Results

Forty patients showing vitiligo were selected from those attending the Dermatology and Andrology out-patient Clinic, Benha Faculty of Medicine, Zagazig University.

There were 11 males and 29 females aging from six years to sixty five years old, having the duration of lesion ranging from one year to 31 years.

Twenty patients presented with localized vitiligo and twenty patients with generalized vitiligo.

Their skin type ranged from type II to IV grades ,as shown in table (1)

Table 1: Description of 40 patients with vitiligo included in the present study.

No.	Sex	Age (y)	Skin type	Treated area	Duration of the lesion	Type of vitiligo
1	Female	6o	111	Fore arm	3	G
2	Female	30	111	Behinde ear	6	G
3	Male	32	1V	Face	11	G
4	Female	45	111	Dorsum of foot	7	G
5	Female	33	111	Dorsum of foot	3	L
6	Female	24	111	Dorsu of foot	7	L
7	Female	14	111	Fore arm	6	G
8	Male	6	111	Buttock	1	L
9	Female	37	111	Thigh	12	G
10	Female	18	111	Fore arm	7	G
11	Male	30	111	Face	11	G
12	Female	22	11	Dorsum of foot	10	G
13	Female	24	111	Nape	4	G
14	Male	26	111	Fore arm	2	G
15	Female	18	111	Fore arm	3	G
16	Male	8	111	Hand	6	G
17	Female	23	111	Eye brow	3	L
18	Male	34	11	Face	2	L
19	Female	36	111	Leg	1	G
20	Female	40	111	Behind ear	2	L
21	Female	28	111	Fore arm	6	L
22	Female	7	111	nape	4	G
23	Male	21	111	face	2	L
24	Female	18	111	eye brow	3	L
25	Female	40	11	thigh	3	L
26	Female	34	111	thigh	6	G
27	Female	26	111	breast	4	L
28	Female	8	111	nape	2	L
29	Female	42	111	nape	6	L
30	Female	23	1V	leg	7	L
31	Male	34	111	back	3	L
32	Male	12	111	nape	3	L
33	Female	33	111	leg	2	L
34	Male	37	11	fore arm	31	L
35	Female	65	111	fore arm	6	G
36	Female	32	111	nape	6	L
37	Female	22	111	leg	4	G
38	Female	37	111	leg+hand	11	G
39	Female	18	111	leg	2	G
40	Male	38	111	abdomen	1	L

G = generalized L = localized

According to our follow up we can summarize the course of repigmentation as follows:

* As regard the repigmentation in the patches treated by 5-flourouracil on dermabraded area . At the second day erythema, edema and erosion appeared, at the fifth or sixth day a crust is formed which fall out by itself leaving a clear translucent membrane. Moderate erythema and edema were seen in the surrounding normal skin. The treatment was stopped at the tenth day as the whole dermal surface of the treated area was exposed.

Epithelialization was completed within 10 days after treatment was stopped. Pigmentation began within 10 days to two weeks after epithelialization was completed. It took place in a brown perifollicular macular pattern within the lesion which then enlarged and coalesced or it began from the margins and spread centripetally.

All patients experienced some discomfort or burning sensation at the first few days.

* The course of repigmentation in minigraft and hair grafts techniques was as follows : The grafts after few days showed scab formation which fall out by itself followed by erythema which changed gradually to faint pigmentation spreading up one or more mm around the edge of the graft .

At the end of nine months different responses were seen by the three methods .

Regarding the patches treated by 5-flourouracil on dermabraded area 16 (40%) patients showed no response (patches pigmented less than 20%) , and 24 (60%) patients showed response .

As regard the patches treated by minigraft technique 10 patients(25%)showed no response and 30(75%)showed response

The patches treated with hair grafts showed exactly the same responses seen with minigraft technique with the same parameters. As shown in table 2 ,3and diagram 1 .

Table 2: Results at the end of 9 months of treatment.

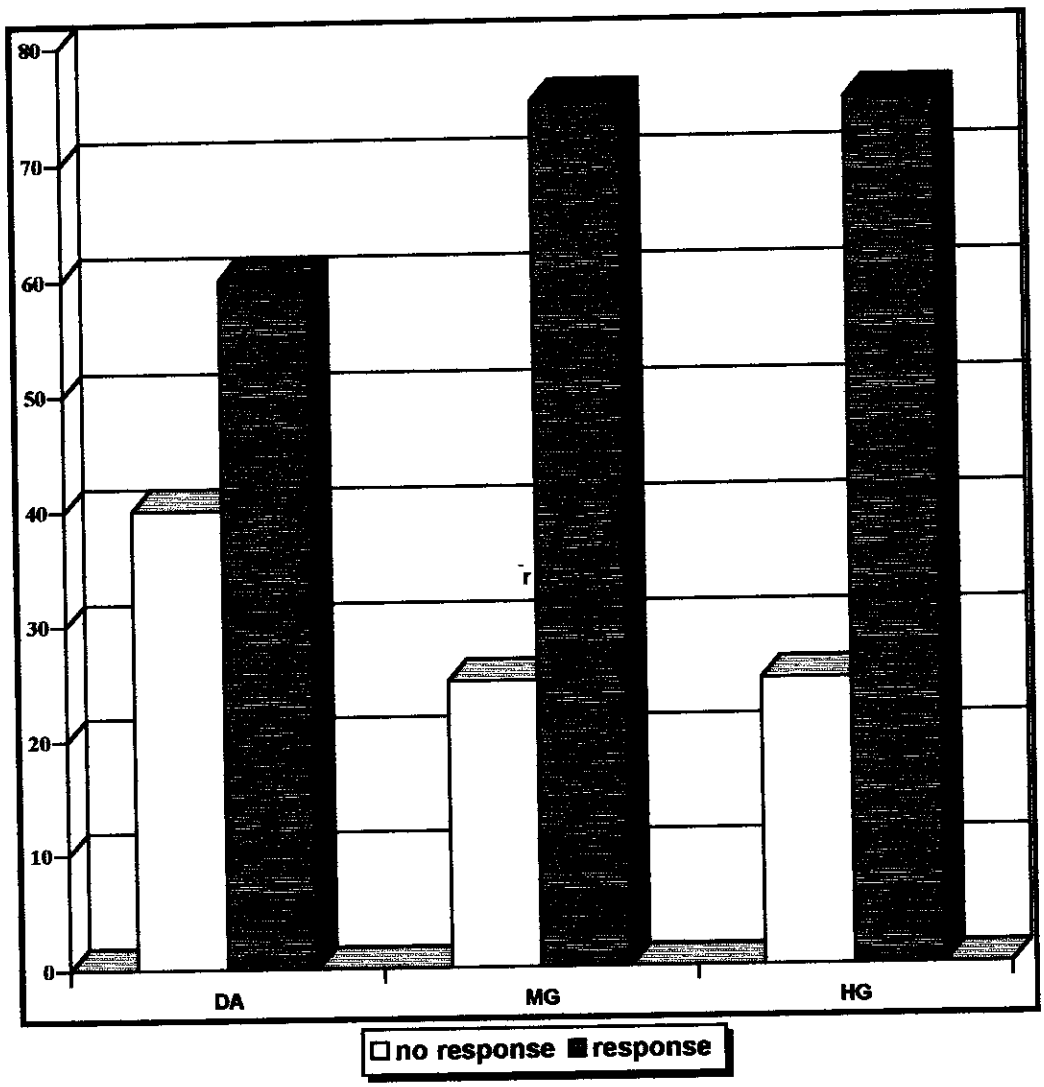
No.	DA	MG	HG
1	N	R	R
2	N	R	R
3	R	N	N
4	N	R	R
5	R	R	R
6	R	N	N
7	R	R	R
8	R	R	R
9	R	R	R
10	R	R	R
11	N	R	R
12	N	R	R
13	R	R	R
14	R	N	N
15	R	N	N
16	N	N	N
17	R	N	N
18	N	N	N
19	R	R	R
20	R	R	R
21	R	R	R
22	R	N	N
23	R	R	R
24	N	R	R
25	R	R	R
26	R	R	R
27	R	R	R
28	R	R	R
29	R	R	R
30	N	R	R
31	N	R	R
32	R	R	R
33	N	R	R
34	N	R	R
35	N	N	N
36	R	R	R
37	N	N	N
38	N	R	R
39	N	R	R
40	R	R	R

R = Respone N= No respone

Table 3: Response by the three methods.

	DA	MG	HG
No response	16(40%)	10(25%)	10(25%)
Response	24(60%)	30(75%)	30(75%)

$X^2 = 2.857.$
$P = 0.239.$



Diag.1 : The response by the 3 methods .

