

THE HEALING OF SURFACE CUTANEOUS WOUNDS: ITS ANALOGY WITH THE HEALING OF SUPERFICIAL BURNS*

JOHN MARQUIS CONVERSE, M.D.†
NEW YORK, N. Y.

AND
A. H. T. ROBB-SMITH, M.D.‡
OXFORD, ENGLAND

INTEREST in the healing of cutaneous wounds produced by the removal of skin grafts was aroused by the fact that the wounds of superficial burns appeared to present a similar process of healing. Brown and McDowell¹ made the same observation, and later Cannon and Cope² used skin graft donor areas to test the effect of coagulants on epithelial growth.

Four hundred and sixty-nine skin graft donor areas were studied. These skin grafts were removed for use in plastic operations and for the covering of raw areas created by burns or trauma. Three types of skin grafts were employed: Thin Thiersch grafts and thicker split (intermediate) grafts which were removed with the Blair skin graft knife. Skin grafts of varying thickness (0.010-0.042 inches) were cut with Padgett's dermatome. The donor sites used were the medial aspect of the arm, the abdomen, the back and the thigh. A few grafts were removed from other regions of the body. The routine post-operative treatment of the donor areas was as follows: Gauze soaked in $\frac{1}{1000}$ adrenaline solution and large saline packs were held with pressure against the bleeding donor area. Then strips of fine-meshed vaselined gauze, impregnated with sulfanilamide powder, were applied to the wound and covered by gauze, cotton and a pressure bandage firmly anchored by adhesive. The dressings over the skin graft donor areas were removed when the latter were healed. The approximate healing time of these donor areas was observed, the dressing being removed when the vaselined gauze could be easily detached from the new epithelial surface of the area. It is obvious that accurate comparative data are difficult to obtain because the thickness of the graft, which is cut with the dermatome, varies greatly with the thickness of the cement which is employed to produce adherence of the skin to the dermatome drum, because of individual variations in the characteristics of the skin of the different patients, and because of variations of the age and general condition of the patients. It is felt, however, that observations in a sufficient number of cases (469) have permitted us to formulate the following conclusions:

1. *The quality of the repair was roughly proportional to the rapidity of healing:*

Donor areas, healing in six to ten days, failed to leave more than a pink area, which rapidly became pale, leaving a faintly visible scar with a soft

* Sections of this paper were read by Dr. Converse before the Moynihan Surgical Club, July 26, 1942, Oxford, England.

† From the American Hospital in Britain (Churchill Hospital), Oxford. At present Capt. M.C., U.S.A.

‡ From the Radcliffe Infirmary, Oxford. Reader in Pathology, University of Oxford.

pliable base. Donor areas, healing in 14 to 21 days, left a more visible, uneven scar with a harder base. Some donor areas remained unhealed for a longer period, and often left retracted, hypertrophic scars.

2. *The rapidity of healing appeared to be dependent upon a number of factors:*

A. *The Thickness of the Graft:*

(1) After removal of thin Thiersch grafts at about the level AB in Fig. 1, healing was achieved in six to ten days.

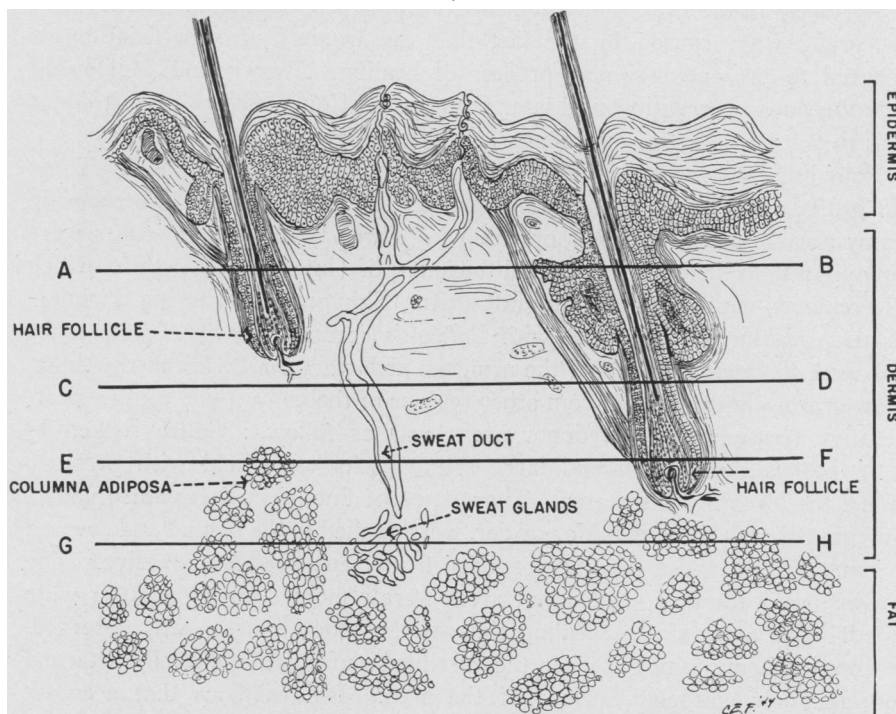


FIG. 1.—Diagram of skin showing levels at which skin grafts are removed. AB, level of a Thiersch graft; CD, level of an intermediate split-graft. EF, level of a thick graft; GH, level of a full-thickness skin graft.

