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Review Article

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SURGICAL MANAGEMENT OF VITILIGO

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INTRODUCTION

The Aim of this clinical review essay is to highlight various surgical modalities employed in the treatment of vitiligo and concisely explain the procedure of each of them along with the merits and demerits. Further, an attempt has been made to briefly compare the different procedures. Hence a literature search was done, primarily with the aid of electronic resources. Multiple databases, such as systematic reviews, PubMed, Medline as well as online journals from reputed publications were adopted for stating the facts and bibliography. Online search engine, Google Scholar, was periodically used to trace the original source of a citation. Pictures have primarily been adapted from the internet. Constant critiquing of the data, to examine and point out any bias has been endeavoured.

The pigment melanin is chiefly responsible for determining the colour of the skin.[1] Melanin is synthesised within the melanocyte and later transferred to the keratinocytes with the aid of melanosomes.[1] See FIGURE 1

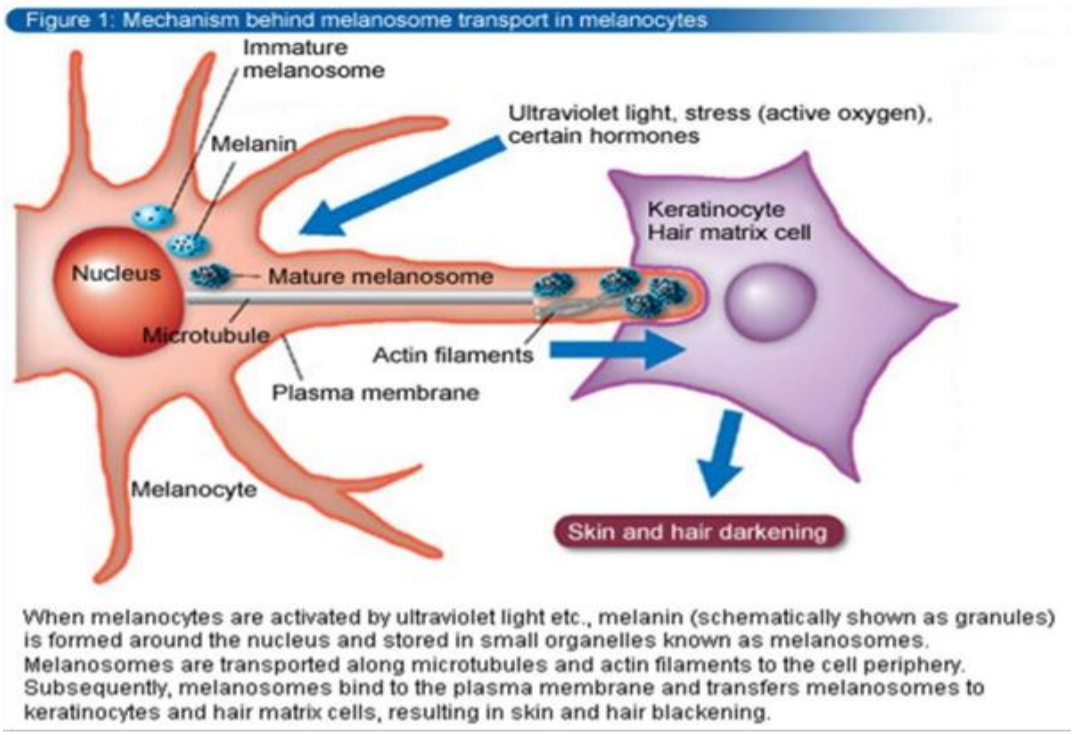


Figure 1: Mechanism of melanin transport (source: internet)

Definition: Vitiligo is best defined as an acquired, progressive disorder characterised by the absence of melanin in the skin and mucous membrane.[2] Clinically vitiligo is characterised by white macules on the skin that can vary in number and site. FIGURE 2.