Some complications were seen in our study:

* The application of 5-flourouracil on the dermabraded area showed hyper-pigmentation which occurred instead of the natural pigment in 5 patients and even hyperpigmentation around the treated area, but all became much lighter with time.

* The patches treated with minigrafts technique showed cobble-stone appearance in 4 patients which may be later treated by dermabrasion.

* The patches treated with hair graft showed over growth of hair in the glabrous skin .

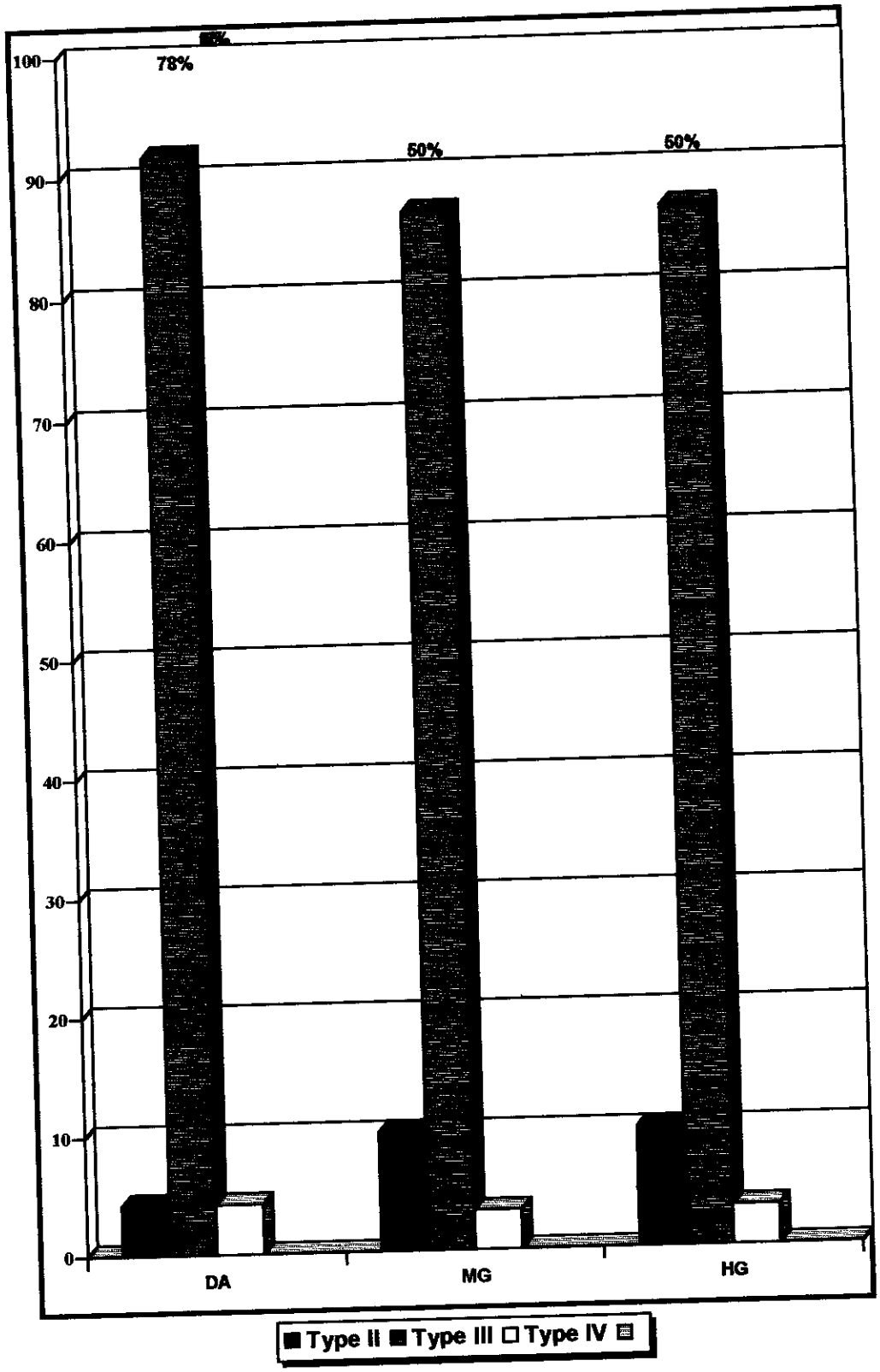
The different variables among all patients in relation to responses of treatment by the three methods of treatment :-

The skin types of our patient ranged from type II through III, and IV in the studied groups. There was no defined relation between skin type and degree of response as shown in table 4 and diagram 2 .

Table4: Relation between skin type and response.

Skin type	DA	MG	HG
II	1(4.2%)	3(10%)	3(10%)
III	22(91.7%)	26(86.7%)	26(86.7%)
IV	1(4.2%)	1(3.3%)	1(3.3%)

$X^2 = 0.781$
$P = 0.9408$



Diag.2 : The relation between response by the 3 methods and skin type .

The age of patients ranged from 6 years to 65 years. There was no relation between age and response by the three methods .as shown in table 5 .

Table 5: Relation between age and response.

	DA	MG	HG
<20years	7(29.2%)	7(23.3%)	7(23.3%)
20-30	7(29.2%)	6(20%)	6(20%)
30-40	7(29.2%)	12(40%)	12(40%)
>40	3(12.5%)	5(16.7%)	5(16.7%)

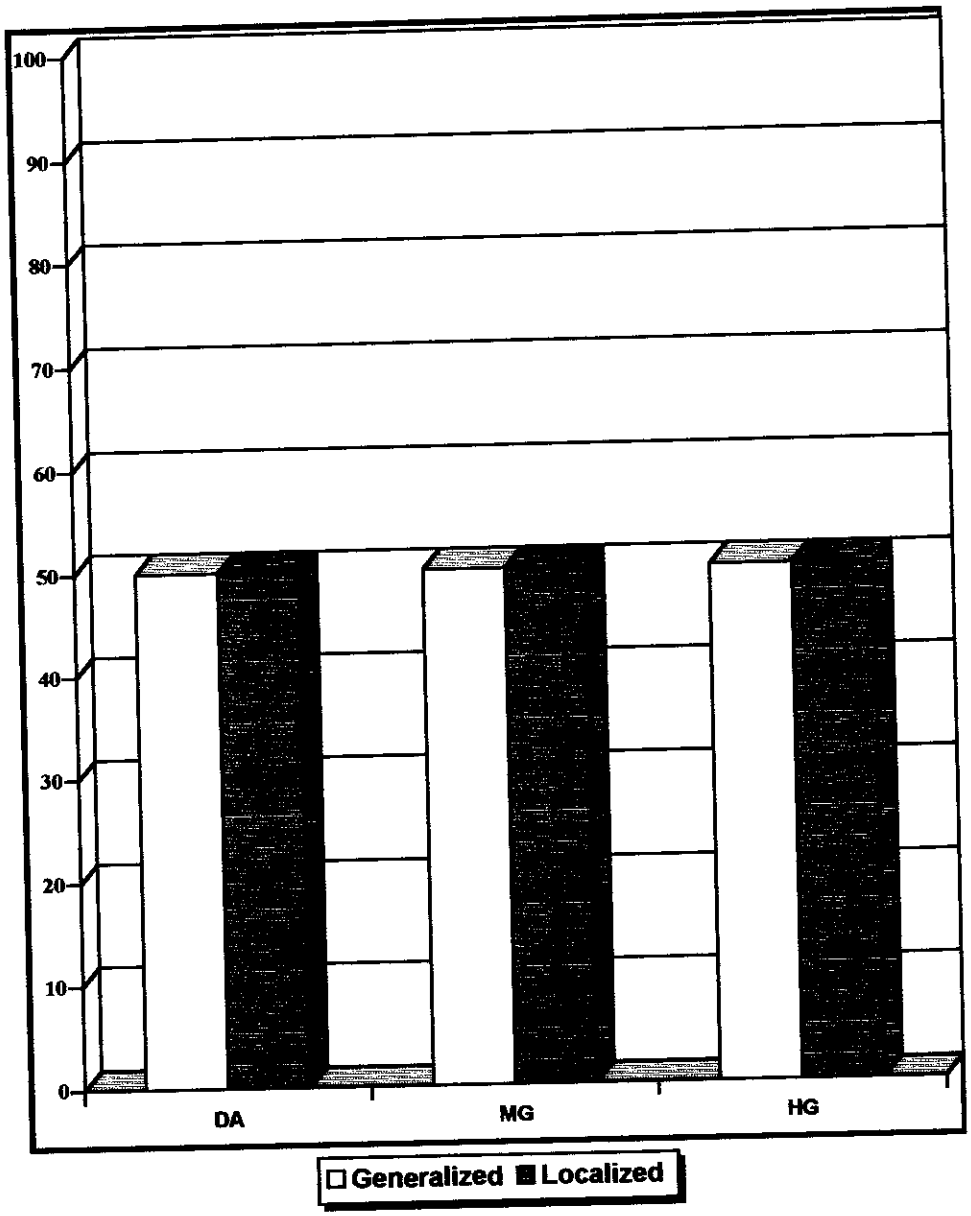
$X^2 = 1.607$
$P = 0.95$

Localized type of vitiligo gave the same response as the generalised one by the 3 methods, As shown in table 6 and diagram 3 .