(2) After removal of split (intermediate) grafts at about the level CD (Fig. 1), healing occurred generally within 14 days.

(3) When grafts were cut along the level EF, towards the base of the dermis, or along the level GH (Fig. 1), at which lobes of fat began to appear, healing was much slower, taking from 21 to 58 days.

B. *The Thickness of the Skin of the Donor Site:*

In four patients, 0.016-inch dermatome grafts were removed simultaneously from the abdomen and from the inner aspect of the thigh. The abdominal areas, in which the dermis is thicker, healed more quickly (average 12 days) than the thigh areas (average 16 days).

C. *The Degree of Looseness of the Skin of the Donor Area:*

In donor areas in which the skin is loosely bound-down to the underlying structures, healing occurred more rapidly by contraction.

D. *Infection:*

In seven cases gross infection with suppuration were noted in the donor area. Cultures were not made. In each case, the dressing, maintained by a bandage, had slipped, failing to protect and immobilize the wound.

In six donor areas from which very thick grafts had been removed, infection was observed after the 23rd day. As a result of the infection,

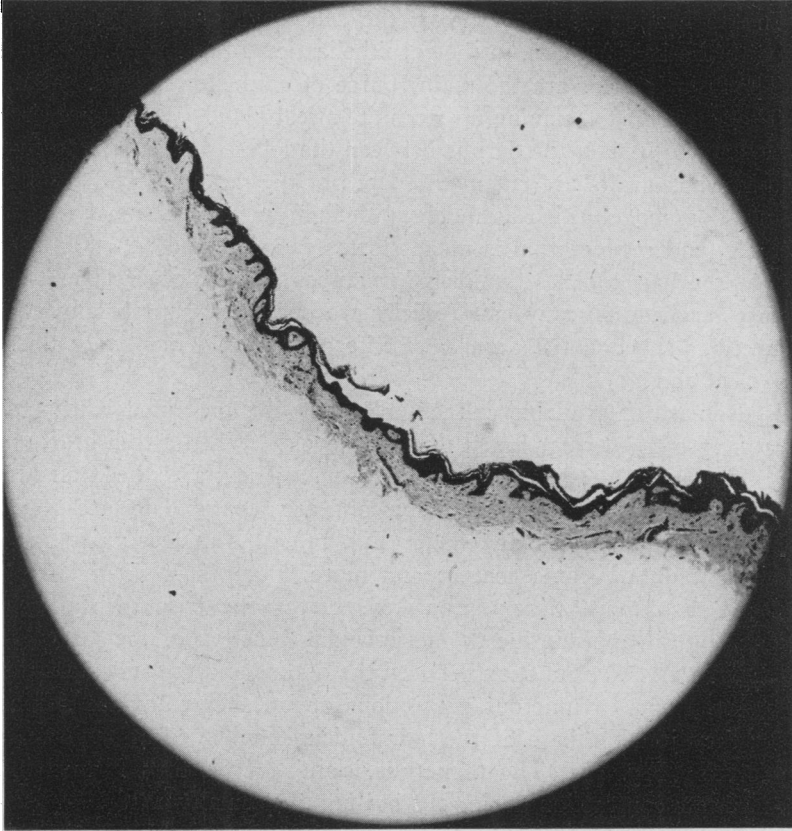


FIG. 2.—Thin graft (0.25 mm.—0.01-in.) removed from the abdomen (about 0.008 on the dermatome calibration) when fixed and embedded showing a portion of the dermis removed. HE $\times 20$ (R.I.S.H. 1585 (6) (42)

necrosis of the remaining dermis was observed which resulted in sloughing followed by granulation of these areas. Healing occurred slowly (average healing time 52 days) leaving an hypertrophic, rough and contracted scar.

PROCESS OF HEALING OF SKIN GRAFT DONOR AREAS

The process of healing of such areas was studied in four patients, who were undergoing a series of plastic operations, and who consented to the removal of biopsies from healing donor areas at various time intervals.

The healing of cutaneous wounds is a dual process, a combination of repair with contraction.

I. *Process of Repair:*

A. *Source of Epithelium* (Figs. 2-10):

The epidermis is removed with the skin graft so that the new epithelial surface must originate from the epithelial elements in the dermis (Figs. 2-8), except from the edges of the defect where there will be regeneration from the surrounding normal epidermis attempting to cover the bare area.

In the study of epithelial repair, histologic sections have revealed the following facts:

1. In the healing of donor areas, the sebaceous glands participate, together with the hair follicles, in the reepithelization (Figs. 3-7).

2. The hair follicles are the main source of epithelium (Figs. 3-8).

3. The sweat ducts, running up from the sweat glands (which are situated in clusters at the base of the dermis between the lobes of fat), help to furnish epithelium when grafts are cut in the depth of the dermis. The sweat duct epithelium does not furnish as much epithelium as an occasional remaining hair follicle, and regeneration is much slower (Figs. 9 and 10). It is to be noted that the hair follicles diminish in number as the deeper layers of the dermis are reached, as many hair follicles are implanted superficially. Horizontal sections through the dermis at different levels demonstrate this fact (Figs. 11, 12 and 13).

