CICATRIZATION OF WOUNDS.

XI. LATENT PERIOD.

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The latent or quiescent period of cicatrization extends from the time of traumatism to the beginning of contraction. During this stage of apparent inactivity, the mechanism which will bring about the reintegration of the tissues is progressively set in motion. A study of the latent period may lead to a better understanding of the secondary causes which directly or indirectly derive from the injury acting as primary cause, and are instrumental in starting regeneration. The purpose of this article is to examine the duration of the latent period, its transition to the period of contraction, and the characteristics of the curve expressing it.

I.

Method.

The experiments were made with wounds of geometric shape, obtained by excision of a flap of skin in the dorsal region of dogs. The animals were of medium size, short haired, and of quiet temper. 24 hours previous to the operation, they were given a warm bath after the hair had been clipped. Later on the same day, the skin of the dorsal region was washed a second time with soap and water. After the animal had been etherized, the skin was shaved, carefully washed with soap and warm water, and covered for 10 minutes with compresses soaked in 75 per cent alcohol. Then the animal was placed on the operating table and the skin was painted with tincture of 10 per cent iodine, which was allowed to dry for 10 minutes.

The wounds were generally obtained by resection of a rectangular flap of skin. In some cases, circular flaps were extirpated by means of a sharp edged tube, 2 cc. in diameter. Hemostasis was secured by compression with gauze pads, or by temporary clamping of the small vessels. No ligatures were used, because after a few days they become centers of colonization for the bacteria existing on the surrounding skin. The measurement of the wounds was made in two different ways. In the earlier experiments, the width of a rectangular wound was ascertained with a compass and its variations were studied, instead of the change in the total area. In the more recent experiments, the area of the wound was measured, according to a technique previously described, and expressed in square centimeters. An accurate appreciation of the area required a great deal of care. It is well known that the skin of the dog is not adherent to the aponeurosis, and is very mobile. This causes the size of the wound to become modified by slight changes in the position of the animal. Therefore, in spite of the precautions which were taken, variations occurred in the area of the wounds which were due only to experimental errors. At the end of the latent period, when the edges of the wound had become fixed to the bottom by granulation tissue, the method was much more accurate.

As the purpose of the experiments was to study the latent period under ordinary conditions, the dressing consisted only of talcum powder, paraffin, or plain gauze. The bacterial condition of the surface was ascertained merely by examination of films. Often the wound could be maintained in a condition of surgical asepsis, that is of mild infection, when the dressing was properly fixed to the skin. Infection was usually carried from the surrounding skin to the wound by the gauze, which moves about on the surface of the skin due to the constant movements of the animal. This could be prevented by stitching a gauze pad to the skin itself. Then a thick cotton pad was applied, fixed by bandages, and protected by a shirt.

Seven experiments are briefly described, and the appearance of the latent period is shown by Text-figs. 1 to 7. The width of the wound in centimeters, or its area in square centimeters, is plotted in ordinates and the time in abscissæ. The latent period is designated

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by the heavy line. The light line expresses the area of the wounds calculated by the formula of du Noüy, which, of course, does not apply to the widths. In Text-figs. 5 to 7 the curves are arbitrary. The observed area, or width, is represented by the heavy points. In the first experiment, the latent period and the two subsequent periods are described, and the curve expresses the complete phenomenon from the excision of the flap to the last stage of epidermization. In the six other experiments, the latent period and the beginning of the contraction period only are shown.

EXPERIMENTS.


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For the calculated curve, the index \(i\) was equal to 0.058.


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II.

DISCUSSION.

