CICATRIZATION OF WOUNDS.

IV. MATHEMATICAL STUDY OF THE EXTRAPOLATION FORMULA AND OF THE CURVE OF CICATRIZATION.

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Several methods may be used to express the form of the curve of cicatrization by an equation, depending on whether the index *i* is or is not introduced into the calculation.[1] In such a curve, during the short time, *dt*, the area cicatrized, *ds*, remains proportional to the area, *S*, of the wound, which is expressed:

$$ds = Ks\,dt$$

If S_o is the initial area, K being a constant, integration gives:

$$T = \frac{1}{K} L \frac{S_o}{S}$$

We can now compute the values of $\frac{1}{K}$, corresponding to the observed numbers of S and T. These values increase regularly, and remain finite. Another factor must, therefore, intervene in the process of cicatrization. If this factor is the perimeter, and if we assume that K increases, the relation between K and the perimeter P is:

$$K = \frac{1}{K_1 + K'P}$$

If we assume that the wound does not alter its form as it cicatrizes,

$$\frac{P}{\sqrt{S}} = K''$$

[1] Carrel, A., and Hartmann, A., *J. Exp. Med.*, 1916, xxiv, 429. du Noüy, P. L., *ibid.*, 1916, xxiv, 451, 461.

from which, if $K_2 = K_1' K''$

$$K = \frac{1}{K_1 + K_2\sqrt{S}}$$

which gives the differential formula:

$$ds = \frac{1}{K_1 + K_2\sqrt{s}} Sdt$$

and by integration:

$$T = K_1 \mathrm{Log}_e \frac{S_o}{S} + 2K_2(\sqrt{S_o} - \sqrt{S})$$

This should represent the curve.[2]

Tables I and II show the results of a few calculations. In the equation the two coefficients K_1 and K_2 remain nearly constant for the same wound. This formula may therefore be considered as representative.

TABLE I.

Patient 263.

Time (T)	Area (S)	Log S	Log $\frac{S_o}{S}$	$\sqrt{S}$	$\sqrt{S_o}-\sqrt{S}$	$T=26 \log \frac{S_o}{S} + 2.6 (\sqrt{S_o}-\sqrt{S})$
days	*sq. cm.*					
0	61.8	1.791		7.86		$K_1=26$, $K_2=1.3$
4	51.0	1.707	0.084	7.13	0.73	4.06
8	41.6	1.619	0.172	6.45	1.41	8.1
12	33.6	1.526	0.265	5.80	2.06	12.2
16	26.9	1.430	0.361	5.19	2.67	16.3
20	21.3	1.328	0.463	4.62	3.24	20.2
24	16.76	1.224	0.567	4.10	3.76	24.4
28	13.09	1.117	0.674	3.62	4.24	28.6
32	10.12	1.0051	0.786	3.18	4.68	32.5
36	7.77	0.890	0.901	2.79	5.07	36.6
40	5.94	0.774	1.017	2.44	5.42	40.5
44	4.5	0.653	1.138	2.12	5.74	44.2
48	3.4	0.531	1.260	1.84	6.02	48.3
52	2.53	0.403	1.388	1.59	6.27	52.0
56	1.88	0.274	1.517	1.37	6.49	56.4
60	1.38	0.140	1.651	1.175	6.685	60.3
64	1.01	0.004	1.787	1.005	6.855	64.2
68	0.74	$\bar{1}.869$	1.922	0.860	7.00	68.1
72	0.54	$\bar{1}.732$	2.059	0.735	7.13	72.0
76	0.4	$\bar{1}.602$	2.189	0.633	7.23	75.6

[2] This calculation was made by Mr. de Rufz de Lavison.

TABLE II.

Patient 360.

Time (T)	Area (S)	Log S	Log $\frac{S_0}{S}$	$\sqrt{S}$	$\sqrt{S_0}-\sqrt{S}$	$T=25 \log \frac{S_0}{S} + 2.5 (\sqrt{S_0}-\sqrt{S})$
days	*sq. cm.*					
0	113.1	2.053		10.6		
4	96.8	1.986	0.067	9.8	0.8	3.6
8	81.6	1.911	0.142	9.02	1.6	7.5
12	67.9	1.831	0.222	8.23	2.4	11.0
16	55.9	1.747	0.306	7.47	3.2	15.6
20	45.5	1.658	0.395	6.75	3.9	19.8
24	36.6	1.563	0:490	6.04	4.6	24.0
28	29.2	1.465	0.588	5.4	5.2	27.7
32	23.1	1.364	0.690	4.8	5.8	31.7
36	18.1	1.258	0.796	4.25	6.4	35.0
40	14.0	1.146	0.907	3.74	6.9	39.9
44	10.8	1.033	1.020	3.28	7.3	43.7
48	8.26	0.917	1.137	2.87	7.8	47.9
52	6.27	0.797	1.256	2.51	8.1	51.6
56	4.75	0.677	1.377	2.78	8.4	55.4
60	3.55	0.550	1.503	1.88	8.7	59.4
64	2.64	0.422	1.632	1.62	9.0	63.3
68	1.95	0.290	1.763	1.397	9.2	66.7
72	1.43	0.155	1.898	1.195	9.4	70.1
76	1.04	0.017	2.036	1.019	9.6	75.0
80	0.75	$\bar{1}.875$	2.178	0.971	9.7	78.7