Table 6: Relation between type of vitiligo and response.

	DA	MG	HG
Generalized	**12(50%)**	**15(50%)**	**15(50%)**
Localized	**12(50%)**	**15(50%)**	**15(50%)**

$X^2 = 0.0$
$P = 1.5$



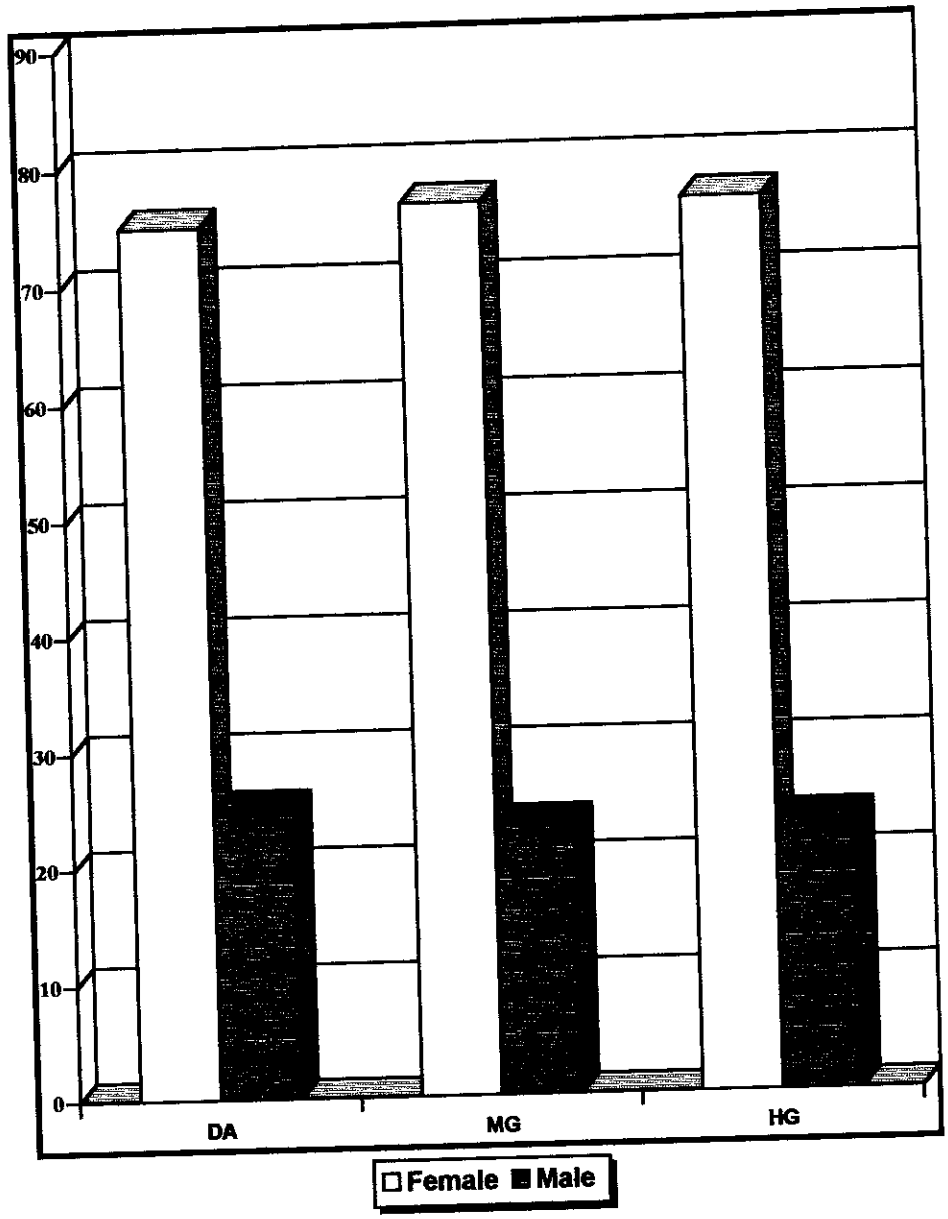
Diag.3 : The relation between response by the 3 methods and type of vitiligo.

The relation between sex of the patients and the response showed no significant relationship as shown .in Table 7 and diagram 4 .

Table 7: Relation between sex and response.

	DA	MG	HG
Females	**18(75%)**	**23(76.7%)**	**23(76.7%)**
Males	**6(25%)**	**7(23.3%)**	**7(23.3%)**

$X^2 = 0.0262$
$P = 0.986$



Diag.4 : The relation between sex and response by the 3 methods .

The relation between site of the treated area whether exposed or not and response showed that non-exposed patches had a better response than the exposed patches as shown in,Table 8 and diagram 5 .

Table 8 : Relation between site of lesion and response.

	DA	MG	HG
Non exposed	**16(66.7%)**	**17(56.7%)**	**17(56.7%)**
Exposed	**8(33.3%)**	**13(43.3%)**	**13(43.3%)**

$X^2 = 0.711$
$P = 0.7006$

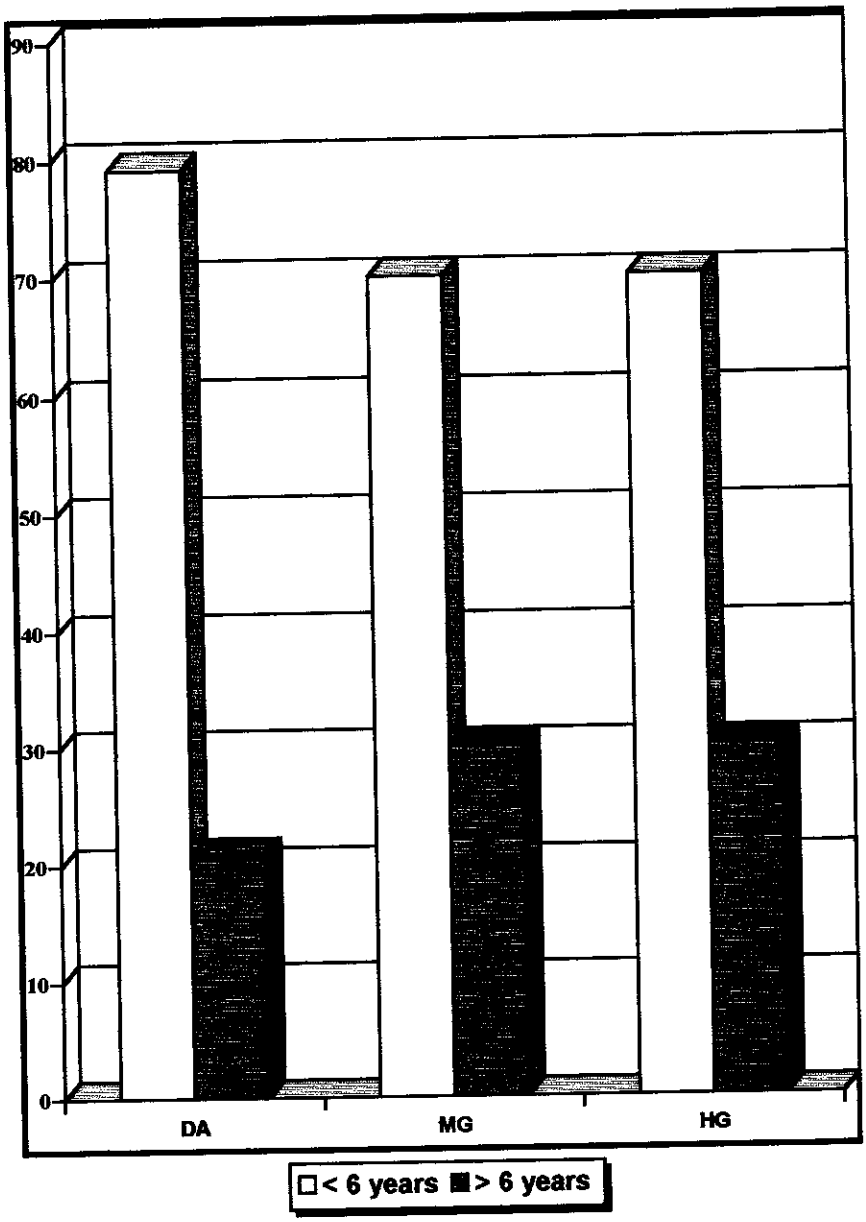
Diag.5 : The relation between site of the lesion and response by the 3 methods .