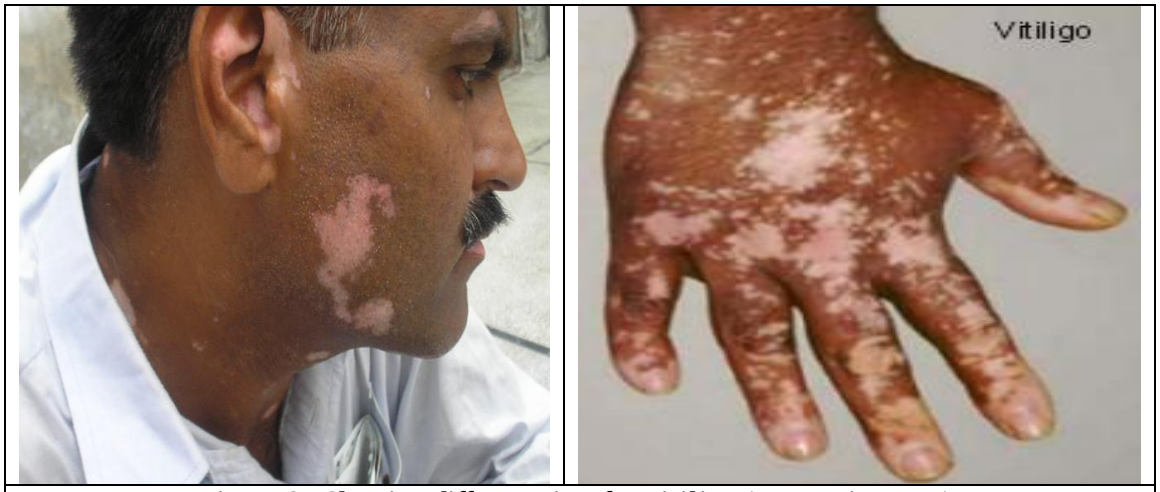


Figure 2: Showing different sites for Vitiligo (source: internet).

Aetiopathogenesis

The exact pathogenesis of vitiligo is unknown, but a few theories have been postulated. The common hypothesis for the aetiopathogenesis of vitiligo is.[3]

1. Autoimmune Hypothesis.[3]
2. Neural Hypothesis.[3]
3. Genetic Hypothesis.[3]
4. Neural Hypothesis.[3]
5. Biochemical Hypothesis.[3]
6. Intrinsic defect of structure.[3]

Figure 3: illustrates the different theories which have been postulated as a cause of vitiligo.

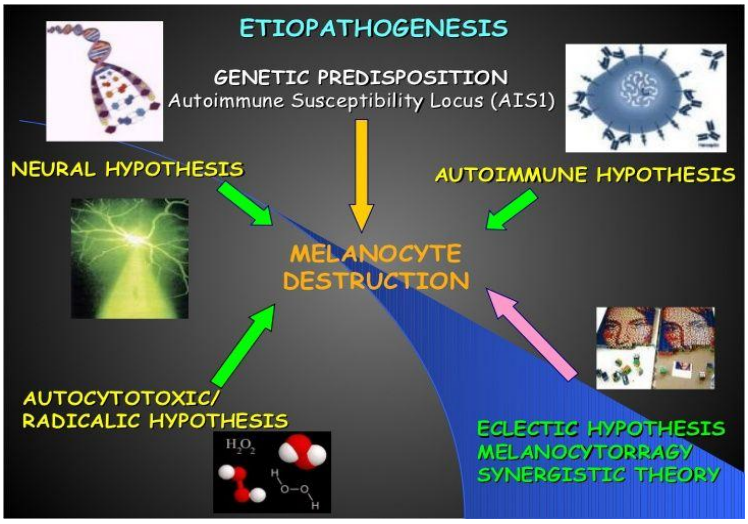


Figure 3: Causes of vitiligo (courtesy internet).

