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Effect of Addition of Macerated Tissues on Healing of Granulating Wounds.

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(Introduced by O. H. Wangensteen.)
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Alexis Carrel[1] showed that extracts of several days' old chicken embryos had the remarkable property of accelerating and maintaining indefinitely the *in vitro* growth of fibroblasts. Carrel and Ebeling[2] showed that homologous and heterologous adult organ tissues (muscle, ovary, etc.) also, accelerated the *in vitro* growth of fibroblasts, but did not maintain growth indefinitely. Recent work purporting to show the accelerating effect of chick embryo extracts on wound healing in animals and man has been done by French and German workers.

The purpose of the present work is to investigate the effect on the healing rate of granulating wounds by applying various organ tissues to their surfaces.

Bilateral circular skin wounds extending down to the superficial fascia and varying in size from about 16 to 70 sq. cm. were made on the backs of 14 dogs. The wounds on the right side were used for experimental purposes and to their surfaces the various tissues under investigation were applied every second to fourth day. The wounds on the left side were used for control purposes. These were always dressed with neutral sodium stearate in which was incorporated Chloramine *T* (Carrel and Hartman)[3] for purposes of maintaining sterility. The size of the wounds on both sides was read every second to fourth day. This was done by tracing the edges of the wounds on cleansed, sterile, old, x-ray film. The wounds healed in from about 35 to 72 days. They were arbitrarily considered healed when their area reached the neighborhood of 0.4 sq. cm. The following is a summary of the data observed:

The experimental wounds in dogs 4, 9, 11, and 14 showed a tendency to slightly earlier healing than the control wounds. All other experimental wounds showed retarded healing compared to the control or a healing time equal to it.

[1] Carrel, A., *J. Exp. Med.*, 1913, xvii, 14.
[2] Carrel, A., and Ebeling, H., *J. Exp. Med.*, 1923, xxxviii, 499.
[3] Carrel and Hartman, *J. Exp. Med.*, 1917, xxvi, 95.

TABLE I.

Dog	Experimental tissue used	*Area at time zero		Area when considered healed		Constants used in formula for prediction		Actual No. days control required to heal	Predicted No. days control required to heal	Difference between actual and predicted No. of days	% error in predicted No. days
		Control	Experimental	Control	Experimental	K	2p				
1	2	3	4	5	6	7	8	9	10	11	12
1	Implantation skin grafts—autoplastic	44.2	42.8	0.3	0.3	.06	200.6	37.0	39.0	2.0	5.4
2	Implantat'n muscle grafts—autoplastic	15.9	16.4	0.4	0.7	.04	89.0	22.0	28.0	6.0	27.0
3	Implantation skin grafts—autoplastic	32.2	33.5	0.4	1.3	.03	159.0	48.0	56.0	8.0	16.6
4	Wolfe-Krause skin grafts—autoplastic	29.7	32.3	0.5	H.	.02	25.7	35.0	38.0	3.0	8.6
5	Spleen pulp—10 day infant	63.4	70.8	0.3	7.4	.03	37.8	49.0	43.0	6.0	12.2
6	Wolfe-Krause skin graft—guinea pig	81.4	84.8	0.4	0.5	.06	153.0	52.0	38.0	14.0	27.0
7	Spleen pulp—calf fetuses, 6-7 months	64.6	64.6	0.5	0.8	.02	8.4	48.5	35.0	13.5	27.8
8	Same as 7	41.6	37.3	0.2	1.8	.02	11.6	45.5	40.5	5.0	11.0
9	Fetal dog liver	65.6	65.0	0.3	0.1	.03	25.4	27.0	41.9	5.1	11.0
10	Same as 11	75.4	75.2	0.6	1.3	.02	18.7	46.0	44.0	2.0	4.3
11	Fetal dog kidney	64.5	66.5	0.6	H.	.04	50.0	47.5	35.0	12.5	26.3
12	Implantation fetal dog skin graft	84.3	93.5	2.0	3.0	.04	62.1	40.0	30.8	9.3	23.1
13	Liver extract—Stearn's	50.3	55.5	0.2	0.3	.05	24.7	45.0	36.0	9.0	20.0
14	Fetal calf liver—powdered	81.7	98.2	1.6	1.4	.03	39.0	48.5	33.5	15.0	31.0
										Average error in prediction for series	18.0

*Area at time zero = starting point for the calculated predictions and not necessarily the original size of the wound, which may have been slightly larger or smaller. H = healed.

In 1919, Lecomte P. duNoüy[4] formulated a general equation for the law of cicatrization of surface wounds:

$$\text{Log } S_t = \text{Log } S_o - K\left(T - \frac{T^2}{2p}\right)$$

$$K = \frac{\text{Log } S_o - \text{Log } S_t}{T \text{ (4th day)}}$$

$$A = \frac{\text{Log } S_o - \text{Log } S_t \text{ (8th day)}}{K} - T \text{ (8th day)}$$

$$2p = \frac{T^2}{A}$$

Using the above formula the time of healing of each control wound was predicted by calculation.

Column 12 of the table (% of error in predicted days) shows that the predictions were correct with errors varying from 4.34% in dog 10 to 31.0% in dog 14. The average error in prediction for the whole series of 14 dogs was 18%.

The causes of error in prediction were chiefly infection of the wound, due to dislodgement of the wound dressing by the dog.

Conclusions. 1. No tissue investigated caused any striking accelerating of healing. 2. The healing time of the control wounds was predicted by calculation with an average error of 18% for the whole series.

[4] du Noüy, Lecompte P., *J. Exp. Med.*, 1919, xxix, 329.