

nerves to degenerate in plasma-clots⁵ in contrast to liquid serum, as such clots develop strong contractile forces in their interior.⁹

Summary. Lateral compression of periph-

eral nerves delays Wallerian degeneration of the compressed zone *in vitro*.

⁹ Weiss, Paul, *J. Exp. Zool.*, 1934, **68**, 393.

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Effect of Cell Growth Activating Tissue Extracts, Locally Applied, on Experimental Skin Wounds.*

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In previous communications from this laboratory¹⁻⁴ it was shown that extracts of adult tissues possess pronounced cell growth-promoting power. Moreover, the growth-promoting activity of tissue extracts was found to be completely independent of the state of proliferation of the tissue from which they are made.^{5,6} Extracts of certain adult organs—heart, smooth muscle, and brain—activate the growth of fibroblast colonies *in vitro* to a greater extent than embryonic extract. The stimulating action of adult tissue extracts in cell growth is not transient. It is possible to cultivate cells indefinitely in a medium which is composed exclusively of adult plasma and extract of adult heart or adult brain.⁷ The growth-promoting property of extracts of adult tissues is not species-specific. The growth of human skin epithelium can, for instance, be activated by extract of adult fowl

heart to a high degree.⁸ The active principle in the growth-promoting tissue extracts is probably a protein or a protein linked group.⁹

In numerous investigations¹⁰⁻²¹ it was claimed that local application of cell growth-promoting embryonic extract accelerates the process of wound healing in man and animals. The extracts of certain adult tissues being more powerful in stimulating cell proliferation *in vitro* than embryonic extract, and moreover, much easier to obtain than the latter, the use of growth-activating adult tissue extracts in wound healing was suggested.⁸ A trial of the effect of the cell growth-stimulating adult tissue extracts on the process of healing of wounds under properly controlled conditions of animal experiments appeared therefore to be desirable.

⁸ Doljanski, L., Hoffman, R. S., and Tenenbaum, E., *Nature*, 1942, **150**, 23.

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¹ Doljanski, L., and Hoffman, R. S., *C. R. Soc. Biol.*, 1939, **130**, 1246.

² Hoffman, R. S., and Doljanski, L., *Growth*, 1939, **31**, 61.

³ Doljanski, L., Hoffman, R. S., and Tenenbaum, E., *C. R. Soc. Biol.*, 1939, **131**, 432.

⁴ Hoffman, R. S., Tenenbaum, E., and Doljanski, L., *Growth*, 1940, **4**, 207.

⁵ Trowell, D. A., and Wilmer, E. N., *J. Exp. Biol.*, 1939, **16**, 60.

⁶ Hoffman, R. S., Tenenbaum, E., and Doljanski, L., *Nature*, 1939, **143**, 764.

⁷ Doljanski, L., Hoffman, R. S., *Growth*, 1943, **7**.

TABLE I.

The Results of Wound Healing Experiments. Each group contains rats with two symmetrically placed skin wounds, one of which was submitted to the tissue extract treatment, and the other was used as a control.

Treatment	No. of rats	Mean closure time in days	
		Exp.	Control
A. Saline adult heart extract	10	19.1	17.7
B. Alcohol precipitates of adult heart extract			
1. Powder	22	18.9	18.5
2. Ointment	14	17.1	15.4
C. Saline embryonic extracts	20	23.1	18.5

In the experiments reported here the question is examined whether adult tissue extracts and cell growth-promoting preparations therefrom, applied locally, are capable of accelerating the process of healing. In addition, the closure time of treated wounds has been compared to that of untreated wounds in the same animal.

The experiments were performed on white rats. Two circular symmetrical wounds, each about 20 mm in diameter, were produced on the back, the skin being excised down to the superficial fascia. The wounds were treated with (1) saline extracts of adult chicken hearts incorporated in an ointment base (40% saline heart extract and 60% lanolin) and (2) with alcohol precipitates of these extracts prepared according to a method previously described,⁹ and applied in the form of an ointment or dry powder. (Tested in tissue cultures, the growth-promoting activity displayed by the alcohol precipitate, dissolved in Tyrode solution, is not inferior to that of the native extracts.⁹)

The ointments were applied to the wounds in a 2-3 mm layer, and the wounds were covered with a gauze dressing. The control wounds were covered with the same ointment base without additional tissue extract. Powder was sprinkled on the surface of the wounds directly, and the wounds covered with gauze and protective dressing. The ointment and the powder were renewed every second day. The experimental and control wounds were measured at intervals of 48 hours. Cases of infected wounds were excluded from the tabulated data.

The experiments showed that extracts of adult heart and alcohol precipitate from these extracts do not accelerate the course of healing of treated wounds as compared with controls in the same animals. The course of all phases of the wound healing process (contraction, formation of granulated tissue, epithelization) is the same in treated as in control wounds.

In view of this result it seemed to us of interest to re-examine the findings of earlier investigators on the allegedly positive effect of embryonic extract in wound healing. 33% saline extracts of 7-day-old chicken embryos were used in these experiments. The wounds were covered with gauze saturated, in the case of the experimental wound, with embryonic extract and, in the case of the control wounds, with Ringer solution. The extract and Ringer solution were renewed daily. Our experiments showed that no acceleration of healing rate could be obtained in wounds treated with embryonic extract, as compared with untreated controls; on the contrary, in wounds treated with embryonic extract, definite inhibition of the healing process was observed.

The results of the experiments reported are summarized in Table I.

Summary. The extract of adult chicken hearts, alcohol precipitates of this extract, and extract of 7-day-old chicken embryos were applied to experimental skin wounds in rats. No acceleration of the wound healing process could be obtained with the preparations used. The period of repair for wounds treated was not shorter than for control wounds in the same animals.