Treatment

The various options to treat vitiligo are:-

1. Medical treatment
1.1 Topical therapy
1.2 Systemic therapy
2. Systemic Phototherapy.[4]
3. Surgical Treatment

The main components of medical therapy are corticosteroids (topical and systemic).[5] and immune-modulators such as topical tacrolimus.[6]

Objectives of Surgery

There are diverse aims and objectives of surgical management of vitiligo, which can be achieved through different techniques.[7] These are:-

a. Introduction of pigments artificially to the depigmented vitiliginous patch. This is done to permanently camouflage the area.[7] Tattooing is a good example.[7]
b. Permanent removal of the depigmented patch. This is achieved by excision with primary closure.[7]
c. Grafting to augment the number of melanocytes in the affected area.[7]
d. Therapeutic wounding of the lesion by various techniques in order to stimulate the melanocytes from the periphery and the black hair follicles to induce repigmentation.[8] Different techniques such as derma-abrasion, needling, cryosurgery, laser ablation, or application of trichloroacetic acid or phenol locally are employed in order to achieve the same.[7]

Selection of candidates for Surger.[8]
Surgical intervention is indicated and useful only when the lesions become refractory and unresponsive to the medical treatment.[8] Evaluation of several factors is necessary, incase surgery becomes imperative.[8]

Stable Disease.[8]
Vitiligo is considered stable under the following circumstances.[8]

1. A lesion showing no progression for a period of at least 2 years.[8] A non-progressive lesion, however, may be active and hence, not responding to surgery.[8]
2. A lesion exhibiting spontaneous repigmentation indicates inactivity of vitiligo and hence indicated for surgery.[8]
3. The most accurate indicator of stable vitiligo is a positive minigraft test.[9] Four to five minigrafts (1.0 mm or 1.2 mm) are implanted 3 to 4 mm apart in an area of achromic.[9] lesion Repigmentation indicates a positive minigraft test.[9]
4. Kobernisation should be absent.[8] This includes new kobernisation as well as at the donor site for the minigrafting test.[8]
5. Several studies have demonstrated unilateral (segmental) vitiligo to be the most stable variant, with excellent response to surgery.[10] However, in case of stable bilateral vitiligo, only upto 50% of the patients respond well to the surgical intervention.[9]

Methods and Size of Lesions
The surgical procedure may vary depending on the area of the lesion to be treated. Simple methods such as suction epidermal grafting and minigrafting are quite beneficial for small or medium-sized lesions. However, in vitro techniques are required for defects which are quite extensive and cover a large area.[11]

Lesions on Exposed Areas
A large majority of patient want lesions, present on the exposed sites, to be treated surgically. Successful repigmentation can be achieved on anatomically refractory sites such as the dorsum of the hand and fingers.[9]

Age
Children are usually not the ideal candidates owing to the invasive nature of the procedures. Nonetheless, highly motivated preadolescents can be considered for Surgery.[8] However they may require sedation or General anesthesia.[8]

Psychological Aspects
Vitiligo has a negative impact on the self-esteem of many patients.[8] Such patients often want to undergo a surgical procedure. It is the duty of doctor to take a pragmatic view of the situation and determine the actual need of the surgical treatment. A psychological evaluation may be required in such cases.[8]

Photographic Records
It is a wise idea to keep a record of the photographs both prior to the surgery and after repigmentation has set in. It helps in ascertaining both the quality and the quantity of the repigmentation as well as adverse effects.[8] It can also safeguard the doctor against the ever-increasing number of litigations.

Expectations of the Patient and the Family
It is not always possible to achieve results in accordance with the expectations of the patients and their family.[8] The repigmented skin is sometimes not comparable with the normal skin of the individual.[8] The results also vary a lot from one patient to another. Nevertheless, it has been observed that most patients are quite satisfied with the final outcome.[8]

Achromia versus Hypopigmentation
Patients with Fitzpatrick skin types 3 to 6 are the ideal candidates for treating completely depigmented lesions. On the contrary, hypopigmented lesions do not repigment equally well. Sometimes, mild to moderate hyperpigmentation has been observed in these lesions.[8]

Donor Site and Procedure
Ideally the donor sites should not be visible.[8] The gluteal region is considered a good and viable choice in the majority of the patients.[8]

Serial Procedures and Multiple methods
More than one sitting is required in many cases to accomplish complete recovery. Also a combination of different methods is considered valuable.[12]

Contraindications[8]
Unstable vitiligo is a contraindication to Surgery.[8] Ruling out a keloidal diathesis in patients who undergo the manipulation of superficial dermis is essential.[8] Additionally, a careful evaluation should be done for the patients who were reported to develop hyperpigmentation in areas of previous trauma.[8]

Cost and Insurance Reimbursement[8]
The cost factor should be ascertained beforehand. Invitro (culture) techniques are usually more expensive. (8) Insurance reimbursement is possible only if the patient is able to establish that the procedure is not merely a cosmetic one. (8)

Types of Surgical procedures
A concise explanation of different surgical modalities is given below.

