THE EFFECT OF TRAUMA ON WOUND HEALING
An Experimental Study*

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The exact nature of the stimulus that initiates and sustains wound healing is not known. It seems probable that when tissues are injured, some type of growth-promoting substance is elaborated.[9] These substances have been referred to by a wide variety of terms,[1,2,7] the most common of which is "wound hormones."[4] Some have felt that these hormones remain only in the immediate vicinity of the traumatized tissues and are capable therefore of exerting only a local and circumscribed effect. Others have conceded the possibility that the hormones may be absorbed and carried by the circulating blood to all parts of the body. If the latter hypothesis were correct, it would be reasonable to expect that a wound made at a time when the titer of these hormones in the blood was high would heal at a more rapid rate than under normal conditions.

In 1941, Young, Fisher, and Young[10] studied the effect of the presence of one superficial skin wound upon the rate of healing of a second similar wound made after an interval of ten or twelve days. Rabbits weighing from 2.0 to 2.5 kilograms were used exclusively. The rate of healing was measured by a planimetric method. All the wounds were left open and undressed. On the basis of a relatively large number of experiments, the authors arrived at the conclusion that in seven out of their ten series the secondary wounds healed at a significantly more rapid rate than the primary wounds. This work, although thoughtfully conceived and carefully executed, is subject to a number of serious criticisms, some of which the authors themselves recognized and acknowledged. Firstly, the use of open wounds introduces such gross factors as: (i) direct mechanical trauma to the wounds, (ii) chemical contamination by food, urine, and feces and, (iii) unlimited bacterial contamination. These factors are variables that can be neither controlled nor accurately measured. Secondly, the wounds were not all treated exactly alike. In order to minimize bleeding immediately after the operation, adrenalin pledgets were applied to some of the wounds and acriflavine to others. Thirdly, because the wound margins slid freely over the underlying tissues and because the size and shape of the wounds varied considerably with the stance of the animals, the method of measuring the wound was not easy or exact. Fourthly, the fact that the end-point of

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healing was not always sharp and precise may have been another source of error. Finally, the authors did not have a true "control" series in their experiments. The secondary wounds were made at a time when the primary wounds were still open and actively healing. Both sets of wounds, present and healing in the same animal at the same time, were therefore in a position to influence each other, and it would not be fair or reasonable to assume, without further evidence, that that influence was exerted only in the direction of the primary wounds upon the secondary wounds but not vice versa.

In 1949, Sandblom,[8] working on the same problem in rabbits, reported similar results. He made two skin incisions, one in front of the other, on the back of each animal. After five days the wounds were excised and their tensile strength was determined by a tensiometer. Fifteen days after the first wound had been inflicted, two new similar incisions were made on the other side of the back. These, too, were excised on the fifth day of healing and their tensile strength measured in the same way. Using this basic pattern, the author, in subsequent experiments, varied the interval between the primary and secondary wounds and the days on which tensile strength determinations were made. He concluded that the secondary wounds healed more rapidly than the primary wounds and, among other things, that the healing curve of the former wounds exceeded that of the latter throughout the first ten days of healing. These experiments are subject to some of the same criticisms as those of Young, Fisher, and Young. The wounds were all on the surface and were therefore exposed to variable influences. Furthermore, as Sandblom pointed out in his report: "A major drawback to the method . . . is that the primary or control wound is identical with and hence inseparable from the stimulus, i.e., the injury. When therefore the control is altered—for example, for studying the strength of wounds at different stages in order to construct the healing curve—the stimulus is changed accordingly. Moreover, the injury is two-fold—it consists of inflicting the wound and excising it later for examination. These facts must be borne in mind when the results are evaluated."

When the present experiments were planned, an attempt was made to profit by the work of previous investigators and to avoid as far as possible some of the difficulties which they had encountered. The primary wounds, involving skin, subcutaneous tissue, fascia, and muscle served only as the source of trauma. They were not also used as controls. The experimental and control wounds were made in the stomachs of separate animals, and every effort was exerted to keep all the conditions identical. Furthermore, the fact that the healing of stomach wounds has been studied intensively under a wide variety of circumstances provided a good base-line for evaluation of the results to be obtained here, not only in the experimental wounds but in the control wounds as well. Young, growing white rats, all of the same strain and each weighing about 100 grams, were used. The animals were kept in cages under ordinary laboratory conditions and were offered water and a complete diet *ad libitum.* They thrived on this regime and continued to gain weight at a normal rate.

