BIO-ELECTRIC CORRELATES OF WOUND HEALING*

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The presence of bio-electric correlates of growth has long been known (Mathews,[4] and Lund[3]). More recently, the development of a new technic has made it possible to determine these correlates with somewhat greater accuracy. They have been studied in Amblystoma (Burr and Hovland[2]), and in chicks (Burr and Hovland[1]). The implication of these studies is that rapidly dividing masses of cells are related in some way to potential gradients which are quite easy to determine. It seemed worth while, therefore, to explore bio-electrically the processes of repair in the healing of a wound. Furthermore, the majority of studies in wound healing have required the use of biopsies which, needless to say, seriously interfere with the continued observation of the process. The bio-electric technic, however, makes it possible to record at frequent intervals correlates of the growth process in each particular wound without interrupting its healing.

Studies by Taffel and Harvey[5] have shown an increasing tensile strength correlated with the passage of time. This increase occurs for the most part during the first 8 to 10 days following the incision, after which the tensile strength tends to remain fairly constant or to increase very slowly. In addition, their observations indicate an inflection in this curve in vitamin C deficient animals.

The determination of tensile strength must involve at least two processes, one of cell proliferation and one of cell differentiation. In normal development the two events do not obtain in the same cell simultaneously. Rather, each cell takes part in the generalized mitosis of a group of cells for a period of time after which it undergoes, with other cells, a period of differentiation. As growth proceeds, new cells go into mitosis and then into differentiation, adding thereby to the new structure. There are no known methods for differentiating these two processes except by microscopic examination. The bio-electric technic offers the possibility of discriminating between the two. It seemed advisable, therefore, to investigate the

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nature of bio-electric phenomena in wound healing and to discover any possible relationship between them and tensile strength and between them and growth or differentiation.

To this end a group of laboratory guinea-pigs was selected, the hair shaved from the right flank, and the potential gradients between three points on the bare area measured. Point A was taken at the cephalic end of the bare area, Point B at the caudal end, Point C in the center where there would subsequently be made a vertical incision traversing the skin and subcutaneous fascia. Between these points, e.m.f. determinations were made, that is, between A and B, between A and C, and between B and C. An incision was made and sutured, and another set of determinations done. These were then continued daily for the next two weeks or until the wound was, to all intents and purposes, healed. In fact, in some instances it was difficult to determine the site of the wound.

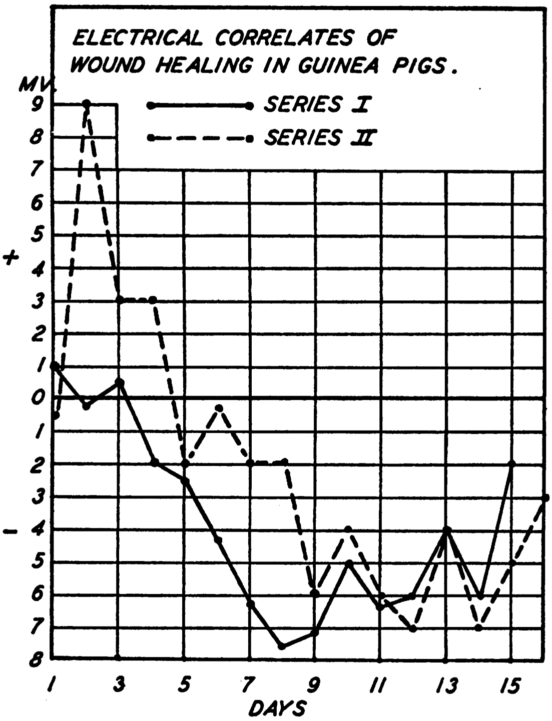

FIG. 1. Graphs of potential gradients between points A and C in normal guinea-pigs. Series I on controlled diet, Series II on laboratory diet. Plot is drawn in mv. against days after operation.

