Original Articles.

THE HASTENING OF WOUND HEALING BY MEANS OF SKIN GRAFTING AND THE USE OF CERTAIN ORGANIC COLORING MATTERS.*

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INTRODUCTION.

WHEN I received an invitation from your secretary to read a paper before this Society I will admit that I accepted with considerable trepidation, as it seemed like "bringing coals to Newcastle" for any one to come to Boston to talk on the healing of wounds.

I should like to say now that I do not pretend to bring before you anything especially new, but want simply to speak about certain well-known procedures.

No attempt will be made even to outline the various procedures which have been employed to hasten wound healing, but I will confine myself to the methods of treatment which in my hands have yielded good results.

The wounds to be considered are those where, for one reason or another, there has been destruction of the whole thickness of the skin over an area of such size, or in such a situation, as to make the usual process of healing stretch out over a period of months, or possibly years.

The course and end results of the unaided healing in these cases is, in many ways, unsatisfactory. Among them, the discomfort to the patient and drain on the vitality; the liability to infection during the treatment; the unstable type of healing and probability of further breakdown, and the frequent occurrence of deformities due to contraction of the scar tissue. The economic aspect of the subject must also be considered, as the actual expense of the extensive dressings and time consumed in making them is a large item, especially if the patients are in the free ward, or in the out-patient department.

The reasons mentioned above should be sufficient to stimulate the surgeons in charge to continue their efforts to hasten the healing, and also might interest the hospital superintendents.

Unfortunately, many surgeons lost interest in the treatment of these extensive wounds after a time, especially if several unsuccessful attempts have been made at grafting, and the patient either remains in the hospital to be dressed by the nurses or internes, or returns for a routine dressing in the dispensary.

METHODS OF AIDING WOUND HEALING.

There are two general methods for aiding the healing of such wounds. First, by the transplantation of skin. Second, by the application of substances which will bring about rapid epithelial stimulation. A combination of the two methods is very advantageous in some instances.

SKIN GRAFTING.

The history of skin grafting will not be taken up, as it was fully considered, as indeed was the entire subject of skin grafting, in an excellent paper by Ehrenfried and Cotton in the *Boston Medical and Surgical Journal* of December, 1909.

Definition. — By "skin grafting" we mean the transplantation of either the whole thickness or a portion of the thickness of the skin from one part of the body to another, for the purpose of closing a breach of surface in the skin; in order to hasten its healing process, and to prevent, as far as possible, future cicatricial contraction. This may be done immediately on a fresh wound, or after repair has set in.

Classification. — In a general way grafts may be divided into *thin grafts*, where only a portion of the thickness of the skin is utilized, as obtained by the methods of Reverdin and Thiersch; and *thick grafts*, where the whole thickness of the skin is used. This latter division includes whole thickness sessile flaps and whole thickness pedunculated flaps. Grafts may be further classified into: *Auto*, or homo, grafts, where the graft is obtained from the same individual; *Iso*, or hetero, grafts, where the graft is obtained from another individual of the same species, and *zoo* grafts, where the graft is obtained from a lower species.

Surface to be grafted. — Whether to graft immediately or to wait until granulations have formed is a matter to be considered. There is no doubt that it is best to graft at once any clean operative defect; for instance, such a one as is left by the removal of a carcinoma of the breast; and such grafts are usually successful throughout. On the other hand, grafts placed immediately on the periosteum of the skull, after avulsion of the scalp, are much less liable to be successful, on account of the poor periosteal blood supply, and it is best to wait until healthy granulations have formed.

Grafts may be placed on a fresh wound, on undisturbed granulations, on granulations slightly rubbed with gauze pledgets, or on the firm base after the granulations have been removed. In my experience, any type of graft will take as satisfactorily, if not more so, on undisturbed granulations as on fresh wounds, provided that the granulations are healthy, firm, rose-pink in color, and are not exuberant.