Punch Minigrafting[8]
It is a minimalistic technique requiring a very few instruments and little training.[8] A graft of 1mm size is considered ideal for the facial region.[8] For other regions a graft size of maximum size 1.2mm is sufficient.[8]

Large sized grafts of around 2.5 to 3mm result in an unsightly effect, also referred to as 'cobblestoning', due to its elevated cobblestone like appearance.[8] Therefore these are not recommended. The fact has been corroborated in quite a large number of patients.[8] In one study about 43% of the patients displayed this effect. Cobblestoning has been implicated as a key adverse effect of minigrafting when large sized grafts (2.5mm to 3mm) were used.[8] The advantage of larger grafts seems to be saving the time and easier handling of the grafts. However the demerits outweigh the merits, since the cobblestone look may be aesthetically unacceptable to the patient. The problem gets even complicated, if no repigmentation occurs. However, this problem can be overcome by using smaller sized grafts of around 1 to 1.2 mm.[8] Below is a diagrammatic illustration of the procedure.[12]

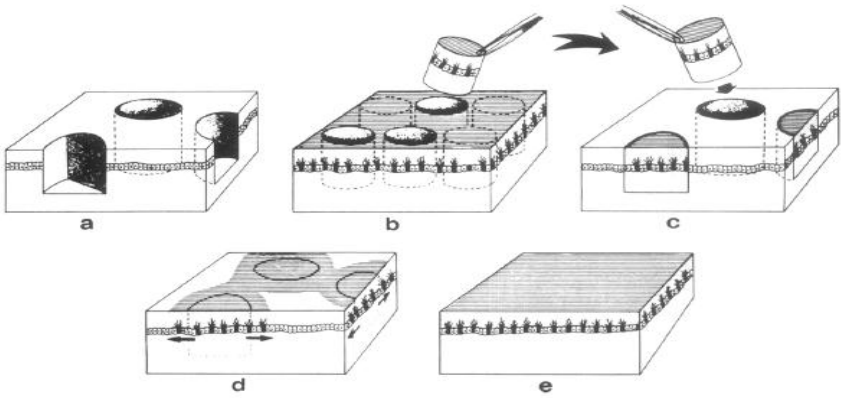


Figure 4: Steps of Punch Minigrafting (a) Punches used to prepare the recipient site. (b) Normally pigmented punches harvested from donor site. (c) Transferred to recipient area. (d) Repigmentation begins. (e) Complete repigmentation.[12]

Suction Blister Epidermal Grafting (SBEG)

The figure below illustrates the principle of Suction Blister Epidermal Grafting.[12]

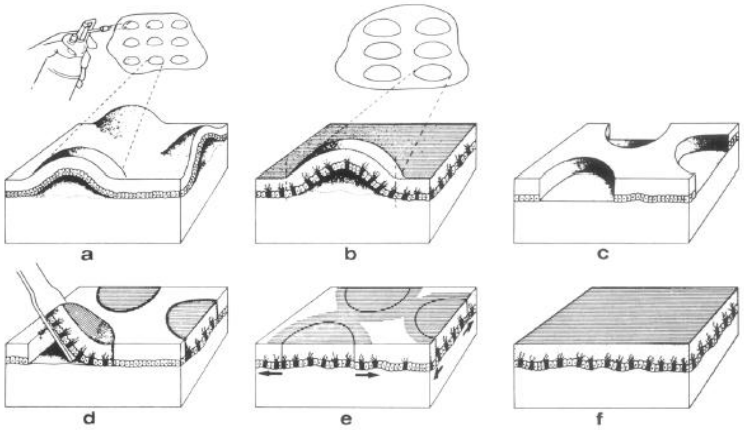


Figure 5: Steps of Suction epidermal grafting. (a) The donor epidermis being raised by liquid nitrogen. (b) Suction to obtain grafts. (c) The epidermis is denuded. (d) Grafting the normal epidermis by suction is achieved. (e) Repigmentation begins in. (f) Repigmentation continues to spread until completely achieved.[12]