This decrease in available epithelium can be demonstrated when cutting skin grafts with the dermatome at different levels. When a thin graft is cut, innumerable small bleeding points are seen. They are the transversely sectioned anastomotic vessels of the skin and are separated by areas of connective tissue containing a hair follicle (Fig. 11). As thicker grafts are cut, the bleeding points become coarser and more widely spaced, and the hair follicles are also more widely separated. Near the base of the dermis, protrusions of fat appear, due to the irregular junction of the fat with the dermis (Fig. 13). The junction between the dermis and the subcutaneous fat is not an even one. Numerous projections of fat, the "columnae adiposae" are seen; they join the base of the hair follicles, implanted at various levels in the dermis (Fig. 1). The numerous islands of fat thus formed in the dermis facilitate contraction during the healing of dermal wounds.

It, thus, results that epithelization takes place from numerous islands of epithelium, which tend to join each other by cellular multiplication and migration. The more numerous these islands are, the more rapid the healing will be.

B. The formation of fibrous tissue and its influence on the quality of the epithelium:

Sections removed from donor areas which have healed rapidly (Fig. 14), show a good quality epithelium over a thin layer of loose connective tissue. This layer is relatively avascular and elastic fibers do not develop until epithelial healing has been complete for some time. Even after five weeks, only very fine fibers are present (Figs. 15, 16 and 17).

When healing has been slow, the appearance is quite different (Fig. 18). Under a thin flat atrophic epithelium, under which there is little rete peg formation and presenting few or no hair follicles, is a thick layer of hori-

FIG. 3

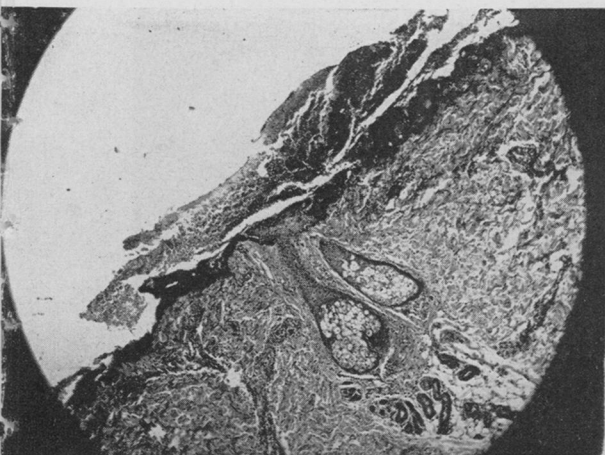


FIG. 4

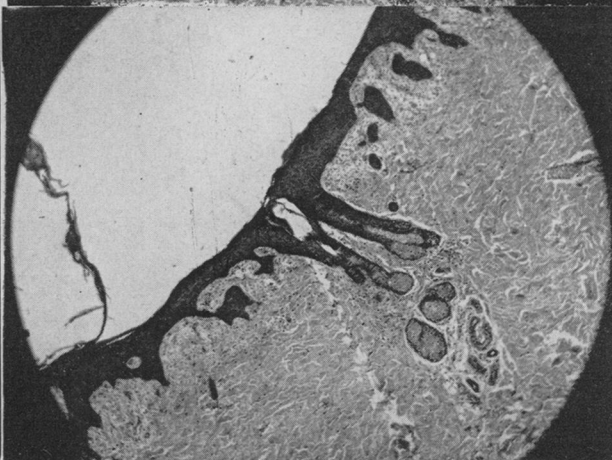
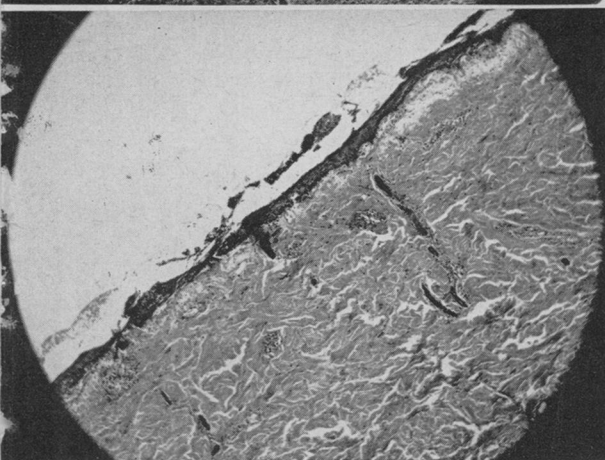
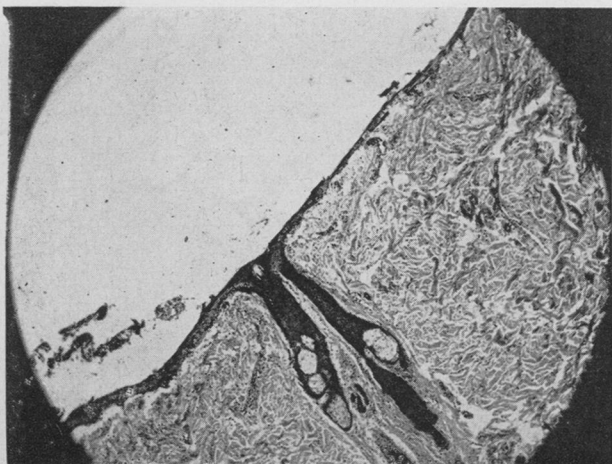


FIG. 5

FIG. 6

FIG. 3.—Donor area two days after removal of a thin graft showing commencing epithelial regeneration from the mouth of a hair follicle and from the sebaceous glands. HE \times 40 (R.I.S.H. 1476 (4) (42)

