained in several forms. However the situation in our country is different as there are few skin banks and there are cultural and religious inhibitions to skin donations. A fresh allograft is the best of all types these are difficult to obtain in cases of emergent needs. Also a fresh allograft is more antigenic than a processed allograft due to its increased cellularity and has the risk of transmission of infective diseases like hepatitis B and C and HIV.[17]

There are various methods which have been described to preserve skin grafts, the most commonly used methods are cryopreservation and chemical treatment with glycerol. Allografts thus treated can be stored for a long time. This makes availability less of a problem as compared with fresh skin allografts but increases the cost due to the processing and storage requirements of the same. The antigenicity and infectivity of these processed allografts is also less than their unprocessed counterparts. The reduced antigenicity delays rejection and makes them stay on the wound for a longer time helping wound healing.

The glycerol preserved allograft has lower antigenicity than the cryopreserved ones as glycerol removes the vital components of the cell and renders the cell non-viable. Also these allografts lower risk of transmissible disease due to the exposure to glycerol and higher temperatures involved in the preservation process.[17,18]

The main benefit of skin allografts is as a biological dressing, as eventually these grafts may need to be replaced by autografts in cases of large areas.

Even though it is only a biological dressing the advantages of using an allograft are many including preventing wound desiccation, prevention of infection, helping maintain better homeostasis in burn patients by reducing water, electrolyte and protein loss through the burn wound.

Allografts are useful mainly in burn patients and in small children in whom mothers skin can be used as allografts

to satisfy huge tissue requirements which are not possibly replaced by autografts from the baby.

Skin Banks in India

The first deceased donor skin allograft bank in India became functional at Lokmanya Tilak Municipal (LTM) medical college and hospital on 24th April 2000. Cryopreservation at −70°C with 15% glycerol as cryoprotectant was used for the preservation of allografts from the year 2000 to 2006. Since 2007, high-concentration glycerol preservation method developed by Euro Skin Bank is being utilized for majority of the allografts. Till 31st March 2010, skin allografts from 249 donors were utilized for 165 patients from this skin bank.[19]

Since then few other skin banks have started in Pune, Chennai, Delhi, Kolkata. But the requirement of allografts is far more than these few skin banks can fulfil. Skin Banking is a prospect which needs to be promoted and funded so that the vast difference between the demand and supply of human allografts may be decreased.

Autografts

Autografts are tissues grafted to a new position on the same individual. They are the gold standard for achieving skin coverage and all other skin substitutes are compared to autografts.

They are commonly divided into three main categories:

- Split-thickness skin grafts (STSGs)
- Full-thickness skin grafts (FTSGs)
- Cultured autologous skin.

Split-thickness skin grafts

STSGs contain the epidermis and a variable thickness of the upper layers of dermis, leaving the remaining layers of dermis in place to heal by secondary epithelialisation from the wound edges and keratinocytes within the adnexa of the deeper dermis.

These types of autografts are most commonly used to resurface large wounds. Split thickness skin grafts require less stringent wound conditions for its take as compared to Full thickness skin grafts.

Full-thickness skin grafts

FTSGs contain the epidermis and the entire dermis. These grafts are preferred in areas where significant scarring or contracture of the grafts would provide harmful aesthetic or functional consequences. Because there is a limited supply of FTSG donor sites, they are usually reserved for reconstructing wounds of the head, neck, hands and areas of the genitals and breasts.

Cultured autologous skin

Cultured autologous skin substitutes are those in which patients skin cells are used to multiply in favourable conditions in the laboratory and then implanted onto various scaffolds for use as skin substitutes.

As these cultured skin substitutes are mostly known by the name of the manufacturer we have listed the same and their advantages as claimed by the manufacturer. We have no experience of the use of these skin substitutes due to their commercial unavailability in the Indian market and prohibitively high costs of using the same at present.