It seems reasonable to believe that the capillary loops of undisturbed granulations are in better condition to immediately penetrate the graft than if these loops have been disturbed or curetted off and have to regenerate before they can penetrate and effectually nourish the newly transplanted skin. This regeneration takes about twenty-four hours, which means that considerable time is lost before the newly formed vascular loops are even ready to enter the grafts. Time is gained, therefore, by placing the grafts on undisturbed, healthy granulations.

Other advantages in placing grafts on such a surface are that there is no pain in the prepara-

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tion of the surface; no loss of blood, which is an important point in cases already much depleted; little likelihood of blood or serum collecting under the graft, and no danger of stirring up infection.

Preparation of granulating wounds. — It is impossible to give definite directions as to the stimulation and treatment of granulating wounds, as each is more or less a law unto itself. However, there is one point to be especially emphasized. The general health of the patient should be built up by every means at our command. One is often impressed when visiting surgical wards or dispensaries at the absolute neglect of this most important therapeutic aid, and it is quite remarkable to observe the change for the better in some of the wounds following the administration of tonics, with forced feeding, fresh air, etc.

There are various ways of stimulating the growth of granulations: Painting with tincture of iodine; touching frequently with nitrate of silver; dressing with balsam of Peru, either pure or mixed with castor oil in various proportions; with dressings saturated with normal salt or boric solutions; with liquor sodæ chlorinatæ and water 1:8; chloral hydrate solution, 2 gr. to the ounce of water; saturated aqueous solution of picric acid; modified styrax ointment; polyantiseptic ointment of Réclus, etc.¹

In dealing with unhealthy, exuberant granulations, a satisfactory and rapid method is to cauterize the surface thoroughly with pure carbolic acid and remove the granulations down to the firm base. Then dress with dry gauze over which is placed sterile boric ointment, or with wet salt gauze. Within twenty-four to forty-eight hours the new granulations will be firm, flat, healthy and ready for grafting. The free use of curved scissors is often desirable.

Another useful method, which takes more time but is equally effective, is to clean and dry the granulations and swab the entire surface with a saturated solution of nitrate of silver; over this paint one or two coats of tincture of iodine, and expose to the air and light. Finally, dress with balsam of Peru, 1 part, castor oil, 3 parts, on old linen, and carry out this procedure each day. A few days of such treatment will make a vast difference in the appearance and condition of an unhealthy granulating area.

Edematous granulations may be reduced with glycerine compresses or be covered with strips of rubber protective and a flat gauze dressing, held in place by a very snug bandage. Strapping the edematous area with zinc oxide plaster is advantageous in some cases.

Method of preparing the skin from which the graft is to be cut. — A satisfactory method of cleansing the skin before removing grafts of any kind is to shave the part selected, then scrub carefully with green soap and water. Rinse with sterile water, sponge with ether followed by alcohol. Then rinse thoroughly with normal salt solution.

Iodine technic is also applicable for disinfecting the skin before cutting all types of grafts, and seems to have no deterrent effect on the healing.

Dr. J. L. Yates, of Milwaukee, first called my attention to this method of cleansing the skin before cutting Thiersch grafts. By the use of this technic perfectly dry grafts can be obtained.

THIN GRAFTS.

Reverdin's method,² 1869. Technic. — The simplest way to obtain these grafts is to transfix a bit of the epidermis with a straight intestinal needle held in an artery clamp. Raise it so that a little cone is formed, and then with a sharp scalpel cut off the tip of the cone. Transfer the graft, still on the needle, to the undisturbed healthy granulations, with the raw surface downward, and press firmly into place with a pledget of dry gauze. Unless the entire wound is to be grafted, it is best to place the grafts near the growing edge of the wound and to arrange them in rows or clusters, leaving a space of about 5 mm. between each graft. I believe that more stable healing is produced when the grafts are placed this distance apart than when they are planted with greater intervals between them. This method gives numerous epidermic islands from which the new epithelium will spread to fill the gaps between and finally meet the stimulated epithelium from the edges of the wound.

Small deep grafts including nearly the whole thickness of the skin may be obtained by depressing the edge of the scalpel and cutting through the base of the cone.

Dress the grafted area with narrow overlapping strips of sterile rubber protective and either expose to the air or cover with a light wet salt dressing. The area from which the grafts are obtained may be dressed with silver foil, sterile boric ointment or any other desirable sterile dressing.