FIG. 4.—Donor area three days after removal of a thin graft showing the epithelial sheet spreading out from a hair follicle. HE \times 40 (R.I.S.H. 1606 (1) (42)

FIG. 5.—Donor area five days after removal of a thin graft. Epithelial regeneration is complete, the epithelium is thicker than in Figure 4. There is a suggestion of rete peg formation and loose subepidermic connective tissue can be seen, particularly at the right hand end of the section. HE \times 40 (R.I.S.H. 1606 (3) (42)

FIG. 6.—Donor area nine days after removal of a thin graft. Epithelial regeneration is complete, the epithelium is much thicker than in Figures 4 and 5. There is keratinization and well-marked, though irregular rete pegs. The newly formed loose subepidermic connective tissue is well shown. HE \times 40 (R.I.S.H. 1476 (6) (42)

FIG. 7.

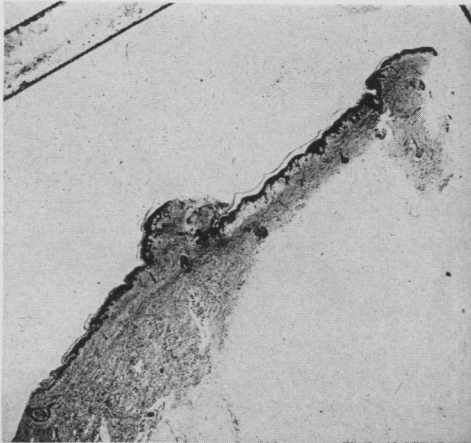


FIG. 8.

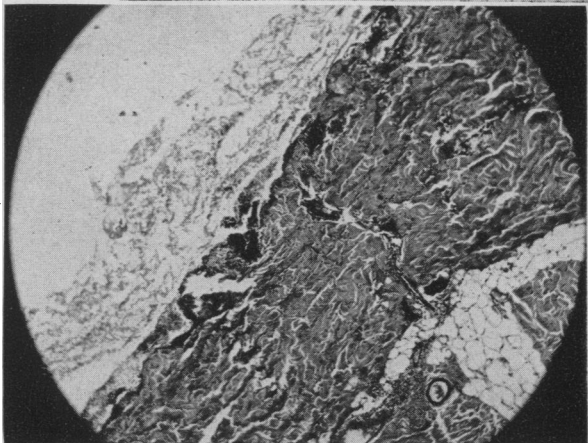
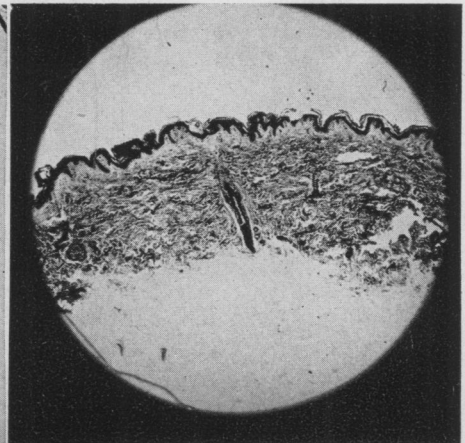


FIG. 9.

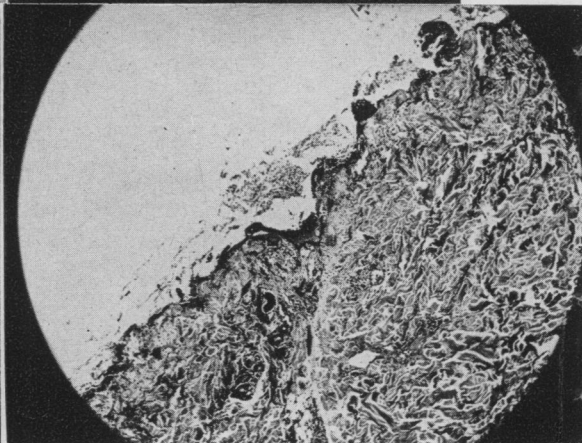


FIG. 10.

FIG. 7.—Comparison of healed donor area with an autograft after 12 days. Immediately after the thin graft had been removed a portion of it was reapplied and the rest of the donor area was allowed to heal. At the extreme right hand, a portion of the normal skin can be seen, then there is the area of regenerated epidermis with irregular rete pegs and loose subepidermic connective tissue, then a nodule where the regenerating epithelium has grown under the graft, then the autograft itself; and the granulating zone can just be made out. HE \times 7.5. (R.I.S.H. 1585 (1) (42)

FIG. 8.—Thick graft (1.36 mm., 0.05-in.) removed from abdomen (about 0.032 on dermatome calibration) when fixed and embedded showing the removal of the dermis and of the hair follicles. HE \times 20 (R.I.S.H. 1585 (5) (42)

FIG. 9.—Donor area three days after removal of a thick graft, only occasional minute islands of epithelium can be seen around the sweat ducts. (Compare with Figure 4). HE \times 40 (R.I.S.H. 1606 (2) (42)

FIG. 10.—Donor area five days after removal of a thick graft; most of the donor area is bare and there is only a small island of epithelium arising in relation to a sweat duct. (Compare with Figure 5). HE \times 40 (R.I.S.H. 1606 (4) (42)

zonally arranged collagen fibrils, completely deficient in elastica (Fig. 19) and the whole dermis is poorly vascularized. These facts explain why these scarred areas present a hard base, why the epithelium is prone to fissure and ulcerate after trauma, and Brown³ has also suggested that a factor in the liability to trauma is the lack of tethering of the epithelium due to the deficiency in rete pegs.