The duration of the lesion was classified into 2 groups more and less than 6 years. The lesions with duration less than 6 years showed better response as shown in table 9 and diagram 6.

Table 9: Relation between duration of the lesion and response.

	DA	MG	HG
< 6 years	19(79.2%)	21(70%)	21(70%)
> 6 years	5(20.8%)	9(30%)	9(30%)

$X^2 = 0.724$
$P = 0.696$



Diag.6 : The relation between duration of the lesion and response by the 3 methods.

The following photographs show the responses in selected cases in our study

Case 1 :

Female patient showing vitiliginous area on forearm

The same patient on the day of treatment , the most distal part was dermabraded and the most proximal part was minigrafted and in between hair grafting was done

The same patient after 2 months of treatment

HG : shows no response

MG : shows no response

DA: shows response

The same patient after 9 months of treatment

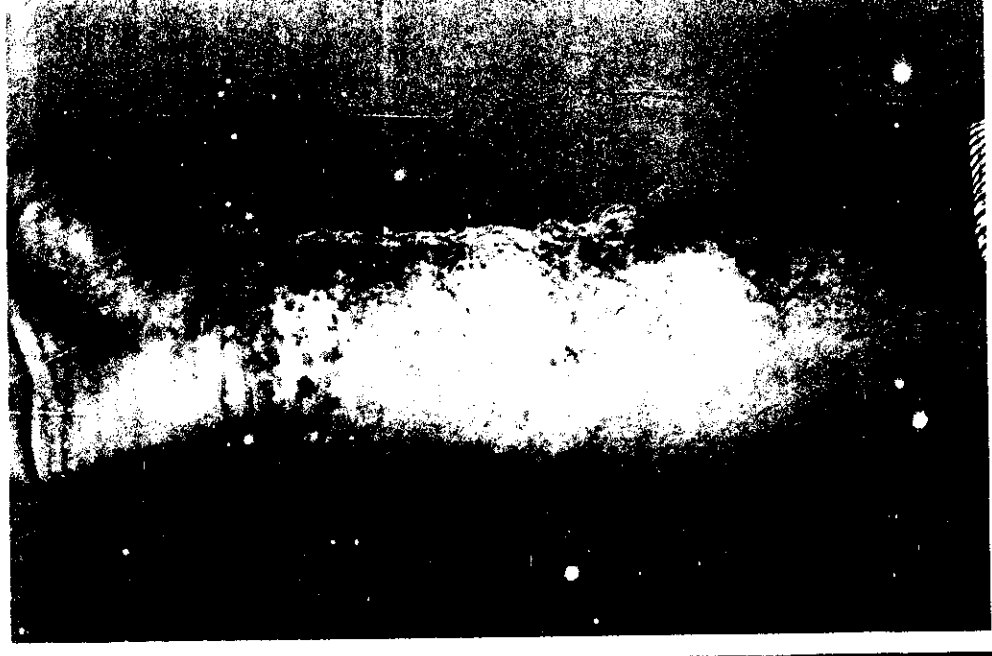
HG : shows no response

MG : shows no response

DA: shows response

Case 2 :

Male patient showing vitiliginous area on forearm



The same patient on the day of treatment , the most distal part was dermabraded and covered , the most proximal part was divided into upper part for minigraft and lower part for hair grafting .

The same patient after 6 months of treatment

HG : shows response

MG : shows response

DA: shows no response

Case 3 :

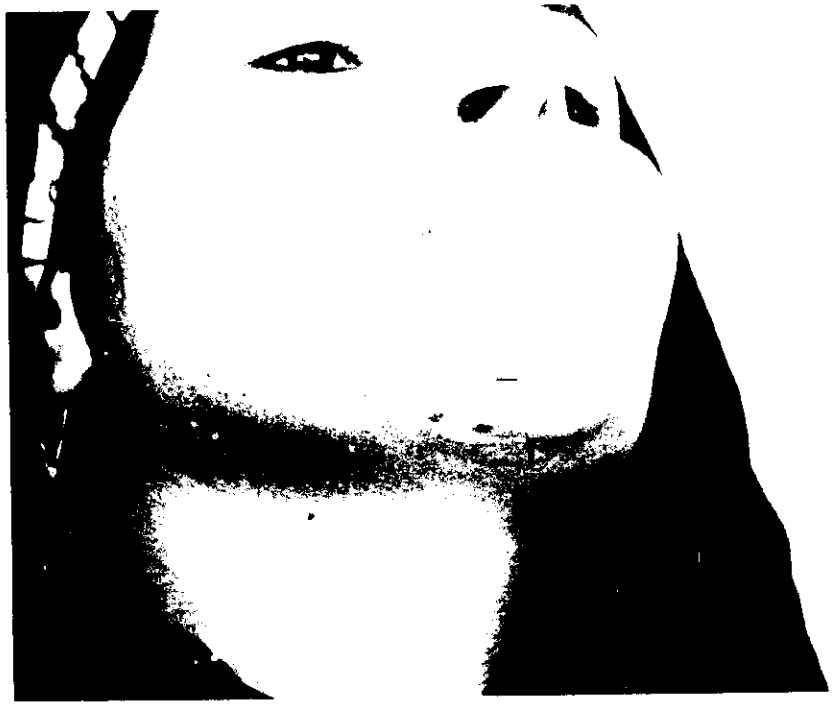
Female patient showing vitiliginous area on the face , divided into 2 parts , the left for DA and the right was divided into upper part for HG and lower part for MG .

The same patient after 9 months of treatment

HG : shows response

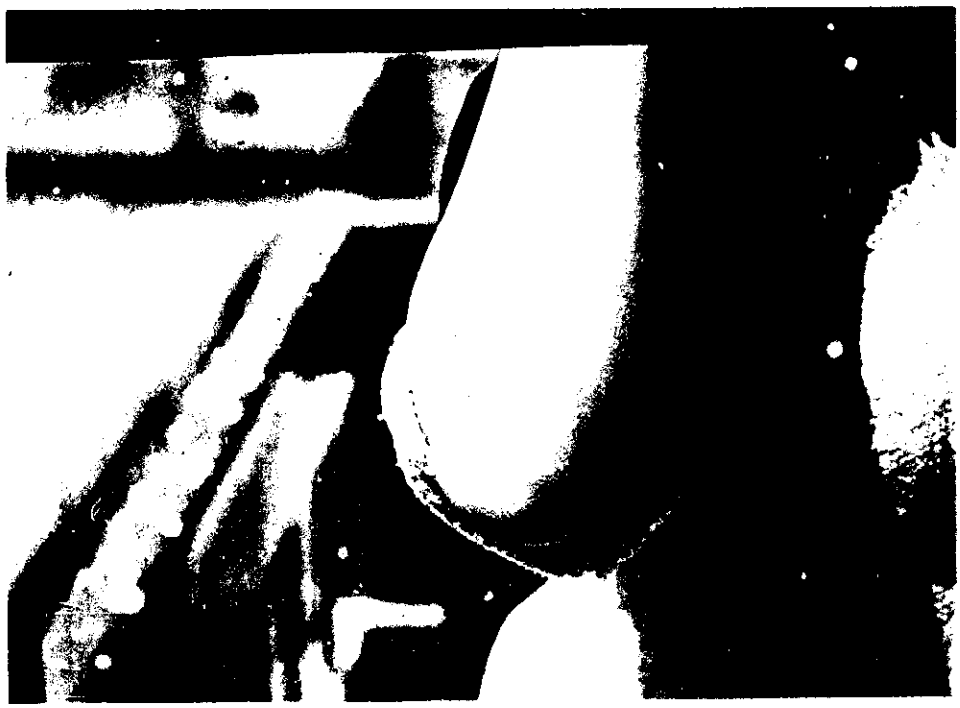
MG : shows response

DA: shows no response



Case 4 :