Kiistala et al in 1964 were the first to report the In vivo separation of viable epidermis.[12] This was achieved by producing suction blisters by means of an angiosterrometer.[13] The drawback of this technique was that it required special equipment.[14]

A new device has been developed to create the blisters by Gupta etal.[14] A 20 ml cylindrical suction cup and 2.5 cm in diameter was connected to a 3 way tap by means of a rubber tube. A 50 ml syringe was attached to the opposite end. No attachment was done on the third end. The donor site was stretched and the suction cup was placed over it. A negative pressure (300 mmHg) was induced by pulling the plunger of the syringe and this resulted in bulging of the skin into the suction cup. A vacuum gauge was attached to the third end to measure the pressure. FIGURE 4. If the pressure was found to be inadequate, the suction was repeated.[14]

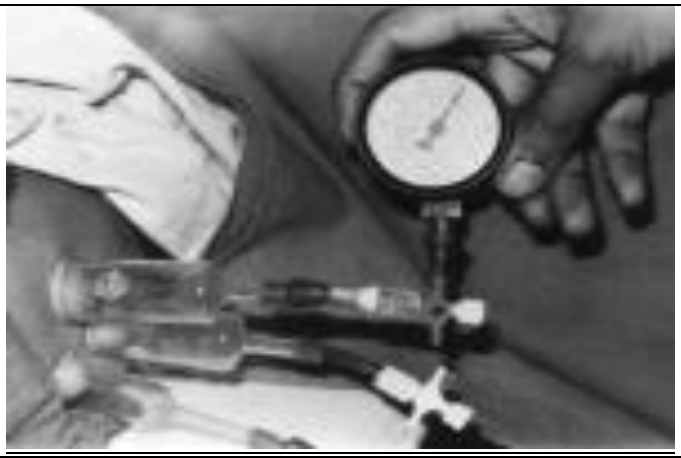


Figure 6. Measurement of the pressure by vacuum gauge.[14]

Figure 7. Suction apparatus in place.[14]

The suction cup adhered to the skin because of the negative pressure. After removing the syringe, both ends of the tap were capped. The apparatus was left in place for a period of 60-90 minutes.[14] FIG 5.

A few vesicles could be observed after some time. The pressure was further increased by 100 mmHg which resulted in coalescing of the small vesicles into large blisters. FIGURE 6.[14]

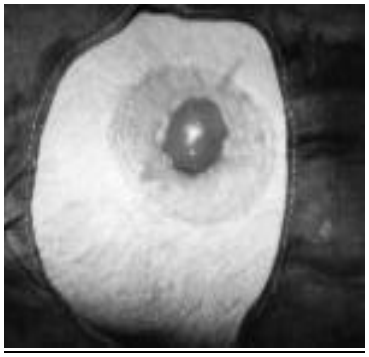


Figure 8: Blister can be seen on the skin surface.[14]

A graft (blister) of about 3 cm size was achieved by a suction cup of 2.5 mm size. Furthermore, the process could be accelerated by application of moist heat to the surrounding skin and injecting intradermal saline to the donor area prior to the procedure. Preparation of the recipient site: - in order to infiltrate the recipient site 2% lignocaine was used.[14] Derma-abrasion, by means of a manual derma-abrader, was done until punctate bleeding points could be seen.[14]

The graft was taken by cutting the roof of the blister at its periphery using an iris scissors.[14] It was everted upon a glass slide, which had been covered with an antibiotic cream.[14] The slide and the graft were then inverted over the recipient site. Jeweler's forceps was used to spread the graft over the area.[14] Non-adherent dressing was applied at both the recipient as well as the donor site. Additionally pressure bandaging was also done on the recipient site. The dressings were removed after a period of one week.[14] This particular study was done on a total of 22 patients. A total of 17 patients showed complete repigmentation by the end of 3 months. FIGURE 7. The results were not up to the mark in other patients with graft rejection being reported in two of them.[14]