As these grafts are obtained without much pain and are applied to undisturbed granulations, general anesthesia is unnecessary. However, when a number of "pin grafts" are to be cut, it is desirable to inject 1% quinine and urea solution, or ½% novocaine, and take the grafts from the anesthetized area.

The procedure is by all odds the simplest method of grafting, but is tedious when a large area is to be covered. Very little skill is required in cutting and placing these small grafts, and they are almost uniformly successful when reasonable care is exercised.

The final healing of an extensive surface is not as stable following grafting by this method as from the methods to be described later, and there is more likelihood of ulceration and future cicatricial contraction. The cosmetic result is also not so good. However, I have used Reverdin grafts placed close together in selected cases with great satisfaction and with excellent results. In fact, on some wounds it seemed impossible to get any other type of graft to take.

The Thiersch method,³ 1886. Technic. — The modified technic, which is in use at the Johns Hopkins Hospital, and with which I am most familiar, is as follows: 'After cleansing the skin as above described place a small sand bag beneath

the arm or thigh in order to give a better surface from which to cut. Arrange the usual sterile dressings about the selected area. Care must be taken that no carbolic or bichloride solutions be brought into the field or touch the grafts, either on the dressings, gloves or instruments.

Firm traction is exerted on the limb. The skin, wet with salt solution, is then put on the stretch, and held as flat as possible by means of two sterile boards about eight inches long placed quite close together at right angles to the length of the limb, one being held by the assistant and the other by the left hand of the operator. The field is soaked with normal salt solution and the edge of a thin sharp Catlin knife is then engaged in the skin between these boards and held almost flat against the limb, and by a sawing motion the graft is cut, the knife closely following the board in the hand of the operator, which is drawn slowly along in front of it. The graft is cut at a level which will include the top of the papillary layer of the corium, and only a slight amount of bleeding will follow.

The graft is then placed, with the raw surface uppermost, upon a piece of protective, and the whole then placed on a board, and by means of a blunt instrument the graft is spread out evenly and to its full extent. It is then covered with gauze wet with salt solution and put aside until required.

Being sure that the wound to be grafted is perfectly dry, the protective on which the graft is spread is placed over the defect, so that the graft is next to the wound. Gradually the protective is lifted up and the graft separated and left in place. It is then pressed down evenly and snugly on the wound with gauze pledgets in order to get rid of air bubbles and to make it adhere as closely as possible. This maneuver is the most satisfactory way of handling Thiersch grafts of every size, and any one who tries it will be convinced of its efficacy and simplicity. If more than one graft is needed, they should be placed so that they overlap a little the edges of the wound and the adjacent grafts.

Immediately over the graft place rubber impregnated mesh and secure its edges with adhesive plaster, in order that it may grasp the grafted area firmly and hold the grafts snugly in position. The mesh is especially indicated where, on account of the position of the defect, the grafts are liable to be displaced. Over the mesh, moist salt dressings may be placed, and the whole secured by a bandage. Silver foil is the dressing most commonly used at the Johns Hopkins Hospital, and is very satisfactory for Thiersch grafts.

A good dressing for the area from which the graft is cut is a sheet of perforated sterile rubber protective, covered with boric ointment, and held in position by adhesive plaster. Over this is placed a light gauze dressing, and the whole secured by a bandage.

Although Thiersch grafts may be cut under local anesthesia, as a rule a general anesthetic is used when grafts of any considerable size are

required. By the method above described very large grafts may be obtained, but this requires more or less skill and considerable practice.

I will mention a few measurements to give an idea of the size of single grafts cut with a Catlin knife: 8 x 16 cm., 10 x 18 cm., 12 x 12 cm., etc. In fact, single grafts have been cut the entire length of the thigh and from 8 to 12 cm. in width.

Thin Thiersch grafts of uniform thickness seem to take better than those of varying thickness. It is very difficult to cut a large graft from a fat or flabby thigh.