Female patient showing vitiliginous area on forearm which was divided into 2 parts , the distal for dermabrasion and the proximal for hairgraft



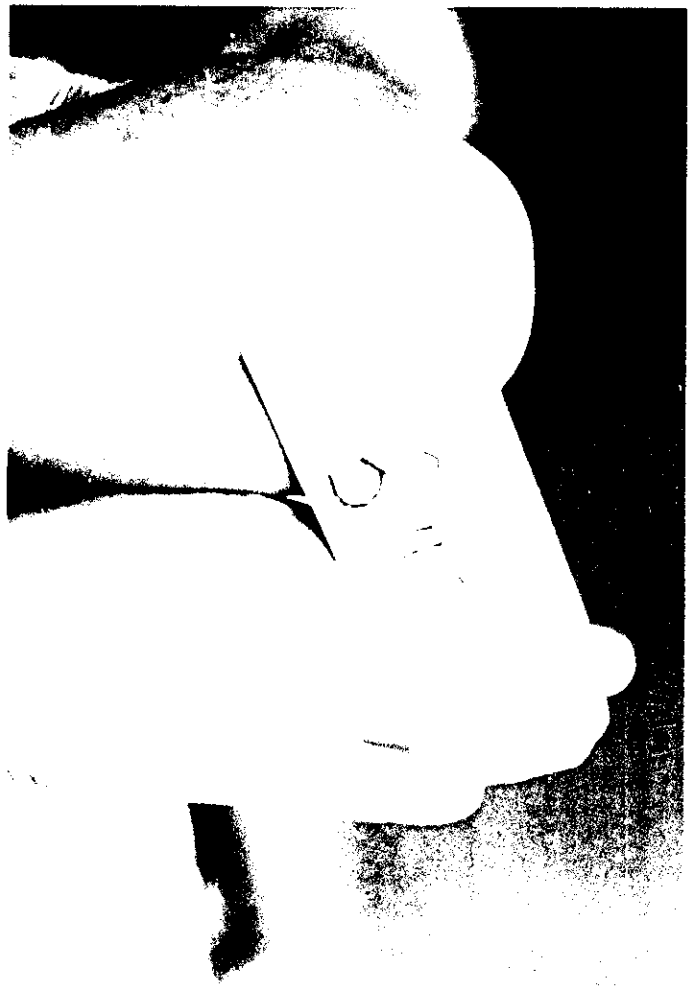
The same patient with another vitiliginous area on the hand for minigraft

The same patient after 6 months of treatment

HG : shows response

MG : shows response

DA: shows response



The same patient after 9 months of treatment

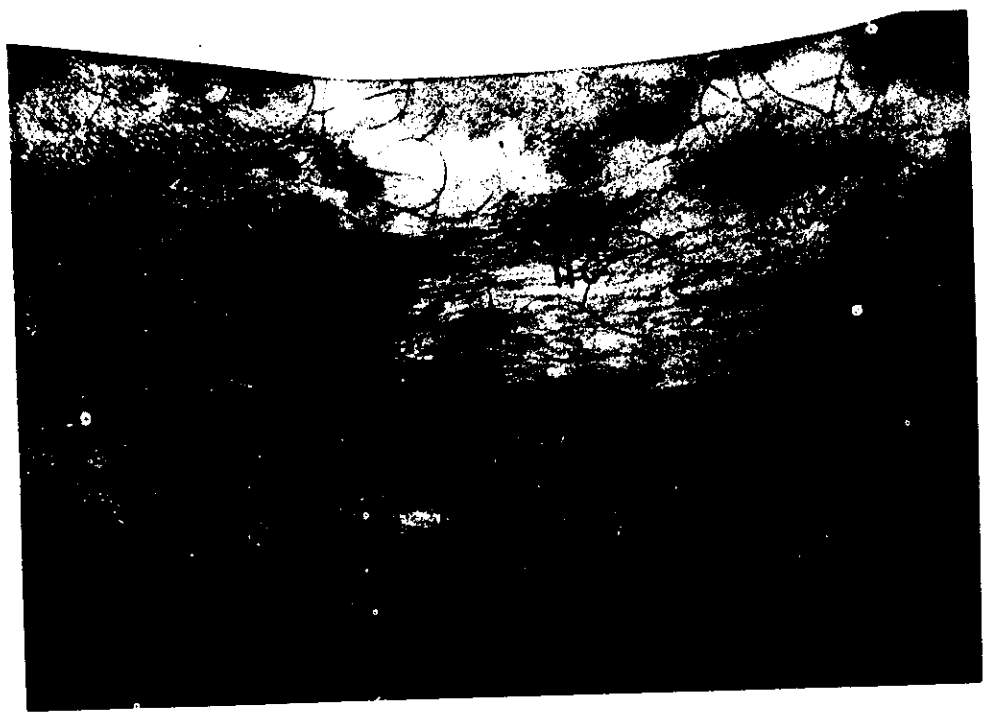
HG : shows response

MG : shows response

DA: shows response

Case 5 :

Male patient showing vitiliginous area on abdomen , divided into 3 parts , the right for DA , the left for MG and in between for HG .



The same patient after 6 months of treatment

HG : shows response

MG : shows response

DA: shows response

Case 6 :

Female patient showing vitiliginous area on the leg , divided into upper part for HG , lower part for DA , and in between MG

The same patient after 6 months of treatment

HG : shows response

MG : shows response

DA: shows no response

The same patient after 9 months of treatment

HG : shows response

MG : shows response

DA: shows

No response

Case 7 :

Male patient showing vitiliginous area on the back .The patch was divided into 3 parts , the upper for MG , the lower for HG , and between DA .

The same patient after 2 weeks of treatment

HG and MG : shows scab formation .

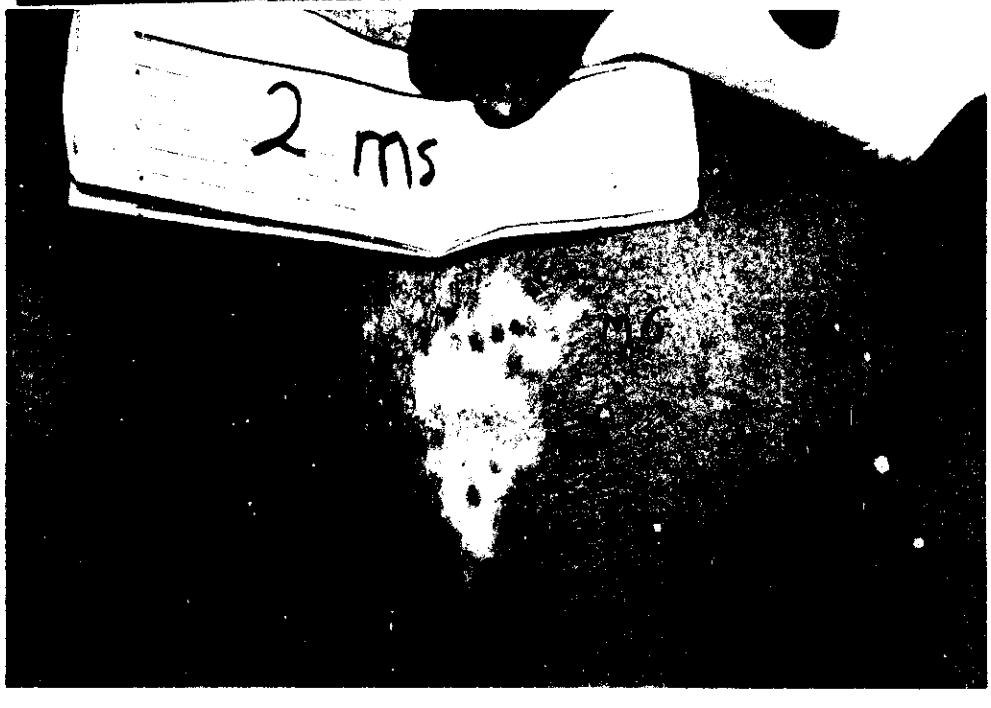
DA : shows erythema and erosion .

The same patient after 2 months of treatment

HG : shows excellent response

MG : shows excellent response

DA: shows no response



Case 8 :

Female patient showing vitiliginous area on the neck .

