

on his initial trip before he imparts that information, and is satisfied that they fully understand the matter; and it frequently is necessary to get an interpreter when one is dealing with Italians and other foreign-born people who do not speak the language.

We have printed instructions. It would be interesting to find out how many of the hundreds given out are read intelligently and carefully. We are doing a great deal in the way of personal instruction of the family directly, or through an interpreter.

As to the physician's duties in case of contagious diseases, there is much to be said. There are all sorts of physicians in Chicago, as elsewhere. Some are antagonistic or careless; some are in sympathy with our work; but there is no one factor that is of as great importance in this entire situation as the physician factor. It is up to the physicians to "get next" to the progressive work that is being done in this line; for if they don't, they will be left behind; progress will be made in spite of their indifference.

We not only put a policeman at the door, but frequently two: one at the front entrance and one at the rear; and two means four, because they work in relays, night and day. It is important; it brings the people to a realization of the fact that we mean business, and it has a salutary effect on them.

Common sense and tact are the greatest factors. You cannot compel the members of a Chicago community, or any large community, to observe strictly any precaution they have never used before and perhaps have never heard of before. Many of these families have had a case of contagious disease for the first time; they do not understand the situation, and if you go at them abruptly you will lose out. This is where experience and tact come in. We try to have inspectors with common sense and education, so far as possible.

We allow nothing to come from the room without being thoroughly disinfected; and we supply bichlorid tablets; we make a solution in a wooden bucket right in the room, and not only are the linen bedding and the nurse's clothes disinfected, but also the bed-clothing, and the floor is mopped daily.

THE TREATMENT OF WOUNDS

A FIRST ARTICLE *

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In the actual condition of therapeutics, aseptic wounds generally heal in a few days. The more ambitious dreams of the surgeons of the pre-Listerian era have been fulfilled. Nevertheless, we have no right to believe that the treatment of wounds has reached its ultimate perfection. We must investigate whether or not it is possible to advance farther. In the treatment of wounds, we content ourselves by protecting the tissues against infection, and we leave to Nature the care of cicatrization. Would it not be feasible to act on the processes of reparation themselves and to activate them? The wounds which now heal in a few days could possibly be caused to heal in a few hours. The treatment of fractures would also be simplified. The development of methods for the stimulation of the growth of epithelial cells, for the inhibition or the activation of the proliferation of connective tissue, for the artificial production of osteogenesis, etc., would greatly improve the therapeutics of the ulcerations of the skin and of the lesions of peripheral nerves, bones and many other tissues or organs. This new evolution of surgery depends on the discovery, partial at least, of the laws of redintegration of tissues of mammals. Cicatrization and regeneration are the expression of the power to persist in its form with which all organisms are

endowed. We are deeply ignorant of the nature of this function of redintegration. It is, as is the function of nutrition, a fundamental property of living matter. To know its nature is as impossible as to know the nature of life. Besides this knowledge would be useless. From a metaphysic standpoint it would be interesting to discover *why* a wound heals. But from a scientific standpoint, it is infinitely more important to know *how* it heals, because it would then be possible to find what stimuli start the complex mechanisms of the regeneration of the tissues. Therefore, the physiologic phenomena of cicatrization must be investigated. It is true that the power of redintegration escapes our methods of research. But the physico-chemical processes which this power, as a directing idea, coordinates and harmonizes in view of the morphologic reparation, can be brought into the field of experiment. We must, therefore, analyze the mechanisms which are instrumental in the cicatrization of a wound, the factors which modify their functions, the stimuli by which they are started, and the causes of their reciprocal cooperation to the common work. Perhaps it will become possible to use some of these agents for the artificial activation of the regeneration of tissues and the treatment of wounds.

MECHANISMS OF THE REPARATION OF A CUTANEOUS WOUND

Since many centuries all surgeons know the anatomic processes of the cicatrization of a wound. On the open surface, granulations appear, and, by their contraction, bring closer to each other the edges of the epidermis. Then the epithelial cells wander on the granulous tissue and a new epidermis is formed. These phenomena can be divided into four periods: quiescent period, period of granulous retraction, period of epidermization and cicatricial period.