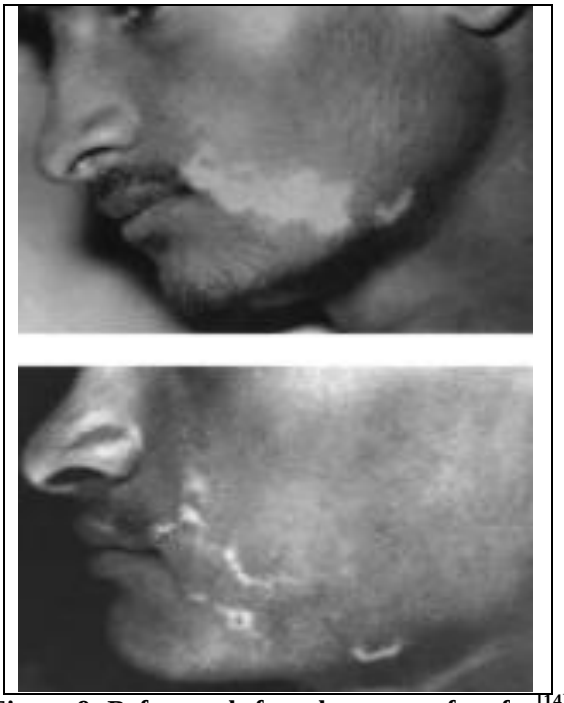


Figure 9: Before and after placement of grafts.[14]

Split thickness Skin Grafting

It is thought that the concept of skin grafting originated in India more than 2000 years ago.[15] The technique was later adopted by the west. The first successful grafting procedure on the human skin was reported in 1823 by a German doctor, Bunger The various types of grafts used in cutaneous surgery are split-thickness skin grafts (STSGs), full-thickness skin grafts (FTSGs), free cartilage grafts, and composite grafts. Split-thickness skin grafts are the ones commonly used to treat vitiligo. The different types of STSGs are given in TABLE 1.

STSG Type	Thickness, in	Durability	Cosmetic Result	Transparency	Donor Site Healing
Thin	0.005–0.012	Least	Poorer	Greatest	Faster
Medium	0.012–0.018	Greater	Better	Least	Slower
Thick	0.018–0.028				

STSG = split-thickness skin graft.

Table 1: Different types of split thickness skin grafts.

The principle of skin grafting is based on three principal biological changes.[16]
1. Graft adherence
2. Revascularisation
3. Contraction

In a Study by Aggarwal etal, 21 patients with 32 vitiligo patches were treated with STSG. 100% re-pigmentation was achieved in 22 patches and around 90-95 % in 10 of them. It took about 4-9 months for reasonable colour matching.[17] No major complications were seen. The aim of this technique, is to replace the depigmented epidermis by healthy epidermis which has been retrieved from the donor site.[17] In the earlier days a dermatome or a knife was used for the purpose of scrapping off the epidermis. Off late several new devices such as Humby's knife.[18] Silver's knife.[14] and even an air driven power dermatome have been introduced in order to harvest grafts of minutely thin grafts.[20] The operator and the assistant stretch the skin in opposite directions and a graft is harvested using any of the above mentioned instruments.[16] The bare recipient area is anaesthetised and the grafts are carefully placed over it.[16] The grafts are immobilized using a surgical adhesive or pressure bandaging which is usually removed after 7 days. Antibiotics are given prophylactically to rule out any infection postoperatively.[16]

However hyperpigmentation and millia are the commonest encountered complications.[16] The efficacy of this procedure is highest according to a systematic review conducted by Njoo etal.[21]

Fliptop Transplantation

In this modification of split thickness skin grafting, a dermo-epidermal flap is created at the recipient area, by leaving one end of the epidermis in contact with the dermis.[22]

The dermal side of the donor area is put on the dermis of the recipient area and covered with the flap. The area is then capped with cyanoacrylate glue. Dressing is applied on both the donor as well as recipient sites. After about 7 days the dressing is removed and repigmentation can be seen.[16]

A fliptop transplantation of 25 grafts on 4 patients by Thomas etal showed 88 % repigmentation.[22] The sample size of this study is however quite small.