The same patient after 6 months of treatment

HG : shows response

MG : shows response

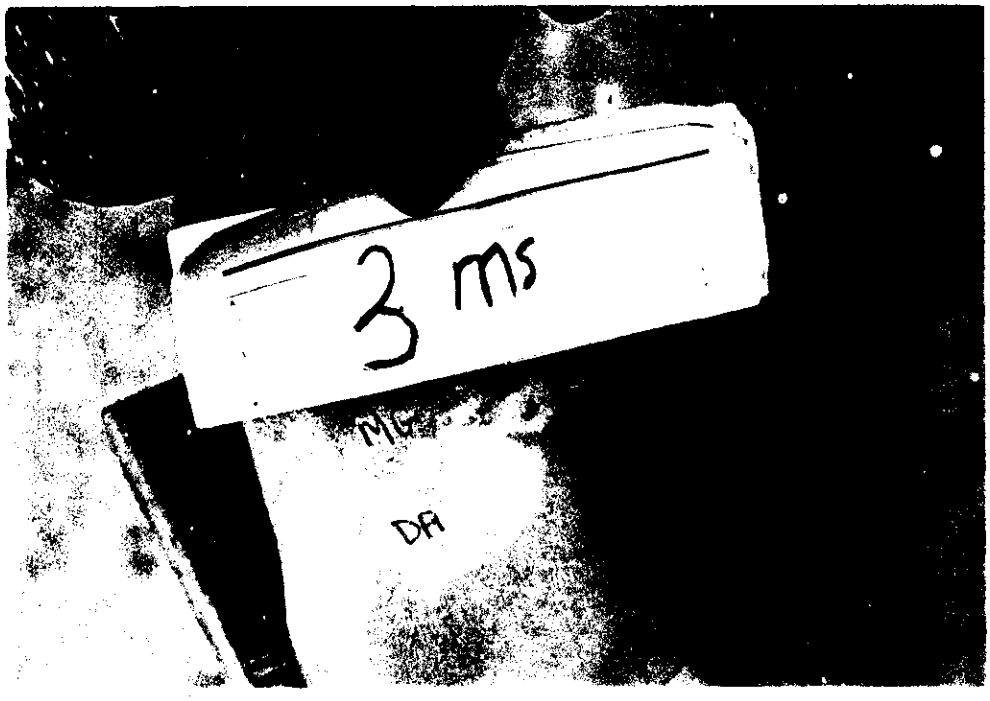
DA: shows response

Case 9 :

Female patient showing vitiliginous area on the dorsum of the foot .

The same patient on the day of treatment , the distal patch was dermabraded and the proximal was divided into medial part for hairgraft and lateral part for minigraft .

The same patient after 3 months of treatment shows no response with the three methods .



Case 10 :

Female patient showing vitiliginous area on the face. The patch in front of the ear for DA , the patch in the forehead was divided into upper part for MG , and lower part for HG .

The same patient after 1 weeks of treatment

HG and MG : shows scab formation and DA shows minimal erythema .

The same patient after 9 months of treatment

HG : shows response

MG : shows response

DA: shows no response

Case 11 :

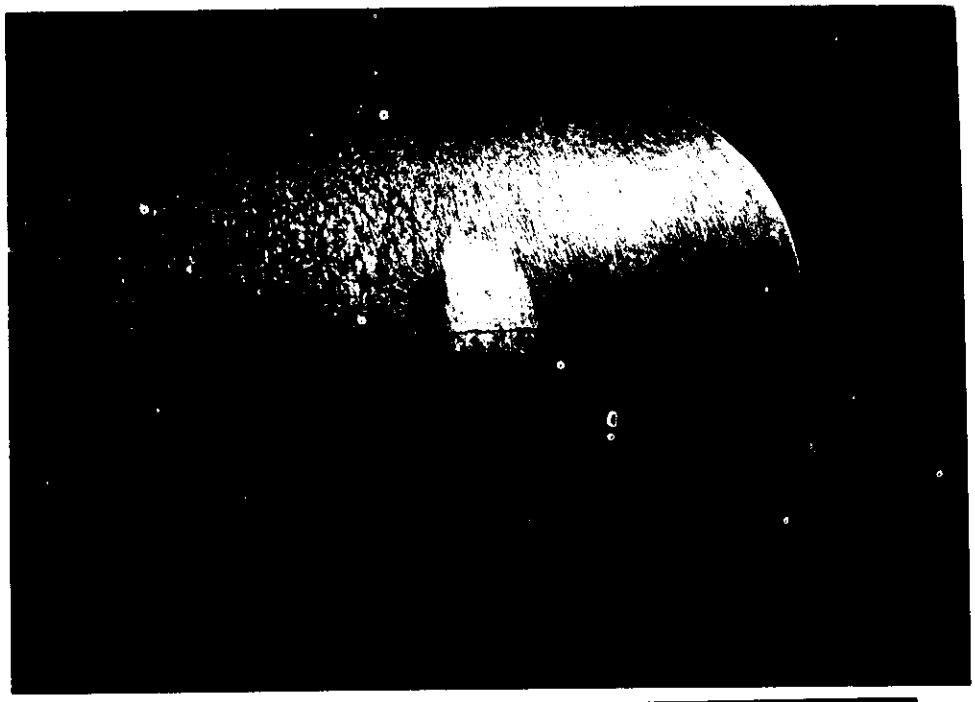
Female patient showing vitiliginous area on the thigh. The patch was divided into 3 parts , the distal for DA , the proximal for HG , and in between for MG .

The same patient after 9 months of treatment

HG , MG , and DA showed response .

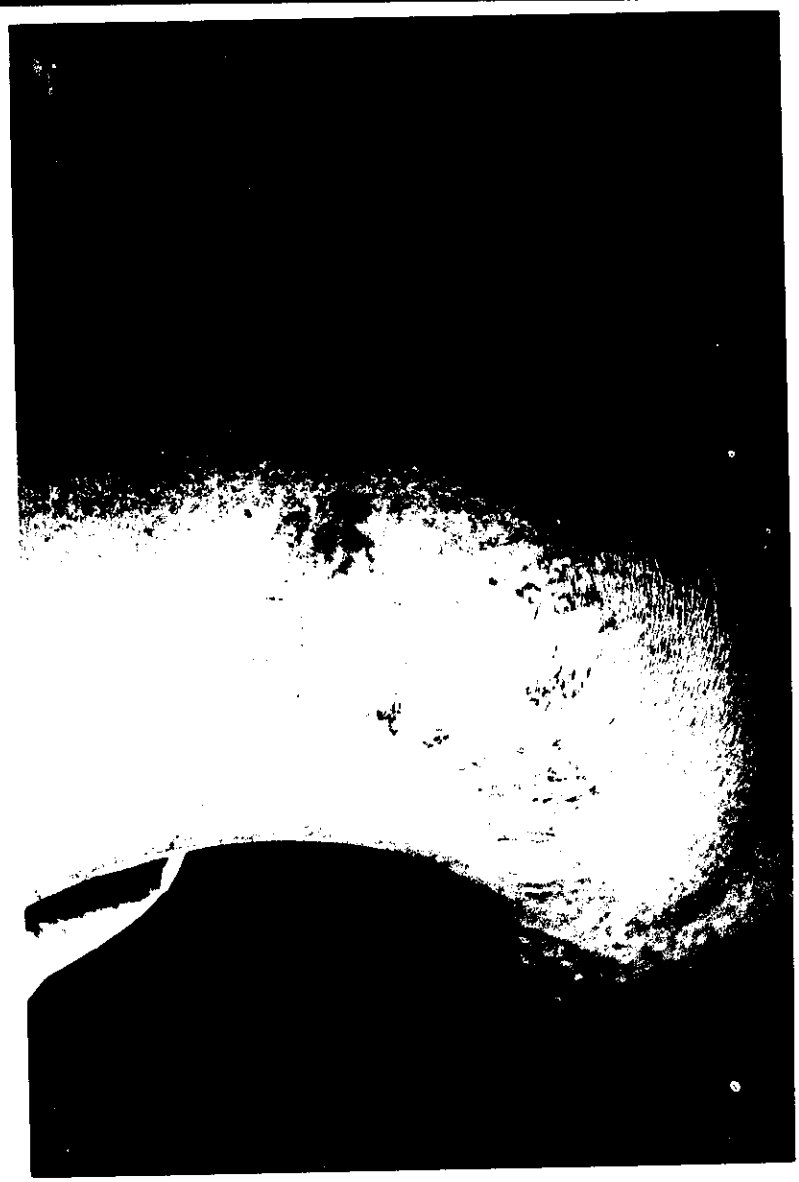
Case 12 :

Female patient showing vitiliginous area on the thigh. The patch was divided into 3 parts , the upper for DA , the lower for HG , and in between for MG .