The experiments on which this article is based were performed chiefly on dogs. The cicatrization of wounds obtained by resection of a flap of skin was observed. The resected flap was of geometrical form, rectangular, trapezoidal or circular. In order that the edges of the old epidermis might be easily seen, I used black animals or I stained the edges of the wound with India ink. It was then possible always to distinguish the new from the old epidermis, and to follow accurately the variations of the dimensions. The dressing consisted of talcum powder and gauze or warm paraffin. The wounds were kept as nearly aseptic as possible. When they became infected the results were discarded.

1. *Quiescent Period*.—The quiescent period extends from the time of the resection to the time of the beginning of the granulous retraction. During the first days the dimensions of the wound do not vary. If we represent graphically by a tracing the time of healing the successive distances between two points A and B taken on the opposite sides of a rectangular wound, the tracing during the quiescent period is horizontal. Suddenly it inclines downward. It is the beginning of the granulous retraction. Often the immobility of the edges of the wound during the quiescent period ceases rather suddenly; there is no period of transition and the active period of reparation starts immediately. The main characteristic of the quiescent period is the great variability of its duration. In some cases it lasts only one or two days, while in others it lasts four or five days.

2. *Period of Granulous Retraction*.—At the end of the quiescent period the edges of the wound begin to advance toward each other. The tracing of the con-

* From the laboratories of the Rockefeller Institute for Medical Research.

secutive distances between the points A and B, taken on the opposite sides of a rectangular wound, shows a sudden inclination downward. Progressively, the inclination of the curve diminishes and, after a few days, it is almost horizontal. The reduction in size of the wound is very active during the first days of the period of granulous retraction. Then it becomes progressively slower until it comes to a standstill. This fact was observed long ago. It was believed that the activity of the granulations depended on their age, while it depends really on the dimensions of the wound.

By measuring the rate of reparation of a rectangular wound, I found that it diminishes progressively from the beginning to the end of the period of granulous retraction. The rate when the wound is 60 or 70 mm. is about 9 or 10 mm. for twenty-four hours. When the wound is one of 40 mm. the rate is about 3 mm. When the dimensions of the wound are only 20 mm. the rate becomes very slow. In all wounds the rate becomes about zero when the edges have reached a distance of about 10 or 15 mm. from each other. It is therefore certain that these differences in the rate of reparation are functions of the size of the wound.

By observing on the same animals large and small wounds, I could see during the same period the larger wound diminishing with a much greater speed than the smaller wound. For instance, two rectangular wounds (Experiment 176) were made on the same animal. The transverse dimension of the one was 66 mm. and of the other 26 mm. During the first forty-eight hours of the period of granulous retraction, the larger wound diminished 20 mm. and the smaller 4 mm. On trapezoidal wounds, it was observed also that the reduction in size of the smaller side is very much slower than the reduction undergone by the larger side. On circular wounds, made on the same animals with cutting tubes 1 and 2 cm. in diameter, the same phenomena were observed. Many other experiments have been performed. It is certain that the *rate of reparation of the granulous period is directly proportional to the size of the wound*: that is, to the effort to be accomplished in order to bring about the redintegration of the parts. It must be noticed that during the period of granulous retraction, the redintegration of the skin of mammals follows the law discovered by Spallanzani on the salamander. If the tail of a fish or salamander is cut off near its base, the new part grows faster than when the tail is cut off nearer the tip. The new part which arises from the basal cut grows more rapidly at first and more slowly later. The rate of regeneration is proportional to the importance of the work to be done. It is remarkable that, on mammals, the reparation of the skin, which is brought about by a very different mechanism, obeys the same general law.

The period of granulous retraction plays a very important rôle in the healing of the middle-sized and the large wounds. Thus, a wound of 60 or 70 mm. can be reduced to one-third and one-fourth of its primitive size. A wound of 30 mm. can be reduced to one-half its size. The importance of the granulous period is less for the small wounds. The effort of the granulations on a wound of about 15 mm. reduces its dimensions to three-quarters or even less of its original size.

The end of the granulous period corresponds to the beginning of the epithelial wandering from the edges of the wound. For a wound of about 30 or 40 mm. the retraction becomes exceedingly slow and even stops completely when the distance between the edges has been reduced to 10 or 15 mm. When the wound is larger,

the retraction stops often when its dimensions are still 20 or 25 mm. In that case the epithelial wandering is very slow and often the result is an ulcer.