Other examples, without the details of calculation, are as follows:

Patient 408.

t observed..........	4.0	8.0	12.0	16.0	24.0	40.0	According to the above formula, $K_1=10$, $2K_2=6$
T calculated........	3.94	8.1	12.3	16.6	24.8	39.3	

Patient 361.

t observed....................................	4.0	8.0	12.0	16.0	24.0
T calculated..................................	3.4	8.2	12.0	16.1	24.1

Patient 366.

t observed..	4.0	8.0	12.0	16.0
T calculated.......................................	4.1	8.1	12.0	16.01

Corrected Formula for Narrow Wounds.

The relation between the length and the width of the wound (the form) seems to play a more important part than the perimeter itself (the length of the outline). To express this in practical form, we have been searching for a formula adapted to long and narrow wounds. In wounds resulting, for instance, from longitudinal incision through muscles, an acceleration of the rate of cicatrization is observed within a few days before complete healing, the gain in time being sometimes 12 or 16 days. It is therefore necessary to introduce a new factor, the action of which was predicted by the calculation. This correction is not necessary in average wounds, because as stated above, the change of rate appears only when the length of the wound is very much greater than its width; in other words, when $\frac{L}{l}$ (L being the length, and l the width) is such that:

$$10 < \frac{L}{l} < 25$$

In this case, as the perimeter is considerably increased in relation to the area, its action becomes then—but only then—important, and this explains why, in the case of ordinary circular or oval wounds, with a more or less hollowed outline, it is unnecessary to pay attention to the individual action of the perimeter.

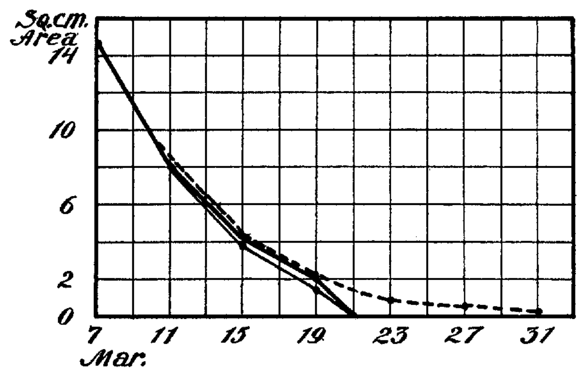
In very long wounds L is practically equal to $\frac{P}{2}$ (P being the perimeter), and may be expressed by $K'\sqrt{S}$. The relation of the outline to the surface then becomes:

$$K' \frac{\sqrt{S}}{S}$$

Experiments showed that when $K' = 1$, this relation is practically equal to $\frac{L}{l}$, and the extrapolation formula becomes:

$$S'' = S'[1 - i(t' + \sqrt{T + t'})] - \frac{\sqrt{S'}}{S'}$$

The following examples show that this equation gives a far better approximation of the date of cicatrization of long and narrow wounds.



TEXT-FIG. 1. Patient 409. Wound of the leg.

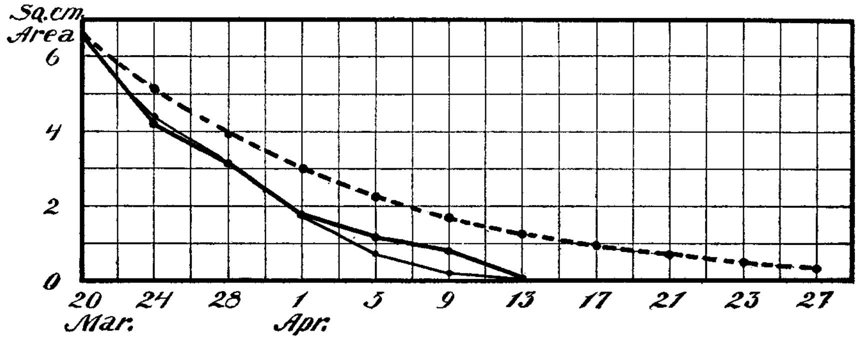
——— observed curve.
——— calculated curve, corrected.
.... calculated curve, uncorrected.

Corrected according to $S'' = S'[1 - i(t' + \sqrt{T + t'})] - \frac{\sqrt{S'}}{S'}$

Uncorrected according to $S'' = S'[1 - i(t' + \sqrt{T + t'})]$

Patient 409 (Text-Fig. 1).