The same patient after 9 months of treatment

HG , MG , and DA showed response .



Case 13 :

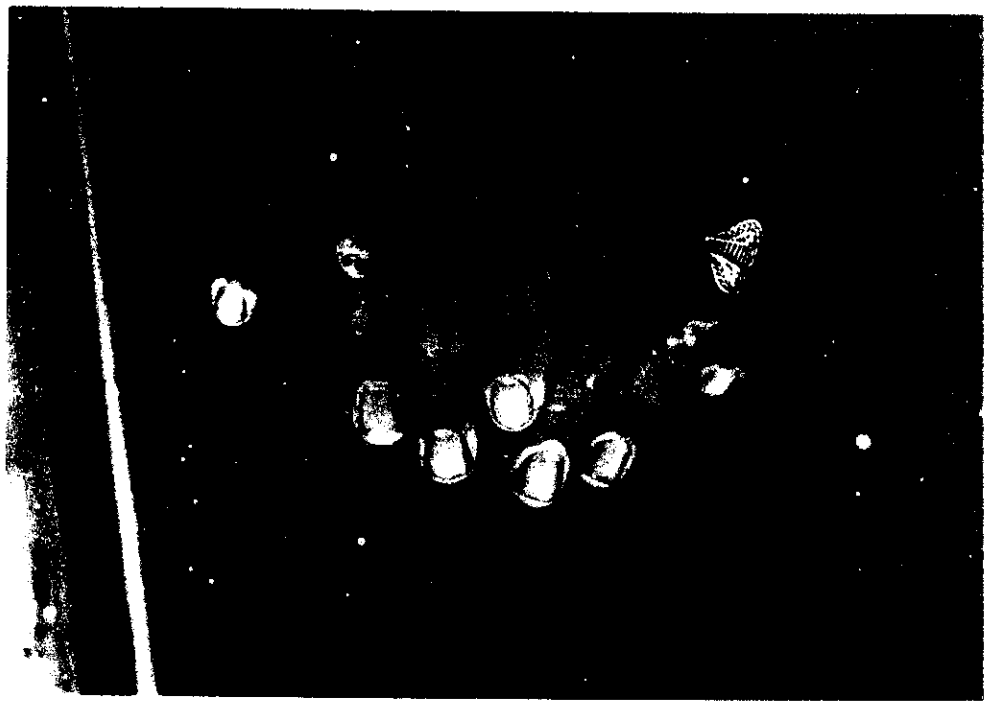
Female patient showing vitiliginous area on the the foot which was dermabraded and another patches on fingers, the right minigrafted and the left for hairgrafting.

The same patient after 9 months

HG: shows response

MG:shows response

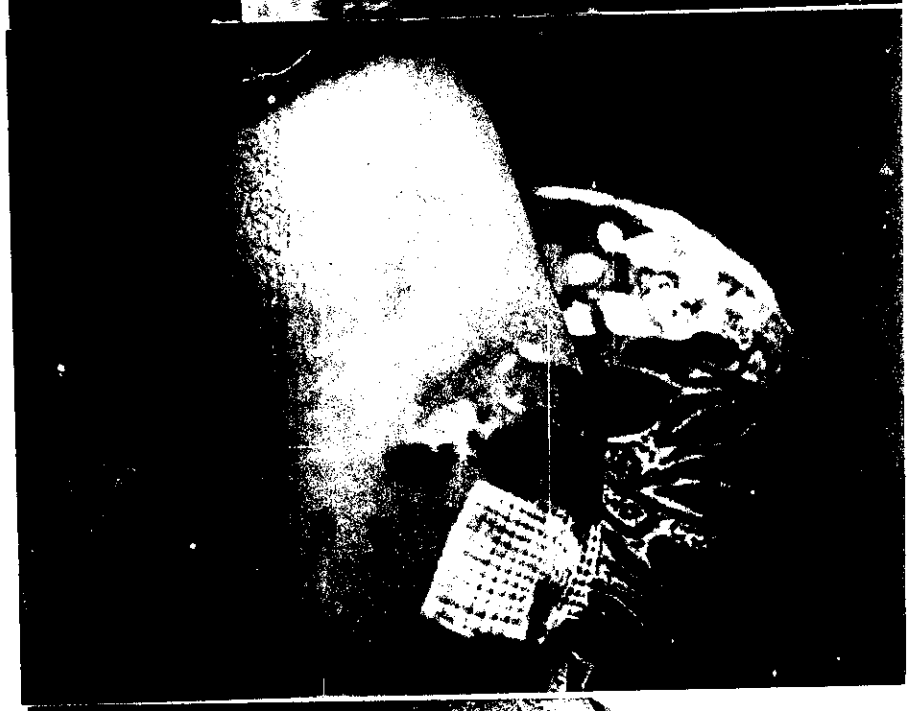
DA:did not show response.



Case 14 :

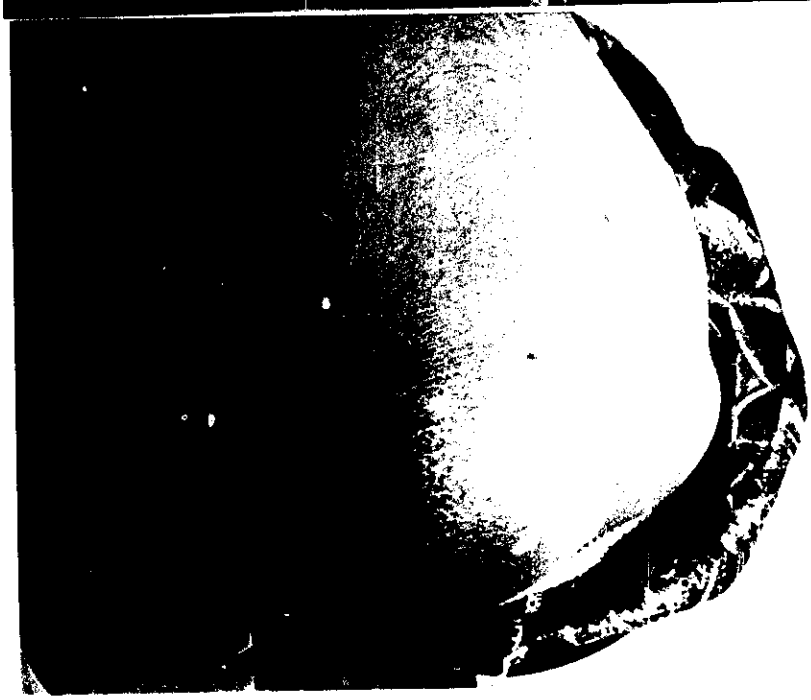
Female patient showing vitiliginous areas on forearm .the right was dermab-raded,the upper left hairgrafted and the lower left minigrafted

The same patient on the day of treatment , the dermabraded area was covered.



The same patient after 6 months

DA,MG.,HG :shows response .



Case 15 :

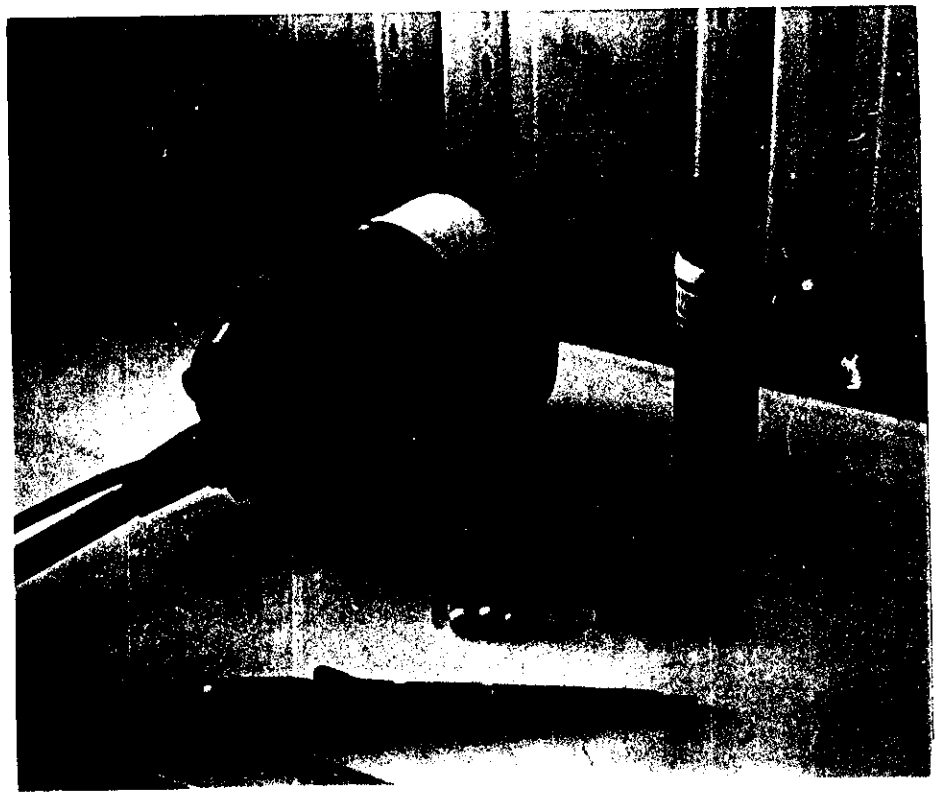
Female patient showing vitiliginous area on the neck. The patch was divided into 3 parts , the dorsal part for DA , the ventral for HG , and in between for MG .