2. Process of Contraction:

All healing wounds contract. Cutaneous wounds, such as donor areas, heal mostly by epithelization and little by contraction. Measurements of the degree of contraction of the wound after the removal of skin grafts were made by comparing (in 62 patients) the size of the piece of skin on the dermatome drum with the size of the healed donor area.

Very little contraction occurs (2-5 per cent) in the donor areas until very thick grafts are removed. Contraction increases to (5-10 per cent) and may reach as high as 20 per cent when the grafts are cut in the base of the dermis where fat begins to appear.

Infection and mechanical and chemical irritation delay epithelial healing, and contraction is increased. We have already noted that contraction occurs more readily when the skin of the donor area is loosely bound down to the underlying tissues. This contraction of the wound is most marked along the direction of the lines of the skin (Langer's lines).

CONCLUSIONS

THE "INTER-ISLAND CONTRACTION"

It would appear that epithelial resurfacing originates from the individual epithelial islands formed from each hair follicle, sweat duct or cluster of sweat glands. Each epithelial island endeavors to join its neighbors not only by cellular division and migration but also by contraction (inter-island contraction). The longer epithelial healing takes to resurface the wound, the more marked this inter-island contraction will be. Such a delay in healing was observed in donor areas, in which the dermis was transected near its base; this was apparently due to the diminution in the number of elements of available epithelium, but infection, and mechanical and chemical irritation produce the same retarding effect. In such cases, a thick layer of relatively avascular inelastic fibrous tissue is laid down which is covered by an atrophic epithelium of poor quality (Figs. 18 and 19).

HEALING OF SUPERFICIAL BURNS

In the past there has been a tendency to attribute success or failure of local burn treatment to the type of treatment used. According to some, the use of certain chemicals over the burn wound has resulted in "healing without scars" of burns. It is true that the necessity of treating the burn with full-thickness skin loss, by early skin grafting is now generally recognized. However, it would appear that within the group of burns generally classified as second degree burns, variations in the quality of the healing of these areas depend upon the extent of the tissue destruction.

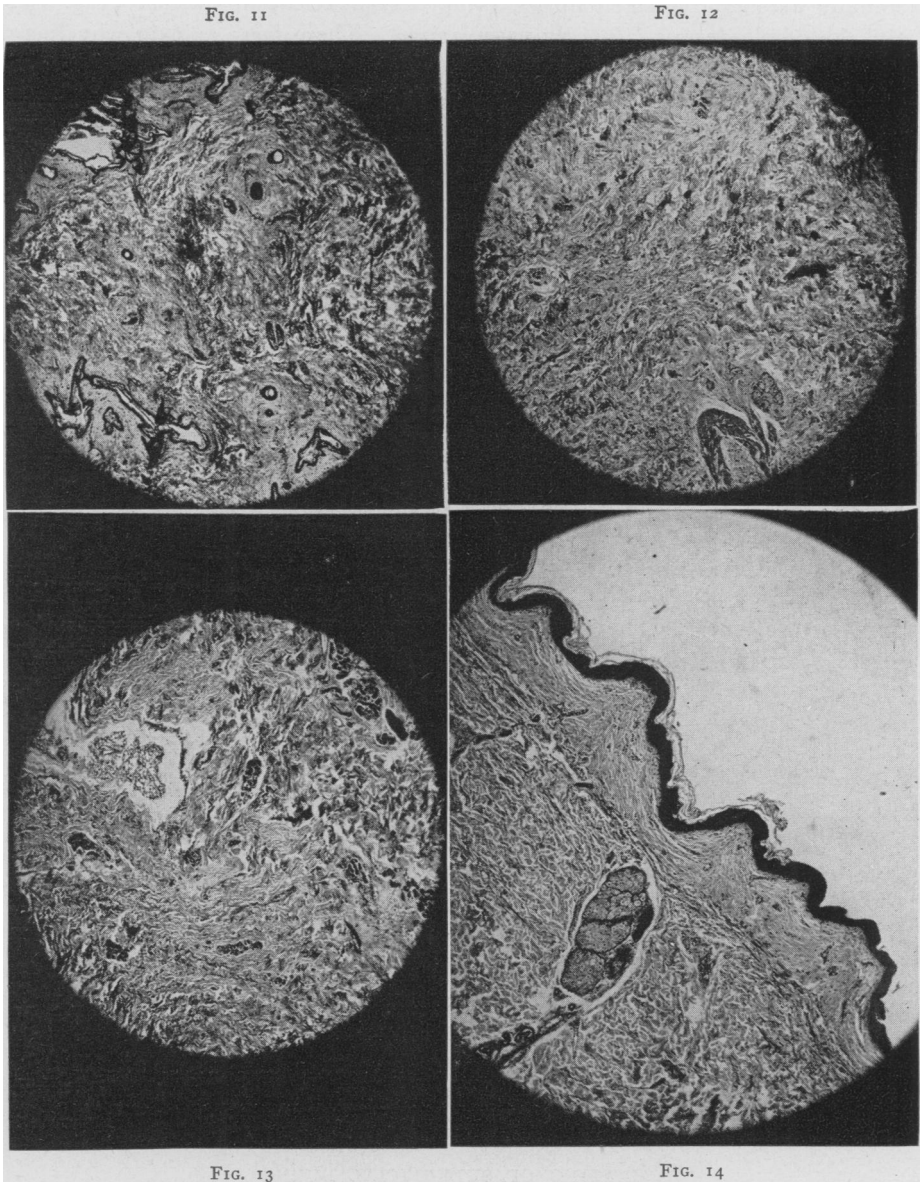


FIG. 11.—Horizontal section of skin of thigh below the epidermic surface, cut 0.18 mm. (about 0.007-in. on the dermatome calibration) when fixed and embedded. The openings of the hair and sweat glands can be seen, also a portion of the epithelium where the deeper epithelial folds occur. HE \times 20 (R.I.P.M. 345/43)