It seems that the epithelial wandering on the surface of the granulations stops immediately their retraction. The epidermization not only coincides with the end of the period of granulous retraction, but it causes it. In the corner of a granulating rectangular wound I deposited a small square graft of skin. After a few days the graft was found surrounded by the normal skin of the edge and the wound had assumed again a perfectly rectangular appearance. This shows that the retraction stopped at the level of the graft, while it still went on in the other parts of the wound. In another case, the epidermization of the upper part of a large square wound was stimulated by a graft, while the lower part remained without epithelium. It was then observed that the distance between the India-ink-stained edges of the old epidermis was still diminishing in the lower part, while it increased in the upper part. The shape of the square wound became trapezoidal. Sometime after complete epidermization it became square again. It is, therefore, certain that the epidermization inhibits the retractive function of the granulations. When the epidermization takes place early, the scar is large and thin. When the epidermization is late, the granulations undergo a stronger retraction and the scar is thick and comparatively smaller.

The function of the granulous period is also to prepare the surface of the wound for the wandering of the epithelial cells. But it seems probable that its main rôle is to bring the edges of the wound to a certain distance—about 10 or 15 mm. in the dog. It is shown by the fact that if the wound is only 10 mm. wide, practically no retraction occurs. It does not occur because it would be useless, since at the distance of 10 mm. the next mechanism of the reparation, that is, the epithelial wandering, can take place easily, as will be shown later.

3. Period of Epidermization.—On a rectangular wound, the edges of which are stained with India ink, it is easy to detect the beginning of the period of epidermization. The new epithelium spreads at first very slowly on the surface of the granulations. It is difficult to locate exactly the free edge of the new epidermis. Nevertheless, by using paraffin dressing, it is possible to see with certainty in a few cases the edge of the wandering epithelium. The new epidermis is exceedingly delicate and a great many external factors interfere with its growth. The best medium for its growth is certainly coagulated fibrin, which can be obtained by using as a dressing paraffin of a certain consistency and melting-point.

The time of the beginning of epidermization does not depend on the age of the wound but on its dimensions. If the wound is large, the epidermization is tardy. It occurs very much earlier when the wound is smaller.

By measuring the distance between two points taken on the free edge of the new epidermis of a rectangular wound, it was found that the growing of the epithelium is exceedingly slow if the distance is more than 12 or 15 mm. But if the edges are located less than 10 mm. from each other, the epithelium wanders more quickly on the granulations. When the free edges of the epithelium are closer, the rate of cicatrization is very much faster. I found, in one case, a rate of 2.5 mm. for a distance of 5 mm. The curve representing the positions of the two points runs at first almost horizontal and progressively inclines itself downward with an accelerated rate.

When at the end of the granulous retraction of a large wound, the edges of the old epidermis are still at a distance of 20 or 25 mm. the new epidermis cannot spread on the granulations and the cicatrization of the wound comes to a standstill.

It seems that the time of the epidermization and its rate depends mainly on the dimensions of the wound. This point has been ascertained by several other sets of experiments.

By observing trapezoidal wounds it was found that the smaller side about 8 mm. wide was completely epidermized while the larger side about 20 mm. wide presented an epithelial band of about 2 mm. along the edges of the old epidermis. On irregular wounds the epidermization begins always on the points where the edges are closer to each other. In lozenge-shaped wounds the epidermization begins in the acute angles and the wound becomes an ellipse. On several kinds of trapezoidal wounds it was always found that the epidermization begins sooner and spreads more quickly between the points which are separated by the shortest distance.

Therefore, it appears that the law of reparation by epidermization is absolutely different from the law of separation by granulous retraction. *The rate of the epidermization is inversely proportional to the dimensions of the wound.* It is very slow when the distance between the edges of the wound is more than 10 or 15 mm. The maximal activity of the epidermization seems to take place when the cicatrization is nearly complete, and when the edges of the new epithelium are very close to each other.