The duration of the latent period varied from 5 to 7 days. It was found, in the course of many other experiments, that the limits of variations may be wider. While the subsequent stages of cicatrization are not affected by external factors, it appears that the latent period may be easily modified in its duration by many local causes, such as mechanical irritation of the tissues, infection, and even by the diet of the animal, as was shown by Clark. The experiments described above deal only with the latent period under ordinary conditions of mild bacterial and mechanical irritation, which was generally obtained by dry gauze dressings. During the first stage of healing, the area was generally found to remain constant. However, in Experiment 7 an increase of the surface, and in Experiment 5 a decrease followed by an increase of the surface, were observed. These changes were probably due to errors of observation. As long as the edges of the wound were not fixed to the bottom by granulating tissue, a slight modification of the tension of the surrounding skin could modify the area considerably. The appearance of the granulation tissue generally announced the end of the latent period. But there was no definite relation between both phenomena. The end of the latent period was marked not only by the growth of granulation tissue, but by an abrupt beginning of the contraction period, which immediately acquired its maximum velocity. In Experiments 4 and 7, there was a transition period which lasted possibly 24 hours, and during which the contraction started slowly. As a rule, the onset of contraction was sudden and a period of maximum activity succeeded the period of complete quiescence.

The formula of du Noüy was found to apply accurately to the beginning of the period of contraction. On the graphs, it may be seen that the light line representing the calculated area follows the observed area almost constantly. There was a perfect coincidence between the calculated and the observed surfaces in Experiment 1, even during the first hours of the contraction. An examination of the seven graphs shows that the phenomenon could not be accurately

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expressed by a curve presenting a point of inflexion. So far, this fact has not been emphasized, and, on account of an insufficient description of the conditions of the experiments, certain curves, in previous publications, were misleading. 5 Recently, Fauré-Frémiet and Vlès 6 attempted to apply to the cicatrization process the equation expressing the monomolecular autocatalytic reaction used by Robertson 7 in his studies on growth. As a consequence of this hypothesis, the curve of the areas must pass by a point of inflexion, in conformity with the equation

\[
\frac{S}{S_o - S} = e^{Ks_o (t - t)}
\]

which necessitates that the rate should be maximum at the time \( t \), where \( S = \frac{S_o}{2} \). One of the curves calculated in this manner agrees fairly closely with that of du Noüy. The other presents a point of inflexion; that is, a maximum in the rate of healing during the period of contraction. There is evidently a close relation between this curve and the observed curve of an experiment previously reported. 5 But the point of inflexion of this observed curve was due to a mere accident. The wound was old and infected, and had begun to cicatrize under a plaster of Paris splint. The observed curve showed the variations of the rate of cicatrization both before and after normal cicatrization had really begun. As these details were not mentioned in the paper, Fauré-Frémiet and Vlès 6 could not help being misled by this accidental fact. Although their formula and the formulas published by de Beaujeu 8 and Lumière 9 show a lack of agreement with the observed facts, there is no doubt that the curve representing the normal process of cicatrization may be expressed by more than an equation, as has already been pointed out by du Noüy. 10

7 Robertson, T. B., Principles of biochemistry, Philadelphia, 1920, 475.
But these equations must apply as well to the beginning of the contraction period as to the end of the epidermization period. A glance at the figures and at the chart expressing the observed and calculated areas of Experiment 1 shows that the coincidence is almost perfect and quite satisfactory, in view of the percentage error necessarily involved in experimental wounds on dogs.

Several equations have already been applied by du Noüy to the curve of cicatrization. The first\(^{11}\) was expressed as follows:

\[
T = K_1 \log \frac{S_0}{S} + 2K_2 (\sqrt{S_0} - \sqrt{S})
\]

The second\(^{12}\) has proven more satisfactory:

\[
S = S_0 e^{-\frac{T}{2p}}
\]

The figures calculated by this last equation coincide almost exactly with those calculated by means of the well known extrapolation formula:\(^3\)

\[
S_n = S_{n-1} [1 - i (t + \sqrt{i + m})]
\]

They applied to the first stage of contraction as accurately as to the later periods of cicatrization.

III.

CONCLUSIONS.

1. The latent period of cicatrization varies generally from 5 to 7 days.
2. It stops abruptly and contraction starts with its maximum velocity.
3. The formula of du Noüy applies to the beginning of the contraction period as well as to the subsequent periods.