The clinical work of harvesting skin specimens from patients and also later engraftment of cultured keratinocytes was performed at the Postgraduate Department of Plastic and Reconstructive Surgery, K.G. Medical University, Lucknow. This study concluded that cell culture currently is not cost-effective in the Indian scenario as the setting up of a laboratory and subsequent running entails huge costs. There is a need to develop indigenous cost-effective and economical technology for cell culture so that it is available to a greater percentage of patients. Also parallel tissue culture laboratories should be developed working in tandem with plastic surgery units.[20]

Epicel

Epicel (Genzyme Biosurgery, Cambridge, MA) is an autologous cultured keratinocyte product indicated for deep partial- and full-thickness burns of total body surface area (TBSA) greater than 30% and large congenital nevus excisions. It requires a biopsy (2 x 6 cm) from the patient. The manufacturing process then isolates, expands and cultures the autologous keratinocytes in sheets for grafting by coculturing with murine keratinocytes.[21]

The entire TBSA can be recreated (1.8 m^2) in up to 4 weeks, although the minimal preparation time for smaller surface areas is 16 days.[21]

Advantages of Epicel include the availability of autologous tissue with permanent cover from a small amount of donor tissue. This is theoretically ideal for patients with high TBSA injuries who have few or no adequate donor sites.[21]

Disadvantages of Epicel include relatively high expense, time required for preparation, fragility of the resultant skin secondary to the thinness of the epidermal grafts and a short window availability for grafting. Practically speaking, patients with high TBSA injuries have the highest potential benefit from this product.[21] At present epicel is not available for use in our country.

Laserskin

Laserskin (Fidia Advanced Biopolymers, Abano Terme, Italy) is an epidermal autograft composite using autogenous keratinocytes from the patient that are cultured in a laboratory and seeded onto membrane consisting of 100% esterified hyaluronic acid, which is laser microperforated.[22]

This product requires premanufacture biopsy of the patients for whom autogenous keratinocytes may be cultured and expanded. After approximately 10 days, autogenous keratinocytes are seeded onto the membrane and sent back to the clinical site for engraftment.[22]

Cultured skin substitute

Cultured skin substitute (CSS) is a CEA with the addition of a cultured autologous dermal layer, making it a more anatomically correct skin substitute. This product was created at the University of Cincinnati and Shriners Hospitals for Children, Cincinnati, OH, and is still in clinical trials but does represent, theoretically, the most advanced autologous skin substitute available.[23]

Culturing autologous fibroblasts and keratinocytes with collagen and glycosaminoglycan substrates creates the product. While passenger melanocytes may be present in the cultures, reports indicate that pigmentation can be uneven and unpredictable.[23]

CSSs have the potential to offer up to 60- to 70-fold expansion of donor skin.[24]

Synthetic skin substitutes

Integra® is a synthetic skin substitute that is acellular and bilaminar. It was developed as a dermal analogue composed of bovine matrix collagen and chondroitin-6-sulphate recovered by a thin layer of silastic (epidermal analogue), which controls the loss of fluids and reduces bacterial invasion.[22] The dermal matrix allows the movement of fibroblasts and capillaries from the recipient bed, thus stimulating repair with a dermal-equivalent structure. Gradually, the collagen is reabsorbed and structured into a new matrix within 3–6 weeks. After that, the silastic lamina can be removed.[25]

Integra® is mainly used for the coverage of deep wounds in full or partial thickness burns with insufficient donor material. Other possible indications are the reconstruction of tissues after excision of post-burn scarring contractures, chronic ulcers and traumatic wounds.[25]

The main advantages of this material are that it provides immediate coverage of large and extensive post-escarectomy areas, its availability, and that it reduces morbidity in donor areas due to the use of thinner grafts. In addition, it reduces the formation of hypertrophic scars (as it inhibits the inflammatory response) and provides better functional outcomes in joints and extremities. This material is also associated with good results because it forms a more elastic tissue when compared to the exclusive use of skin grafts. The main disadvantages of this material are its high cost, the requirement of proper training for its correct use and a high risk of the development of hematoma or seroma, which causes the loss of the component when applied immediately after debridement.[26]

Integra has long been known to offer reliable immediate coverage after excision of deep burns, improve take of thin epidermal autografts, decrease hypertrophic scarring by limiting the inflammatory response, show better function and range of motion of joints and extremities and offer improved cosmetic outcomes for patients.

Outside burn literature, few randomized controlled trials involving Integra exist that evaluate its efficacy. Advantages of Integra include its immediate availability for wound coverage, improved cosmesis and tissue elasticity compared with STSG alone, reduced donor site morbidity and scarring due to the use of thinner STSGs (0.005 in) and avoidance of the theoretical risk of infectious disease transmission present with allograft material. Integra may be ideal for use with autogenous cultured keratinocytes because the bilaminate substitute requires 3 weeks for maturation before it is suitable for graft take.