FIG. 12.—Horizontal section of skin of thigh, below the epidermic surface, cut 0.36 mm. (about 0.028-in. by the dermatome calibration) when fixed and embedded. There are no hair follicles and the sweat ducts can only be made out with difficulty and are scanty. HE \times 20 (R.I.P.M. 345/43)

FIG. 13.—Horizontal section of skin of thigh, below the epidermic surface, (about 0.034-in. by the dermatome calibration) when fixed and embedded. The coiled sweat glands are seen as well as intradermic protrusions of fat. HE \times 20 (R.I.P.M. 345/43)

FIG. 14.—Healed donor area 32 days after the removal of a thin graft. The epidermis is keratinized and of moderate thickness. Rete pegs are not marked but there is the normal undulation of the skin, and hair follicles. The contrast between the new-formed subepidermic connective tissue which is becoming collagenized and the coarse collagen fibers of the original dermis can be clearly seen. (Compare Figures 6 and 18). HE \times 40 (R.I.S.H. 1476 (3) (42))

During two years' service at the American Hospital in Britain (1940-1942) 191 burns were observed. These burns were seen at all stages, some as early as two hours after injury, others after complete healing, often because of the need for secondary plastic operations. The youngest patient was age 5 the oldest, 64. The patients were civilians as well as belonging to the Armed Services. The causes of the burns were variable; 143 were related to the War (gasoline explosions, plane crashes, incendiary bombs, flash burns of high explosives, accidents in war industries); 48 were of the usual civilian type. Early treatment had often been carried out in other hospitals, and the methods of local treatment employed were very variable: irrigation methods (saline baths, irrigation envelopes); coagulation methods (tannic acid and silver nitrate, gentian violet, triple dye, sulfadiazine in triethylanolamine); lightly applied dressings of wide-mesh vaselined gauze (*tulle gras*) and moist saline dressings; pressure dressings with fine-mesh vaselined gauze; plaster encasements and splints. The healing of these burn wounds was observed, and 63 biopsy specimens were removed for histologic examination.

In defining the depth of the burn, it would seem more logical to use anatomic terms. Table I shows the terminology used in this paper.

TABLE I
CLASSIFICATION OF BURNS

Superficial Burns (partial skin loss)	<table border="0"> <tr> <td style="font-size: 2em; vertical-align: middle;">{</td> <td style="padding-left: 0.5em;"> <i>Epidermal burns:</i> Erythema. Epithelial desquamation. <i>Dermal burns:</i> Blistering. Destruction of superficial layers of the dermis. <i>Deep dermal burns:</i> Destruction of the dermis down to the deep layers. <i>Mixed burns:</i> Small areas of total skin loss alternate with areas of deep dermal burns. </td> <td style="font-size: 2em; vertical-align: middle;">}</td> </tr> </table>	{	<i>Epidermal burns:</i> Erythema. Epithelial desquamation. <i>Dermal burns:</i> Blistering. Destruction of superficial layers of the dermis. <i>Deep dermal burns:</i> Destruction of the dermis down to the deep layers. <i>Mixed burns:</i> Small areas of total skin loss alternate with areas of deep dermal burns.	}	<table border="0"> <tr> <td style="font-size: 2em; vertical-align: middle;">{</td> <td style="padding-left: 0.5em;">Heal well.</td> <td style="font-size: 2em; vertical-align: middle;">}</td> </tr> <tr> <td style="font-size: 2em; vertical-align: middle;">{</td> <td style="padding-left: 0.5em;">Heal slowly, with contraction; may require skin grafting.</td> <td style="font-size: 2em; vertical-align: middle;">}</td> </tr> </table>	{	Heal well.	}	{	Heal slowly, with contraction; may require skin grafting.	}
{	<i>Epidermal burns:</i> Erythema. Epithelial desquamation. <i>Dermal burns:</i> Blistering. Destruction of superficial layers of the dermis. <i>Deep dermal burns:</i> Destruction of the dermis down to the deep layers. <i>Mixed burns:</i> Small areas of total skin loss alternate with areas of deep dermal burns.	}									
{	Heal well.	}									
{	Heal slowly, with contraction; may require skin grafting.	}									
Deep Burns (total skin loss)	<table border="0"> <tr> <td style="font-size: 2em; vertical-align: middle;">{</td> <td style="padding-left: 0.5em;">Destruction of the whole-thickness of the skin into, or beyond, the fat.</td> <td style="font-size: 2em; vertical-align: middle;">}</td> </tr> </table>	{	Destruction of the whole-thickness of the skin into, or beyond, the fat.	}	<table border="0"> <tr> <td style="font-size: 2em; vertical-align: middle;">{</td> <td style="padding-left: 0.5em;">Heal with difficulty, producing contractions and deformities. Skin-grafting the rule.</td> <td style="font-size: 2em; vertical-align: middle;">}</td> </tr> </table>	{	Heal with difficulty, producing contractions and deformities. Skin-grafting the rule.	}			
{	Destruction of the whole-thickness of the skin into, or beyond, the fat.	}									
{	Heal with difficulty, producing contractions and deformities. Skin-grafting the rule.	}									

1. *Epidermal Burns.*—These burns are characterized by erythema, often followed by an epithelial desquamation. A detailed study of the early histologic changes in experimental burns has been made by Leach⁴ and exactly comparable changes have been observed in man.