4. *Cicatricial Period.*—The dimensions of the scar can easily be measured when the edges of the old epidermis are stained with India ink, or when the animal is black. It was found that the scar of a large wound is comparatively smaller than that of a small wound. On the same animal, two wounds of 66 mm. and of 26 mm. were observed. The 66 mm. wound gave a scar of 22 mm. and the 26 mm. wound a scar of 13 mm. The scar of the large wound was only one-third the size of the wound, while the scar of the small wound was one-half the size of the wound. If the wound is still smaller, 10 or 12 mm., the scar is almost the same size as the wound. This is the natural result of the law of granulous retraction.

The evolution of the scar is very slow and the cicatricial period of a wound very long. As soon as the epidermization is completed, the distance between the points A and B of the edges of the old epidermis grows greater. The tracing shows a slight movement upward of the line representing the different values of the distance A and B. The points A and B have a tendency to go back to their former position. This progressive enlargement of the scar lasts for a long time and its result should be a complete redintegration.

The mechanisms which are instrumental in the cicatrization of a wound are coordinated in such a way that the reparation is continuous and progressive. Nevertheless, the reparation presents phases of maximum and minimum activity during which the rate is higher or lower. During the quiescent period, the end of the period of granulous retraction and the beginning of the period of epidermization, the rate of the reparation is slow. It is maximum at the beginning of the period of granulous retraction and at the end of the period of epidermization. The two mechanisms are adapted to the healing of small and middle-sized wounds, the width of which is not over 40 mm. In a wound 30 or 40 mm. in width or smaller, the retraction of the granulations

is very efficient, since it can quickly bring the edges to a distance of 10 or 15 mm. This distance is very favorable to the epidermization. Therefore, at the same time when the rate of reparation by granulation becomes very slow, the epidermization starts and the reparation goes on without interruption, although by a different mechanism. But if the wound is larger, 60 or 70 mm., the retraction of the granulations cannot bring the edges to the minimum distance. They remain at a distance of about 20 mm. and the reparation comes to a standstill because the epidermization cannot take place easily under these conditions. The mechanisms are very efficient for the healing of the injuries to which the animals are exposed in their every-day life. But they do not work as satisfactorily for the larger wounds.

VAPOR ANESTHESIA APPARATUS

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In 1905 I first presented my apparatus for vapor anesthesia to the medical profession. At that time it seemed quite complicated. It consisted of three bottles connected by tubing, one of which was for ether, one for chloroform and the other being a bottle containing hot water or hot neutral oil for warming the vapor, and having a tube through which the vapor was delivered to the patient. Each bottle was provided with a stop-cock, and a mixture of chloroform and ether could be given. The ether bottle contained a drum for assisting in vaporizing the ether. I have perfected the different parts and

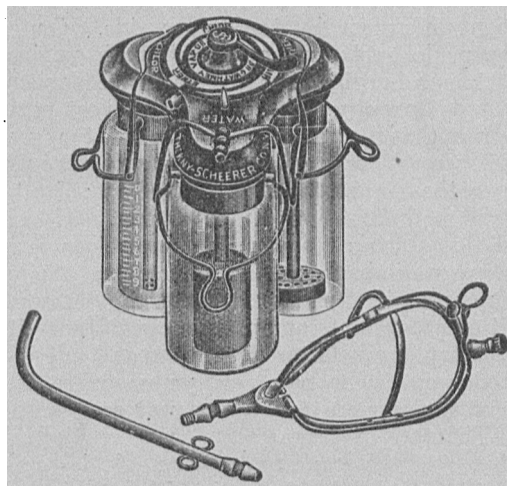


Fig. 1.—This shows the three bottles of the vaporizing apparatus, with the single stopcock. The figure at the right below shows the tubular frame of the mask through which the vapor passes to the gauze covering. The tube at the left below is used in delivering the anesthetic in operations about the mouth or throat in which the mask cannot be used.

now present a simplified apparatus consisting of three bottles with one stop-cock. The drum in the ether bottle has been modified (as suggested by Dr. Charles E. Boys, Kalamazoo, Mich.), so that it now vaporizes all of the ether, and it does not necessitate refilling the bottle as often as before. A small bottle holding 10 drams of chloroform has also been placed within the chloroform bottle. This is enough chloroform for a long operation. The end of the tube in the chloroform bottle has been closed and a number of pinhole perforations made at the bottom of this tube, so that it is impossible to waste the chloroform as the air passes through. The last improve-