Series A. Experimental group—50 animals. A measured 4 cm. incision was made in the interscapular area, to one side of the midline, and extended through the skin, subcutaneous tissues, and paraspinous muscles down to the bony thoracic cage. The wound was then carefully closed in two layers with fine silk sutures. Five days later the secondary wound was made. This consisted of an incision measuring 1 cm. in length and extending completely through the wall of the cardiac portion of the stomach. The wound edges were immediately approximated in one layer with a running, continuous Connell suture of #000 plain catgut, which loses its tensile strength well within four days.[6] The abdominal wall was closed in two layers with fine silk sutures. The operative procedures were performed under drop-ether anesthesia, and strict aseptic technique was observed. On each of the 4th, 6th, 8th, 10th, and 12th postoperative days ten animals were sacrificed. The strength of the stomach wounds of eight of these was immediately determined by distending the stomachs with air and measuring the bursting pressures;[5] the stomachs of the remaining two animals were preserved intact for histological examination.

Series A. Control group—50 animals. The above regime was carefully duplicated in every particular, including the two administrations of ether anesthesia but omitting the infliction of the primary wound. Histological studies and determinations of the tensile strength of the stomach wounds were similarly made from the 4th to the 12th postoperative days.

Series B. Experimental and control groups—100 animals. This series differed from Series A only in the respect that the stomach wounds were made fifteen days after the primary wounds instead of five days.

With rare exceptions, the primary and secondary wounds in Series A and B healed *per primam.* The few animals that demonstrated evidence of wound infection, even if only of minor degree, were discarded. The averages of the bursting strengths for each postoperative interval and the standard deviation were computed. Fisher's[3] formula for small samples was applied to determine statistical significance.

Results

The curves of healing of the secondary stomach wounds in both series showed no statistically significant deviation from normal (Charts I and II). Histological examination also failed to show any constant or appreciable variation in the degree of exudative or fibroblastic response. The tensile strength of the wounds could be measured accurately only during the 4th, 6th, and 8th postoperative days, when the stomachs burst almost invariably through the wounds. On the 10th and 12th days, in both the experimental and control animals, the bursting points were located more often in some part of the intact stomach wall than in the wounds themselves. The absolute strength of the wounds in these latter two periods of healing could therefore not be determined by this method, and all that can be said is that the wounds in both the experimental and control groups were stronger than the adjacent stomach walls.

Conclusions

In young, growing white rats, trauma in the form of relatively large, soft tissue wounds did not affect the rate of healing of secondary wounds in the stomach that were made after five and fifteen days respectively. These experiments lend further confirmation to the concept, already firmly supported by other data, that a healing wound is a basic and elemental biological process that proceeds autonomously at its own constant pace, un-

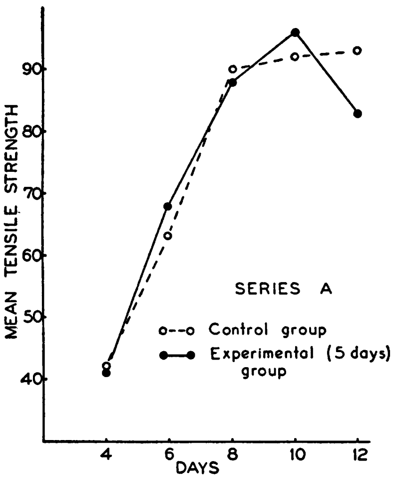

CHART I

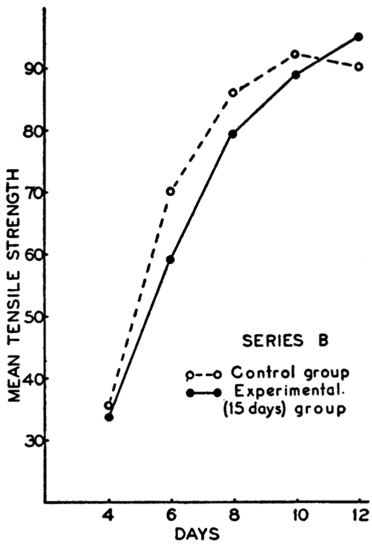

CHART II

altered and undisturbed by any but the most overt and gross stimuli. Wound sepsis, severe hypoproteinemia, and almost total vitamin C deficiency may impair or retard wound healing, but an influence that clearly and indisputably accelerates it still remains to be demonstrated.

REFERENCES

1 Bier, A.: Deut. med. Wschr., 1917, *43,* 833.
2 Carrel, A.: C. rend. Soc. biol., 1924, *90,* 29.
3 Fisher, R. A.: *Statistical methods for research workers.* Edinburgh, 1934.
4 Habelandt, G.: Sitzber. Preuss. Akad. Wiss., 1921, p. 221.
5 Harvey, S. C. and Howes, E. L.: Ann. Surg., 1930, *91,* 641.
6 Howes, E. L.: J. Am. M. Ass., 1928, *90,* 530.
7 Marchand, F.: *Der Process der Wundheilung.* Stuttgart, 1901.
8 Sandblom, Ph.: Ann. Surg., 1949, *129,* 305.
9 Wiesner, J.: *Elementarsttuktur.* Wien, 1892.
10 Young, J. S., Fisher, J. A., and Young, M.: J. Path. Bact., Lond., 1941, *52,* 225.