Disadvantages of Integra include its relative expense, learning curve for use and its higher risk for seroma/hematoma formation after initial placement because of its use on acute wounds.[26]

Biobrane®

It is a biosynthetic skin substitute composed of a bilaminated membrane formed by nylon mesh filled with type I porcine collagen (dermal analogue) and covered by a thin lamina of silicone (epidermal analogue).[27] It has small pores that allow the drainage of the transudate and is considered a semi-impermeable substitute. This material enables fibroblasts and capillaries to invade the wound and repair the dermal defect. Reepithelialisation is possible due to the presence of keratinocytes at the wound's edge. Its major indications are for the treatment of superficial and medium clean burns of partial thickness that are not caused by chemicals or petroleum-based products, the temporary coverage of donor areas in partial skin grafts and the protection of autogenous mesh grafts.[28]

Because of the large clinical experience of Biobrane since its development in 1979, Biobrane has become the standard for skin substitute coverage of thermal injuries by which other products are compared.[28]

Newer substitutes (under evaluation)

No article on skin substitutes can be complete without mention of substitutes which are under trial at present. These in the next few years may revolutionise the treatment of burns and the way skin substitutes are perceived. This list as the list of skin substitutes is endless and some of the most interesting and promising ones are given below.

The C-PVA nanofibres along with novel growth factor are promising new biomaterials that could be used as dermal substitutes for accelerated wound healing.[29] Trials are currently under way in animals and human trials are still some way off.

Adipose-derived stem cells and platelet-rich plasma are being added to skin substitutes as a method of increasing the replacement of these substitutes by native recipient cells.[30]

Indoleamine 2,3-dioxygenase-expressing skin substitutes have been tried as an effort to reduce the amount of scar formation and prevent engraftment of xenografts in the areas covered by these substitutes.[31]

Although their use in developing countries is still far off, these newer skin substitutes will offer even more options to the plastic surgeon.

CONCLUSION

Skin substitutes are a heterogeneous class of therapeutic devices that vary in their biology and application. Although there is no single perfect skin substitute, certain characteristics can be considered when evaluating alternatives.

Because no single product meets all criteria of an ideal skin substitute, each patient case requires careful evaluation to determine the most appropriate solution.

Although many acute and chronic wounds may benefit from a tailored multidisciplinary approach that utilizes one or more of the products discussed, each patient should be evaluated for other possible therapies before use of skin substitutes especially in the Indian set up where the cost of the use of these skin substitutes may be much higher.

REFERENCES

1. Kumar P. Classification of skin substitutes. Burns 2008;34:148-9.
2. Colocho G, Graham WP 3rd, Greene AE, Matheson DW, Lynch D. Human amniotic membrane as a physiologic wound dressing. Arch Surg 1974;109:370-3.
3. Shores JT, Gabriel A, Gupta S. Skin substitutes and alternatives: A review. Adv Skin Wound Care 2007;20:493-508.
4. Halim AS, Khoo TL, Yussof SJ. Biologic and synthetic skin substitutes: An overview. Indian J Plast Surg 2010; 43(Suppl):S23-8.
5. Pigeon J. Treatment of second-degree burns with amniotic membranes. Can Med Assoc J 1960;83:844-5.
6. Nakamura T, Yoshitani M, Rigby H, Fullwood NJ, Ito W, Inatomi T. Sterilized, freeze-dried amniotic membrane: A useful substrate for ocular surface reconstruction. Invest Ophthalmol Vis Sci 2004;45:93-9.
7. Hanumanthappa MB, Gopinathan S, Rithin S, Rai DD, Shetty G, Shetty K, *et al*. Amniotic membrane dressing versus normal saline dressing in non-healing lower limb ulcers: A prospective comparative study at a Teaching Hospital. Int J Biol Med Res 2012;3:1616-20.
8. Keswani MH, Patil AR. The boiled potatopeel as a burn wound dressing: A preliminary report. Burns 1985;11:220-4.
9. Gore MA, Akolekar D. Evaluation of banana leaf dressing for partial thickness burn wounds. Burns 2003;29:487-92.
10. Wainwright DJ. Use of an acellular allograft dermal matrix (Alloderm) in the management of full-thickness burns. Burns 1995;21:243-8.
11. Lukish JR, Eichelberger MR, Newman KD, Pao M, Nobuhara K, Keating M, *et al*. The use of a bioactive skin substitute decreases length of stay for pediatric burn patients. J Pediatr Surg 2001;36:1118-21.
12. Trent JF, Kirsner RS. Tissue engineered skin: Apligraf, a bi-layered living skin equivalent. Int J Clin Pract 1998;52:408-13.
13. Waymack P, Duff RG, Sabolinski M. The effect of a tissue engineered bilayered living skin analog, over meshed split-thickness autografts on the healing of excised burn wounds. The