Phlebitis of the long saphenous vein has followed cutting Thiersch grafts from the left thigh, and for this reason the right thigh should be used whenever practicable. As far as I can ascertain, no case of phlebitis has followed cutting on this side.

When more skin than is required is cut, it can be grafted on the area from which it came with complete success.

What seems to be a failure at the first dressing will sometimes turn out very well.

Some grafts are quite dry during the healing process, while others are moist. In the moist variety a strong, characteristic glue-like odor is often noticed; this is probably due to the secretions which are held in by the dressings.

Thiersch grafts adhere to the underlying tissues for a much longer time than whole thickness grafts, and the majority of Thiersch grafts, especially on breast cases, that I have examined were still adherent throughout the greater part of their extent, even after several years.

The Thiersch graft cut by one method or another is that chosen by the majority of surgeons, and the healing of an area covered with the large thin grafts is very much more stable than the healing following the small thin grafts of Reverdin.

THICK GRAFTS.

Whole thickness pedunculated flaps.—Before the technic for the transplantation of whole thickness sessile flaps was perfected and proved so successful, whenever a thick graft was necessary better results were obtained by living pedunculated flaps, either from neighboring or distant parts, with subsequent amputation of the pedicle.

Transplantation from distant parts is as a rule very trying to the patient because of the enforced position, and in addition a considerable defect is left. However, the raw area as well as the under surface of the flap may be covered by thin or thick grafts.

Sliding plastic flaps from neighboring parts are of great value in the treatment of certain defects. Also pedunculated flaps from distant parts, which are brought into position by either a single or double transfer. I will not take up the special methods advocated by various surgeons on account of lack of time.

The pedicle may be amputated in from five to fourteen days, and the edges of the separated base should then be shaped and sutured into position.

Pedunculated flaps which are properly cut, as

a rule are successful. By this method a considerable thickness of subcutaneous fat may be transplanted with the flap.

Sessile whole thickness flaps: LeFort,⁵ 1872; Wolf,⁶ 1875; Krause,⁷ 1896. *Technic.*—After cleansing the skin, and drying it carefully, mark out lightly with a scalpel an elongated ellipse, in order that the edges of the wound can be easily approximated after the flap is removed, remembering that the skin after being cut immediately shrinks to about two thirds of its original size transversely, and a little less in its length. Remove the skin with the underlying fat by a few clean sweeps of the knife down to the fascia or aponeurosis covering the muscle. Then lay it on the palm of the hand, raw side up, and trim off the fat in one piece with curved scissors. Buttonhole the flap here and there or perforate with a leather punch, and press down snugly on to the fresh wound, or on carefully dried, healthy granulations. I believe that better results can be obtained by preserving a perfectly dry technic until the graft is in place.

The rubber-impregnated mesh is advantageous as a splint for this type of graft also. It is wise to make the flap additionally secure by means of numerous superficially placed fine silk sutures, where accurate approximation is desired, as, for instance, on the face. Moist salt dressings over the rubberized mesh are usually the most satisfactory, and should be kept on from twenty-four to forty-eight hours. Then remove the dressing down to the mesh and either replace the moist dressing or anoint with some bland ointment and expose to the air. Silver foil is also an excellent dressing for whole thickness grafts.

After transplanting whole thickness grafts to the palm of the hand or fingers for the relief of contractions, I have found it advantageous to put the part up in a plaster cast, and leave it undisturbed for three weeks.

The skin may be taken from almost any situation where there is sufficient laxity of tissue to admit the suturing of the edges after removal of the graft. The graft should be selected with due regard to the type of skin which is to surround it. For instance, it is advisable, where transplantation to the face is proposed, to select the inner fore part of the upper arm, as it is thin and practically hairless.

As an example of the contraction of a whole thickness graft, immediately after cutting, the following measurements may be of interest: As marked out on the skin of the thigh before cutting, 14 x 3.75 cm.; after removal, 10 x 2.5 cm.; area of wound after removal of the flap, 16 x 6.5 cm. It is important to handle the skin as little as possible.

The ideal result desired in whole thickness grafting is elasticity, softness, movability and normal color. Krause says all of these are obtained in one third of the full takes, but my experience shows a considerably larger percentage.