Inspection of the data collected in this manner showed a marked change in the potential gradients between the normal skin and the area of injury. Perhaps the most astonishing finding was that the site of injury was not consistently negative to the normal tissue, as would be expected by the theory of injury potentials. On the contrary, for the first 24 or 28 hours after the injury, the wound area was positive to the cephalic point A on the normal skin. The potential gradient between these points tends to rise for 24 or 48 hours and then rapidly declines until on the 3rd or 4th day the wound becomes negative to the normal skin and becomes increasingly negative until it reaches a maximum on the 8th or 9th day (cf. Fig. I, Series 2). Beginning on the 8th or 9th day and lasting for 24 to 48 hours, the potential gradient drops, to be followed on the 10th to the 12th day by another rise in potential. This is repeated on the 12th to the 14th day, and on the 15th or 16th day the gradients return to approximately normal limits. The animals used in this experiment were laboratory animals fed on a laboratory diet and were given no special treatment. Comparison of this curve with that obtained by Taffel and Harvey shows an interesting parallelism. The tensile strength measurements show a rapidly rising curve during the first 8 days. The bio-electric measurements show a similar rise. After the 8th day the tensile strength seems to approach a plateau. The bio-electric determinations show alternating periods of growth and differentiation after the 8th day. While examination of the curve shows rather small changes in the potential gradients they, nevertheless, are statistically reliable.

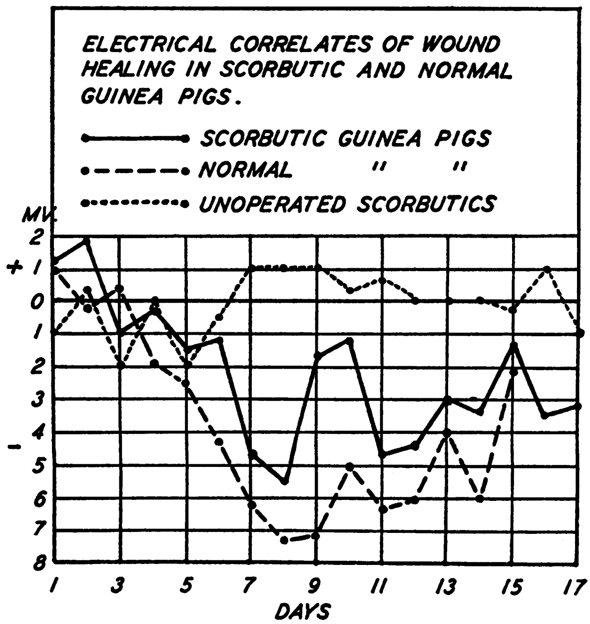

Fig. II. Graphs of potential gradients between points A and C in operated normal and scorbutic pigs and in unoperated scorbutics. Plot is drawn in mv. against days after operation.

In order to investigate this matter further, a second series of animals was studied under somewhat different conditions. Thirty guinea-pigs from the laboratory stock were taken, ten of which were placed on a controlled laboratory diet. It is to be noted that this diet is different from that of the first series. These animals received an incision in the right flank as described above and were read daily. The curve of the e.m.f. determinations appears as the solid line in Figure I. It will be noted that the curve is quite parallel to that obtained on the normal laboratory diet, the only difference lying in the fact that the rising negativity of the wound appeared earlier and rose higher. Since the only difference between the two groups was that of diet, it is possible that this may explain what seems to be a slight acceleration of the time of onset of the growth process. However, once started, the alternation of growth and differentiation is strikingly parallel in both groups of animals. Twenty of the animals were put on a vitamin C deficient diet. Ten of these were with no wounds in the skin and ten with wounds. Daily readings were made on all. The potential gradients in the operated and unoperated scorbutics and in the normals on controlled diet are plotted in Figure II. It will be seen that in the unoperated scorbutics a reasonably constant base-line appears through the whole period of the experiment. The scorbutics operated upon, however, show changes in the potential differences which closely parallel the normals, save that the magnitude of the potential differences is less. In addition, they show the same delay in the onset of the potential rise as was seen in the animals on the normal diet as contrasted with the control diet. The same alternation of growth and differentiation seems to be indicated as in all the other groups except possibly in the last 48 hours of the study.

The observations here recorded indicate that it is possible to measure with some certainty bio-electric concomitants of growth and differentiation in the healing of wounds in the guinea-pig. They suggest that the growth process is not a continuous one except in the early stages, but rather that after the 8th day it alternates with periods of differentiation. The bio-electric correlates of growth in the animals on a control diet seem to rise faster and reach a greater magnitude than is the case in the scorbutics or the animals on a normal diet.

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