Smashed Skin Grafting

A relatively new technique in the field of vitiligo surgery is smashed skin grafting. It is a modification of split thickness graft. The graft after being retrieved from the donor site is 'smashed ', using simple instruments like a scissor. It is then transplanted onto the donor site.[23] The illustrations given below depict the procedure.

Figure10: - Harvesting the skin.[23]

Figure11: - Smashing of the harvested skin.[23]

Figure12: Immediately after Transplantation.[23]

In a study by Krishnan etal, 26 patients were treated using the smashed skin technique. 90% of them achieved repigmentation with excellent colour matching within 6 months of the surgery.[23]

In addition to above mentioned methods, numerous cellular methods are employed to manage vitiligo.[24,25] These include:-

1. Autologous noncultured epidermal cell suspension.[26]
2. Autologous cultured pure melanocyte transplantation.[26]
3. Autologous cultured melanocyte - epidermal grafts.[26]

Autologous non cultured epidermal suspensions

These were first developed by Olsson and Juhlin.[20] It primarily consists of three principal steps.[26]

1. The recipient area is 5 to 10 times the donor area. The skin from the donor area is harvested either by split thickness graft or suction blister grafting.[26]
2. A basal layer cell suspension rich in melanocytes is prepared.[26]
3. Finally the suspension is applied over the recipient area.[26]

Furthermore the cell suspension is prepared by following steps.[26]

a) Trypsinization
b) Separation of dermis from epidermis
c) Centrifugation

The recipient site is properly cleaned and anesthetized. By means of a pippete or a syringe, the suspension is evenly spread over the entire area which is then covered by a collagen film and dressed properly.[26] To avoid postoperative infection antibiotics are prescribed.[26] Pigmentation starts after a period of 4 weeks and is complete by 3-6 months.[26] The advantage of this procedure is that it can cover very large areas and gives good results. Nonetheless there have been a few concerns about the safety of this method.

Autologous cultured pure melanocyte transplantation

In this innovative procedure, melanocytes cultured in vitro are used to treat vitiligo.[27,30] Gluteal skin is used as a donor site and collected by shave excision.[26] Typsinization is employed to separate the dermis from the epidermis. Disassociation of melanocytes and keratinocytes is achieved by vortexing.[26] The melanocytes are then seeded in a medium which contains growth factors.[26] In vitro culture of melanocytes is done for a period of 15 days to one month.[26] Once ample numbers of melanocytes are grown, they are separated from the culture plates.[26] The recipient spot is denuded by either derma-abrasion or carbon dioxide laser ablation. Transplantation of the suspension on the recipient site, on an average density of 1000-2000 melanocytes per square millimetre is the final step.[26] A gauze which has been soaked in a culture medium is used to secure the site.[26] Finally an occlusive dressing is applied for 7-10 days.[26] The advantage of this procedure is that it can cover very large areas and gives good results.[26] Nonetheless there have been a few concerns about the safety of this method. Mutation and possibility of carcinogenic changes are possible risks.[27]

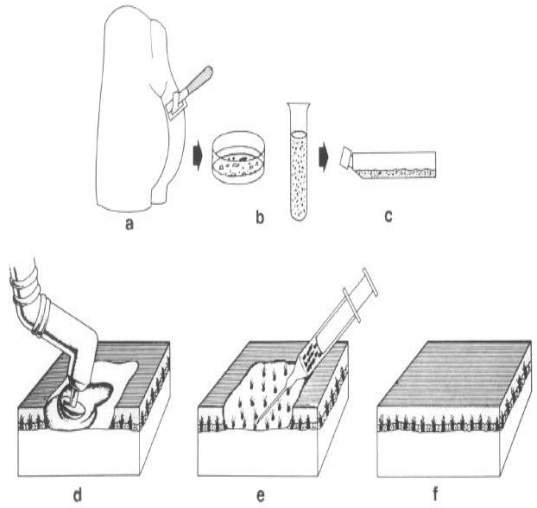


Figure 13: Showing steps of in vitro cultured melanocyte suspension. (a) Skin is harvested from gluteal region. (b) Epidermal suspension is obtained. (c) Melanocytes cultured in vitro. (d) Derma-abrasion of recipient site. (e) Inoculation of the cell suspension. (f) Gradual re-pigmentation in following months.[12]