The operative procedure in securing thick grafts is undoubtedly much greater than for thin grafts, but, on the other hand, the healing following thick grafts is as stable and firm as normal skin. I

believe that the ultimate result in selected situations will more than justify the discomfort experienced by the patient. I have not yet seen a contraction occur under a whole thickness graft, but under an area healed by thin grafts contraction is not uncommon, especially in the palm of the hand.

Thick grafts are usually obtained under general anesthesia, preferably nitrous oxide, but can be removed perfectly well under local anesthesia after outlining the flap or blocking a nerve.

As the success of the flap depends on the blood supply of its new bed, it follows that sessile flaps should not be placed on uncovered cartilage, nor be used for bridging over defects, but that pedunculated flaps be used for this purpose. However, sessile flaps can be successfully placed on tendons, fascia, muscle, cortical and spongy bone, periosteum, and even on the dura mater.

Krause advised against the use of whole thickness sessile flaps in face plastics, as he says there is liability to blotchy brown pigmentation, and that cyanosis may persist in the flap for months. Furthermore, that the surface of the flap may become irregularly shriveled, and although these changes in no way impair the efficacy of the flap, he advised Thiersch grafts or pedunculated flaps for this region. As all of these conditions may occur also in thin grafts, I use whole thickness sessile flaps on the face in preference to thin grafts, as I have found the lasting and cosmetic results have been so much better.

There is a prevalent idea that whole thickness sessile flaps must be small in order to heal successfully. My experience has been that you can transplant as large a graft of this type as you can safely provide, and the larger the grafts, the fewer the scars between them.

Vascular sprouts have been demonstrated in epidermic grafts on the second day, and in cutis grafts on the third day. Under whole thickness grafts a layer of adipose tissue regenerates within a comparatively short time, and this is most important, as it prevents contraction and insures early movability.

Whole thickness grafts which are placed on untouched granulations project at first above the level of the surrounding skin, but during the process of healing they assume the normal level.

The Thiersch method will, of course, remain the method of choice on account of its simplicity and smaller operative action, and on account of the large areas which can be covered at one grafting, but in such localities as the elbow, palm of the hand, knee and heel, and in other regions where there is considerable pressure and friction, the thin grafts will not stand the strain, and grafts of whole thickness are indicated.

Iso or hetero grafts.—There is much difference of opinion as to the advisability of utilizing iso or hetero grafts, and many surgeons insist that only auto grafts should be used. Lexer,⁸ at the meeting of the German Surgical Congress in 1911, went so far as to state that it was useless to try iso grafts as none of them ever took and, furthermore, none of them ever lasted longer than three

weeks. There is no doubt but that there are certain individuals on whom iso grafts will not take, the reason for which I am not yet prepared to say. On the other hand, I have seen individuals on whom iso grafts from a number of different people have taken without difficulty. Of course auto grafts are more likely to succeed, but a study of the results obtained by means of iso grafts at the Johns Hopkins Hospital, and also my own experience with these grafts, have convinced me that both thin and thick iso grafts are well worth trying, and that very good lasting results may be secured in some cases if the grafts are obtained and transplanted with the proper technic.

Even though an iso graft should not last more than three weeks, as Lexer claims, it has the power of markedly stimulating sluggish wound edges, and would be useful for this purpose alone.

In reviewing the first 550 cases grafted at the Johns Hopkins Hospital, there were 42 cases in which iso Thiersch grafts were applied.⁹ Twenty-one were complete takes, 16 partial takes, and 5 were total failures, thus showing that iso grafts are well worth trying.

When iso grafts are used it is of great importance that the individual from whom the grafts are obtained be healthy, as cases of syphilis, tuberculosis and smallpox have been reported as having been transmitted in this way.

Zoö grafts.—Both thin and thick zoö grafts have been used, and a number of successful cases have been reported in the literature. The skin of dogs, lambs, rabbits, guinea pigs, frogs, etc., has been used. The most uniformly successful reports seem to follow the use of skin from a young pig. My own results with zoö grafts have been disappointing. Most of the grafts would apparently take and would bleed when cut into, but within a few weeks they would melt away.