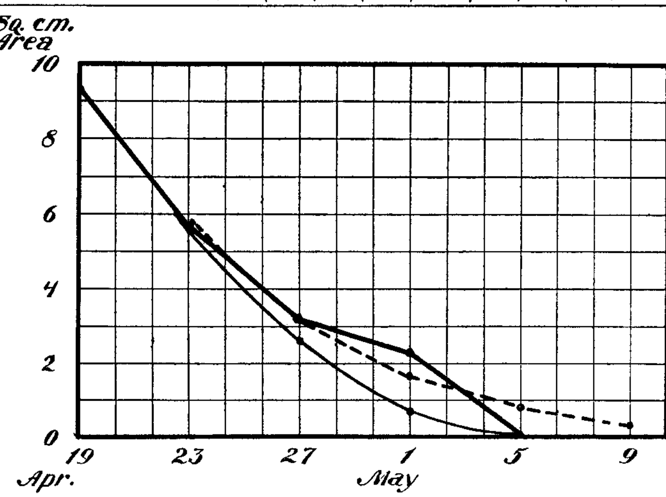
1916 Mar.	7	11	15	19	21	23	27	31
Observed area	14.6	8.2	4.3	2.0	0			
Calculated area (corrected)		8.2	3.95	1.4	0			
" " (uncorrected)		8.5	4.4	2.1		0.9	0.6	0.4
Length of wound (L) cm.	13.2	12.3	10.6	7.4				
Width of wound (l) cm. maximum	1.6	1.0	0.6	0.3				
$\frac{L}{l}$	8.2	12.3	17.6	24.6				



TEXT-FIG. 2. Patient 318. Wound of the leg. Normal rate until Mar. 20, 1916.

Patient 318 (Text-Fig. 2).

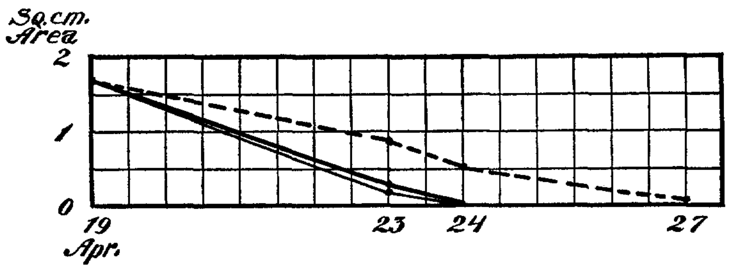
1916 Mar.	20	24	28	Apr.1	5	9	13	17	21	25	27
Observed area................	6.5	4.2	3.1	1.8	1.15	0.8	0				
Calculated area (corrected).....		4.3	3.1	1.8	0.7	0.2	0				
" " (uncorrected)...	6.6	5.1	3.9	3.0	2.25	1.7	1.28	0.95	0.70	0.5	0.37
$\frac{L}{l}$........................	10.0	10.6	11.6	13.8	17.0	25.0					



TEXT-FIG. 3. Patient 415. Wound of the thigh.

Patient 415 (Text-Fig. 3).

1916 Apr.	19	23	27	May 1	5	9
Observed area..........................	9.3	5.6	3.2	2.3	0	
Calculated area (corrected)................		5.5	2.6	0.72	0	
" " (uncorrected)............		5.7	3.2	1.65	0.78	0.35
$\frac{L}{l}$..................................	7.5	9.1	12.8	13.4		



TEXT-FIG. 4. Patient 415. Wound of the leg.

Patient 415 (Text-Fig. 4).

1916 Apr.	19	23	24	27
Observed area	1.7	0.3	0	
Calculated area (corrected)		0.22	0	
" " (uncorrected)		0.9	0.5	0.2
$\frac{L}{l}$	9.0	12.5		

As the acceleration of the rate of cicatrization often occurs suddenly, the curves drawn by means of the above formula merely give a more exact determination of the date of complete healing. This formula goes to zero, which corresponds to the cicatrization.

As the perimeter becomes important only when the relation of $\frac{L}{l}$ is above 10, the wound generally cicatrizes according to the uncorrected formula, until it suddenly begins to decrease in size. As soon as the relation between the two extreme dimensions (length and width) reaches a number between 10 and 20, the perimeter apparently becomes important, and reduces the time which should have been necessary for the cicatrization under ordinary circumstances. The fact that both epithelial borders are close to each other probably plays an effective part in this phenomenon.

The time taken is always 4 days.[3]

The corrected and uncorrected formulas can be simplified by expressing the calculated area of a wound after a certain period, as $n \times t$ days. If $t = 4$, $nt = 4n$.

[3] du Noüy, *J. Exp. Med.*, 1916, xxiv, 451.

If the first calculation is 1, the second 2, the third 3, and so on, up to the n^{-1} and the unknown nth; then the area S_n, at the end of $n \times t$ days will be

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

and the correction

$$-\frac{\sqrt{S_{n-1}}}{S_{n-1}}$$

or, if $t = 4$,

$$S_n = S_{n-1}\,[1 - i\ (4 + \sqrt{4n})]$$