The same patient after 9 months of treatment

HG , MG , and DA showed response .

Some instruments used in the study

Dermabrador with diamond fraise and local anaesthetic (freon , ethyl chloride) used in DA



Dermabrador with 3 mm punch, tissue glue and infil-terative local ana-esthetic used in MG and HG .

Discussion

Although the treatment of vitiligo has improved in recent years, it is still unsatisfactory in a certain number of patients.

Topical and systemic methoxasalen therapy combined with the use of various U.V. sources and local therapy with corticosteroid was proved to be fairly effective. However, these treatments often require long term administration but many patients achieve only partial improvement.***(Tsuji and Hamada., 1983)***

Several surgical procedures for the treatment of depigmented skin have been reported, including minigrafting***(Flabella, 1988)***, thin theirsh graft***(Behl et al., 1964 ; Olsson and Juhlin 1997)***, and injection of non-cultured melanocytes ***(Olsson et al 1998)*** and suction blister***(Kim and Kang 1999)***,.

The aim of this work was to evaluate 3 surgical modalities in the treatment of vitiligo. The first modality was dermabrasion followed by topical 5% fluorouracil cream application for 10 days from the day of treatment. The second was autologous minigrafting and the third was hair grafting .

Dermabration followed by topical 5% flourouracil :

Tsuji and Hamada (1983) used 5-fluorouracil after dermabrasion for treatment of vitiligo. They noticed no effect in lesions treated with either epidermal abrasion

alone or 5-fluorouracil cream alone. They stated that trauma alone is not an effective initiative factor to induce repigmentation and that 5-fluorouracil absorption and its efficacy are greatly enhanced by removing the epidermal barrier.

The mechanisms by which 5-fluorouracil cream induces repigmentation of vitiligo lesions is unknown. But there are two hypotheses might explain how it works :

1- 5-Fluorouracil produces melanocytes colonization in vitiligenous epidermis by stimulating the division of epidermal melanocytes that migrate into the affected area after epithelialization of the dermis occurs*(Africk et al., 1971)*.

Tsuji and Hamada (1983) showed also that repigmentation was initiated perifollicularly in most cases. In addition, the same authors described that the repigmentation may be also in the form of diffuse pattern.

Klus et al (1965) in a study of the effect of dimethyl benzanthracence on the melanocyte of hairless mice, demonstrated a rapid diffuse pigmentation of the skin. In hairless mice of course the entire hair matrix including the melanocyte is absent, this may suggest that the melanocytes responsible for repigmentation in vitiligo are derived not only from hair follicles but also from the epidermis.

2- At the cellular level fluorouracil competes with desoxyuridine and its derivatives for the enzyme thymidylate synthtase which is a potent inhibitor for a variety of cellular activities and readily kills most cells including pigment cells.***(Tsuji and Hamada 1983)***

In our study, 16 (40%)showed no response and 24(60%)showed response .

Four patients out of those 16 showed only hyperpigmentation at the border surrounding the vitiligenous area. According to ***Tsuji and Hamada (1983)*** hyperpigmentation may occur around the vitiligenous skin where no erosion had occurred. Presumably this effect is from some action of the absorbed drug on adjacent perilesional melanocytes .

By comparing our results with other studies:

Tsuji and Hamada (1983) used 5-fluorouracil on dermabraded vitiligenous area, their result revealed that 18 out of 28 (64%) showed response, the remaining 10 (36%) including 2 patients with segmental vitiligo showed no response. Their result is nearly similar to our study

In another study by ***Szekeres Morvey ,(1985)*** they tried treatment of vitiligo by dermabrasion followed by 5-fluorouracil cream. The result revealed that three patients with symmetrical type of vitiligo out of 5 patients responded with repigmentation, two other patients with segmental vitiligo failed to respond to this treatment. A result which is more or less compatible with our study .

In Cairo, Egypt another study , ***Ghoz (1996)*** using dermabrasion followed by 5-fluorouracil he found that three patients out of eight showed good response and five showed minimal to no response. A result which is more or less similar to ours .

The only complication seen with dermabration was hyperpigmentation wich became much lighter with time

As regard the minigraft technique :

It is suitable for repigmentation of several types of stable leukodermas ***.(Falabella, 1986)***

Patient selection is important. It is not always possible to detect stable vitiligo based on a history of 6 months, therefore the minigraft test should be always performed because the result will tell us whether vitiligo is still showing activity or not. In active vitiligo the

minigraft test will be usually negative.***(Klaus et al., 1965;Flabella et al 1995)***

In this study, patients with positive Koebner (as known from the history) were excluded from grafting technique. According to ***Boersma et al (1995)*** exclusion of these patients is a must even if there is initial spread of pigment from test grafts because all grafts are liable for depigmentation .

The mechanism of pigmentation is most probably due to migration and multiplication of melanocytes with the resultant diffusion of melanin as demonstrated by ***Billingham et al, (1970)*** in spotted guinea pig.

Regarding the results of our study, 30 patients out of 40 (75%) showed response, and 10(25%) patients showed no response. .

According to this finding, it is expected that cases responding to minigraft test are considered to be suitable for several sittings of minigrafting .

Our result goes with the study done by ***Falabella (1983)*** who tried treatment of vitiligo by minigraft technique his result revealed that 15 patient out of 22 attained response .

Another study by, ***Boersma et al , (1995)*** on 19patients with vitiligo selected after positive minigraft test was done, 14 showed response , the remaining

showed minimal to no response A result which is more or less similar to our study .

In a recent study , (***Malakar and Dahar , 1999)*** on 1000 cases , test graft was done , 880 cases showed positive test graft , 656 (74.5%) of them showed response , and the remaining cases showed minimal to no response . These results go with our study .

The only complication seen in our study was the Cobblestone appearance of minigrafts ,this was seen in four patients out of the ten patients who did not respond, those lesions where opposite major joints (elbow and knee). This sequel may be due to the discrepancy in the thickness between the donor skin and the recipient sites resulting in no allayment of the dermis and epidermis of the graft and recipient sites.

On the other hand ***Boersma et al ,(1995)*** advice avoidance of minigraft against bone structures, tendons, nerves or superficial veins because these structures prevent proper preparation of the acceptor areas. In the same study he advised making holes in the acceptor areas about 1 mm deeper than the thickness of the minigrafts.to avoid cobble- stone apprarance

Silicone gel sheet dressing is now used to prevent post minigraft cobblestone ***(Agawal et al 1999)***

As regard the hair graft technique:

Hair graft was first used in the correction of various hair problems***(Choi et al., 1992)***. As repigmentation usually begins in the perifollicular areas, hair follicles are believed to harbor a reservoir population of inactive or precursor melanocytes specially located in the lower third of hair follicle.***(Ortonne et al., 1979; Arrunategni et al., 1994).***Recent studies have suggested that these are present in the upper two third of hair folicle ***(Grinchei et al 1996,Horikawa et al,1996)***

Kim and Choi et al , (1995) observed that pigmented hair regrew after amputation of the hair bulb suggesting that a melanocyte reservoir exists outside the bulb .

It is speculated that normal grafted hair follicles might have some positive effects on the recovery of pigmentary problems.***(Gun et al., 1998)***

The results of hairgraft and minigraft techniques in our study were identical .

Comparing our results with the study of ***Gun et al., (1998),*** he found that 13 patients out of 21 showed response and the rest showed no response. A result which is more or less compatible with our study .

According to ***Mutalik , (2000)*** it is difficult to draw any fixed guideline for treatment of vitiligo , and treatment must be individualized depending upon the extent and stability of the disease , and surgical treatment must be for obtaining the best possible cosmetic results .