2. *Dermal Burns.*—Blistering is the rule. In the histologic sections studied, blisters were due to an epidermo-dermal separation produced by the exudation of fluid. In one section, the layer of separation was deeper than the junction of epidermis and dermis, in the dermis itself.

When the base of the blister is red, smooth and moist, healing may be expected in the absence of infection in 7-10 days. Epithelization in such superficial burns originates, possibly from a few remaining islands of basal epithelium, and from the hair follicles and the sweat ducts. The histologic picture is the same as that observed in the healing of a donor area after the removal of a thin skin graft (Figs. 3-6 and 14-17).

When the base of the blister is grey and dry, the dermis is more deeply involved, and healing will be slower because a layer of burned dermis must first be eliminated as a slough. Histologic examination has shown that

FIG. 15

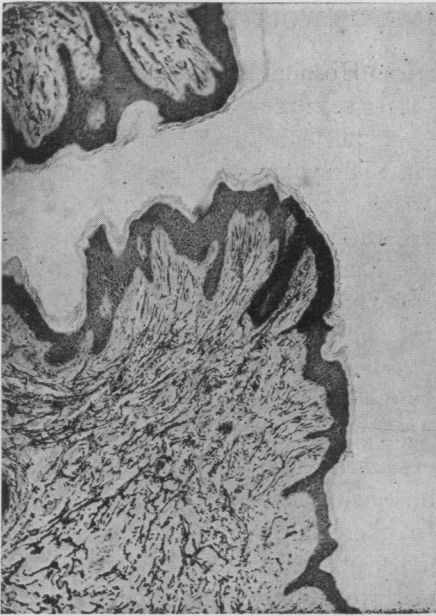


FIG. 16

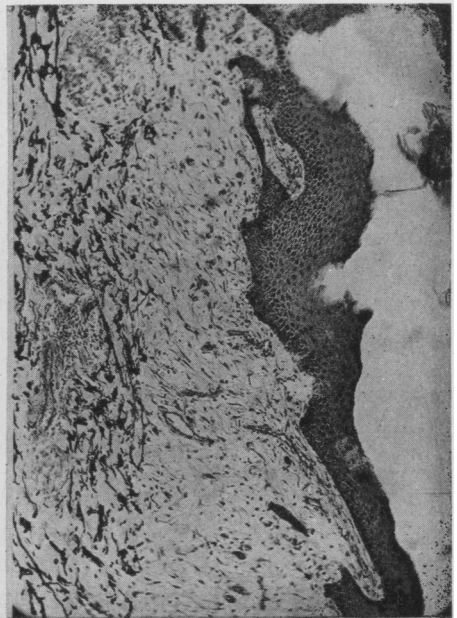


FIG. 17



FIG. 18

FIG. 15.—Normal skin to show elastic fibers. There is an imperceptible transition from the coarse fibers of the dermis to the fine fibers of the subepidermic region. Orcein $\times 120$ (R.I.S.H. 1585 (1) (42)

FIG. 16.—Healed donor area 12 days after removal of a thin graft from the abdomen (0.008-in. by the dermatome calibration). The elastic fibers of the original dermis can be clearly seen, but no elastic fibers have developed in the newly-formed, subepidermic loose connective tissue. Orcein $\times 120$ (R.I.S.H. 1585 (1) (42)

FIG. 17.—Healed donor 32 days after removal of a thin graft from the abdomen (0.008-in. by the dermatome calibration). The elastic fibers of the original dermis can be clearly seen and very fine elastic fibers have developed in the new-formed subepidermic connective tissue. (Compare with Figures 14-16). Orcein $\times 120$ (R.I.S.H. 1476 (3) (42)

FIG. 18.—Healed hypertrophic-scarred donor area 65 days after removal of a thick graft from the abdomen (about 0.034-in. by the dermatome calibration). There is a layer of atrophic epidermis with no formation of rete pegs and absence of hair follicles though sweat glands are present. The newly-formed subepidermic connective tissue has become collagenized, but deep to it are bundles of horizontally-arranged closely-knit collagen fibers. The original dermis can just be made out at the bottom of the photomicrograph. HE $\times 40$ (R.I.S.H. 1476 (2) (42)

although the structural pattern of the dermis has been maintained, yet the physicochemical characters of the collagen have been profoundly altered.