Apligraf Burn Study Group. Burns 2000;26:609-19.
14. Haynes B. The history of burn care. In: Bosivich J, editor. The Art and Science of Burn Care. Rockville, MD: Aspen Publication; 1987. p. 3.
15. Piccola N. Use of frog skin as a temporary biologic dressing. Proc Am Burn Assoc 1992];24.
16. Chiu T, Burd A. "Xenograft" dressing in the treatment of burns. Clin Dermatol 2005;23:419-23.
17. Mat Zaad AZ, Khoo TL, Dorai AA, Halim AS. The versatility of a glycerol-preserved skin allograft as an adjunctive treatment to free flap reconstruction. Indian J Plast Surg 2009;42:95-9.
18. Khoo TL, Halim AS, Saad AZ, Dorai AA. The application of glycerol-preserved skin allograft in the treatment of burn injuries: An analysis based on indications. Burns 2010;36:897-904.
19. Gore MA, De AS. Deceased donor skin allograft banking: Response and utilization. Indian J Plast Surg 2010;43(Suppl):S114-20.
20. Agarwal R, Singh AK, Dhole TN. Early experience with autologous skin culture for wound therapy. Indian J Plast Surg 2007;40:104-6.
21. Wright KA, Nadire KB, Busto P, Tubo R, McPherson JM, Wentworth BM. Alternative delivery of keratinocytes using a polyurethane membrane and the implications for its use in the treatment of full-thickness burn injury. Burns 1998;24:7-17.
22. Lobmann R, Pittasch D, Muhlen I, Lehnert H. Autologous human keratinocytes cultured on membranes composed of benzyl ester of hyaluronic acid for grafting in nonhealing diabetic foot lesions: A pilot study. J Diabetes Complications 2003;17:199-204.
23. Harriger MD, Warden GD, Greenhalgh DG, Kagan RJ, Boyce ST. Pigmentation and microanatomy of skin regenerated from composite grafts of cultured cells and biopolymers applied to full-thickness burn wounds. Transplantation 1995;59:702-7.
24. Grzesiak JJ, Pierschbacher MD, Amodeo MF, Malaney TI, Glass JR. Enhancement of cell interactions with collagen/glycosaminoglycan matrices by RGD derivatization. Biomaterials 1997;18:1625-32.
25. Stern R, McPherson M, Longaker MT. Histologic study of artificial skin used in the treatment of full-thickness thermal injury. J Burn Care Rehabil 1990;11:7-13.
26. Jeschke MG, Rose C, Angele P, Fuchtmeier B, Nerlich MN, Bolder U. Development of new reconstructive techniques: use of Integra in combination with fibrin glue and negative-pressure therapy for reconstruction of acute and chronic wounds. Plast Reconstr Surg 2004;113:525-30.
27. Banes AJ, Compton DW, Bornhoeft J, Hicks H, Link GW, Bevin AG, *et al*. Biologic, biosynthetic, and synthetic dressings as temporary wound covers: A biochemical comparison. J Burn Care Rehabil 1986;7:96-104.
28. McHugh TP, Robson MC, Heggers JP, Phillips LG, Smith DJ Jr, McCollum MC. Therapeutic efficacy of Biobrane in partial- and full-thickness thermal injury. Surgery 1986;100:661-4.
29. Sundaramurthi D, Vasanthan KS, Kuppan P, Krishnan UM, Sethuraman S. Electrospun nanostructured chitosan-poly(vinyl alcohol) scaffolds: A biomimetic extracellular matrix as dermal substitute. Biomed Mater 2012;7:045005.
30. Trottier V, Marceau-Fortier G, Germain L, Vincent C, Fradette J. Using human adipose-derived stem/stromal cells for the production of new skin substitutes. Stem Cells 2008;26:2713-23.
31. Li Y, Tredget EE, Ghaffari A, Lin X, Kilani RT, Ghahary A. Local expression of indoleamine 2,3-dioxygenase protects engraftment of xenogeneic skin substitute. J Invest Dermatol 2006;126:128-36.

How to cite this article: Singh AK, Shenoy YR. Skin substitutes: An Indian perspective. Indian J Plast Surg 2012;45:388-95.

Source of Support: Nil, **Conflict of Interest:** None declared.