Autologous Cultured Melanocyte-Epidermal Grafts

This technique is somewhat similar to the above mentioned technique.[31,34] However, the key difference is, that the melanocytes and keratinocytes are cultivated together. Hence eventually an epidermal sheet is cultured which is transplanted on the recipient site.[26]

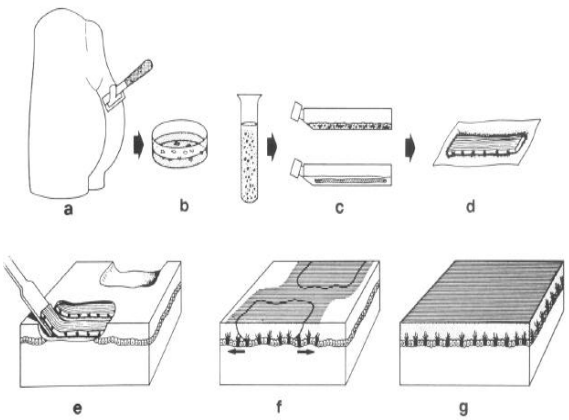
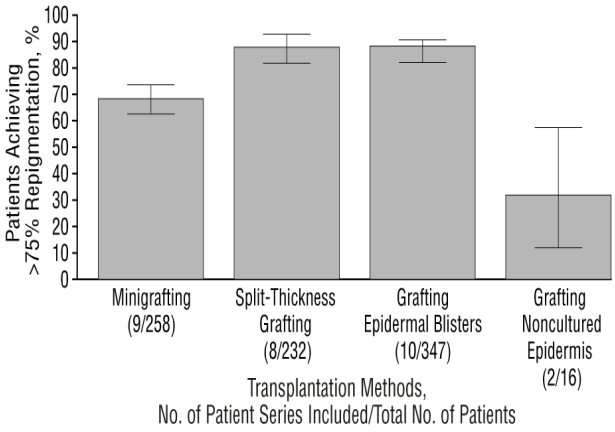


Figure 14: Steps of In vitro cultured epidermal sheets. (a) Skin fragment shaved off from donor site. (b) Epidermal suspension obtained. (c ,d) Epidermal sheet with melanocytes cultured in vitro in 21 days. (e) New epidermis planted on the recipient site. (e) Re-pigmentation starts around the graft. (f) Complete re-pigmentation.

Comparison between different modalities

A systematic review by Njoo etal to compare the efficacy of various surgical modalities was done.[21] See Figure. A total of 63 different studies were analysed.[21] Split thickness was grafting was found to be the most successful (confidence interval 95%). SBEG also showed excellent results (87% success, 95% confidence interval), while non-cultured epidermal suspension (NCES) was found to be the least efficacious. On the contrary, a comparative study between NCES and SBEG, by Budania etal, on 41 patients considered NCES to deliver superior results as compared to SBEG.[35]



	Minigrafting	Split-Thickness Grafting	Grafting Epidermal Blisters	Grafting Noncultured Epidermal Suspensions
No. of Included Patient Series:	9	8	10	2
Total No. of Patients:	258	232	347	16
Patients Successfully Grafted, %	68 (175/258) [62-74]	87 (201/232) [82-91]	87 (301/347) [83-90]	31 (5/16) [11-59]

Table 2: Graphical Comparison Of Repigmentation Following Different Surgical Techinques.[21]

CONCLUSION

In spite of a wide array of surgical options, there is no 'ideal' management or specified protocol for surgically treating the condition. The type of procedure employed, remains to be the prerogative of the clinician depending upon his preferences and competency. Having said so, surgery has emerged as a useful last resort. Proper surgical training of the dermatologists, as opposed to random hit and trial, would be a welcome step in treating this condition, which continues to be an enigma for the 'sufferers' and 'carers' alike.

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