3. *Deep Dermal Burns*.—A thicker layer of dermis is destroyed, exposing the base of the dermis which appears as grossly punctated. Often one may see numerous small islands of epithelium, resembling minute pinch-grafts

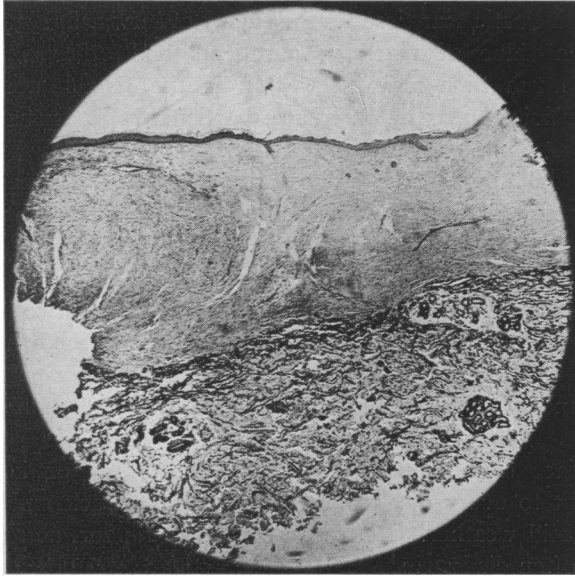


FIG. 19.—Healed hypertrophic-scarred donor area 65 days after removal of a thick graft from the abdomen (about 0.034-in. by the dermatome calibration). The elastica of the original dermis can be seen, but there is virtually no elastica in the newly-formed subepidermic connective tissue or the underlying collagen bundles. Note the thickness of the newly-formed tissue (1.6 mm., 0.066-in.); whereas, in a healed donor area, after removal of a thin graft, the new-formed connective tissue is only 0.36 mm. (0.013-in.) thick. Orcein $\times 20$ (R.I.S.H. 1476 (2) (42). (Compare with Figure 17).

from which epithelization spreads as a pearly-white thin layer. Healing is prolonged, particularly in infected cases. The healed epithelium is often thin, parchment-like and prone to cracking. Histologic examination in the healed stage shows an appearance similar to that described in a healed deep donor area, save that the zone of horizontal collagen fibrils is greater (Figs. 18 and 19).

CONCLUSIONS

SKIN GRAFTING AFTER SUPERFICIAL BURNS

In superficial burns when the deeper layers of the dermis are involved, (deep dermal burns, mixed burns) healing occurs with considerable contraction (inter-island contraction). Although the burn has not caused destruction of the full-thickness of the skin, a loss of skin surface is noted (invisible loss). This contraction and loss of skin surface following superficial burns is noted particularly:

1. When the skin of the area is loosely attached to the underlying structures, *e.g.*, the skin of the dorsum of the hand, or of the eyelids (resulting in ectropion).

2. In the vicinity of joints where it tends to interfere with their normal function.

The newly healed skin is smooth, shiny and very tight; it is often keloidal. Avascular and inelastic scar tissue is the enemy of serviceable repair. Without minimizing the value of massage, ointments and other physical therapy methods, too much time may be wasted in the rehabilitation of patients following superficial burns by their use, particularly in burns of the hands. Roentgenotherapy may be useful to reduce and soften hypertrophic scars, but if scar-epithelium overlies scarred dermis, the best treatment is their complete replacement by thick skin grafts. The presence of a thick dermal pad under the epithelium has been the reason for the serviceable repair given by the split graft.

Skin grafting is indicated in superficial burns for two main reasons:

1. For the relief of skin deficiency, of tightness, following inter-island contraction of deep dermal and mixed burns; particularly on the dorsum of the hand, around joints, for ectropion of the lids or distortion of the features of the face.

2. To replace skin of poor quality. Thin, shiny or keloidal skin is poorly resistant to every day trauma. It tends to crack and ulcerate, even as a result of cold weather. Return of sensation is poor, and the appearance of the skin is often disfiguring.

SUMMARY

1. In the study of superficial burns, a comparative study of 500 donor areas of partial thickness skin grafts were done. The following facts were noted:

1. The quality of the repair was roughly proportional to the rapidity of healing.

2. The rapidity of healing was dependent upon:

- A. The thickness of the graft removed.

- B. The thickness of the skin of the donor site.

- C. The presence or absence of infection.

3. Epithelial healing originates from the epithelial elements in the dermis, hair follicles, sebaceous glands, sweat ducts. The number of these elements decreases in depth of the dermis and so healing is slow.

4. In slow-healing areas, abnormal fibrous tissue is laid down in excessive amounts. The epithelium formed is of poor quality.

5. Contraction following healing is appreciable in areas from which grafts have been cut near the base of the dermis. In deep dermal burns and in mixed burns, such a contraction has been observed and is called "inter-island contraction."

2. From 191 burned patients, 63 biopsy specimens were removed. The extent of the anatomic destruction of the burn wounds and the mode of healing of these wounds were observed.

3. An anatomic classification of burns is proposed.

4. A description of the clinical and pathologic aspects of superficial burns is given.

5. The need for skin grafting certain superficial burns because of the tightness produced as a result of inter-island contraction or because of the poor quality of the healed skin is noted.

REFERENCES

- ¹ Brown, J. B., and McDowell, F.: *ANNALS OF SURGERY*, **115**, No. 4, 658, 1942.
- ² Cannon, B., and Cope, O.: *ANNALS OF SURGERY*, **117**, No. 1, 85, January, 1943.
- ³ Brown, J. B.: *Int. Abst. Surg.*, **67**, 105, August, 1938.
- ⁴ Leach, E. H., Peters, R. A., and Rossiter, R. J.: *Quart. J. Exp. Physiol.*, **32**, 67, May, 1943.