Changes in pigmentation.—It is interesting that grafts from a negro which have been successfully transplanted on to a white person gradually fade and assume the color of the host, and vice versa. This has been established by a number of observers, and has also been the experience at the Johns Hopkins Hospital.

It must be borne in mind that some auto white grafts become deeply pigmented during the process of healing, and this pigment remains in the grafted area. This fact must be remembered where pigmentation of white grafts on the negro takes place. In the few cases reported where black skin transplanted on to a white person remained pigmented, this same process might have occurred after the natural pigment had been disposed of.

From observation I am convinced that the actual change in the color occurs. There are several theories concerning these changes, but lack of time prevents their consideration here.

Vitality of grafts.—It is not necessary to apply grafts immediately after cutting, and grafts which are kept moist and cold can be transplanted after a number of days or weeks with as good results as when just cut. This is very important,

as grafts can be cut at the time of operation when the patient is under a general anesthetic, and applied later, if conditions for immediate grafting are not satisfactory.

REFERENCES.

- ¹ *Modified styrax ointment*: Olive oil, 100 gm.; liquid styrax, 50 gm.; rosin, 35 gm.; rosin elemi, 35 gm.; yellow wax, 44 gm. (Fouchard.)
- ² *Poly-antiseptic ointment*: Iodoform, 1 gm.; orthoform, 4 gr.; antipyrin, 5 gm.; salol, 3 gm.; ac. boric, 3 gm.; bichloride of mercury, .1 gm.; ac. carbol, .5 gm.; vaseline, 200 gm. (Besson.)
- ³ J.: Bull. et mém. Soc. de Chir. de Par., Dec. 8, 1869.
- ⁴ Verhandl. d. deutsch. Gesellsch. für Chir., Berlin, 1874, p. 69; 1886, p. 17; 1888, p. 66.
- ⁵ Ann. Surg., March, 1909, p. 417.
- ⁶ Gaz. des Hôp., 1872, nr. 7.
- ⁷ Brit. Med. Jour., Sept. 18, 1875, p. 360; Glasgow Med. Jour., July, 1876, p. 420.
- ⁸ Sammlung klin. Vorträge, 1896, n. 143.
- ⁹ Arch. für klin. Chir., heft 4, 1911, p. 827.
- ¹⁰ Johns Hopkins Hosp. Rep., vol. xv, p. 307.

(To be continued.)

CHRONIC INTERSTITIAL NEPHRITIS. ACUTE INDIGESTION AS AN IMPORTANT SYMPTOM.

BY MALCOLM SEYMOUR, M.D., BOSTON.

THAT gastro-intestinal disturbance in the course of chronic interstitial nephritis is not uncommon is evident not only from the number of cases which come to our attention, but also from the newspaper reports of similar cases.

Almost daily we read of the death from acute indigestion of some prominent public or private individual.

The cause of death here is evidently not indigestion in itself. There must be some underlying factor, and in a large majority of cases involvement of the kidneys will be found.

To be sure, not every case of gastric disturbance in the adult has a contracted kidney and uremia as a foundation, but if greater care be used in finding a cause of the indigestion or dyspepsia, attention will oftener be directed to the kidneys.

Many writers have called attention to our inability to make a correct intra-vitam diagnosis of chronic interstitial nephritis. This is due many times to careless history taking, hurried examinations, under-valuation of supposedly unimportant symptoms, and erroneous interpretation of urinary findings.

It is not my purpose to go into a lengthy discussion of chronic interstitial nephritis, but to direct attention to the too frequently overlooked evidences of renal involvement, with special reference to the altered digestive function and to the analysis of the urine.

Chronic interstitial nephritis is essentially intransient in its course. Its onset is masked by other deteriorative processes and compensatory changes. Once established, it is slow and persistent, spectacular signs and symptoms are usually lacking, and it is the apparent absence and meagerness of signs, especially in its earlier stages, which characterize the disease. This applies not only to the symptomatology and physical manifestations, but to the excretory function of the kidney.