significantly, hence the data for individual Groups have been omitted.

Discussion. The work of Binkley and coworkers(10) has indicated that the non-protein sulfhydryl of rat liver consists mainly of glutathione or precursors of glutathione, *i.e.*, cysteinyl glycine and y-glutamyl cysteine. We have no data as to the nature and amounts of compounds which comprise the non-protein sylfhydryl of mouse liver, nor which ones are concerned in the observed changes in non-protein sulfhydryl occurring as a result of the experimental procedures to which the mice have been subjected. Changes in non-protein sulfhydryl observed in the present experiments probably were due chiefly to changes in relative rates of synthesis and breakdown of glutathione in the liver. Further experimentation may reveal whether decreases in liver non-protein sulfhydryl concentration are a usual concomitant of stress situations and shock, and what mechanisms are involved in the effects noted to date.

Summary. Mice were subjected to severe stress by scalding, ligation trauma, injection of a toxic dose of a bacterial polysaccharide, or exposure to cold. Each of these procedures produced a marked decrease in liver non-protein sulfhydryl concentration. In some experiments, a moderate decrease in liver protein sulfhydryl concentration also occurred. Mice recovering from scalding exhibited marked increases in liver non-protein sulfhydryl concentration to values well above the original control level.

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An Inhibiting Effect Observed in the Course of Normal Wound Healing. (19854)

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The experiments described herein were initiated to attempt to account for the slowing-down of the proliferation of granulation-tissue in the last phase of wound healing prior to closure by epithelization. One possibility is that this slowing-down of the proliferation is caused by the liberation of an inhibiting factor in the organism.

To test this hypothesis, 2 experimental wounds of equal size were produced at different time intervals, so that any inhibiting influence produced in the last phase of the first wound healing process could be made to coincide with the active phase of proliferation of the granulation-tissue in the second wound.

Material and methods. Four series of experiments were performed on male albino rats of about 200 g weight. 1) A circular skin wound, 20 mm in diameter, was produced after depilation on the back of the animal on one side of the dorsal midline, and a second wound of equal size added symmetrically on the other side of the dorsal midline after an interval of 6-7 days (16 animals). The healing wounds were outlined on every second day and the values thus obtained plotted in curves. The exact technic of wound production and measurement has been described

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Exp.	2 wounds separated by:		Mean healing times ± S.D.* (days)	Diff. of mean healing times ± S.D.* (days)
	days			
1	6–7	1st wound	26.4 ± 1.1	12 ± 2.8
		2nd	38.4 ± 2.6	
2	10	1st	25.9 ± 1.1	1.9 ± 1.5
		2nd	27.8 ± 1	
3	14	1st	26.8 ± 1.7	3.8 ± 2.6
		2nd	30.6 ± 1.9	
4	18–23	1st	26.9 ± 1	3.7 ± 1.9
		2nd	30.6 ± 1	
Control exp.				
1	2 wounds produced simultaneously on 1 animal:			
		Right wound	22.5 ± .7	.6 ± 1.1
		Left	21.9 ± .9	
2	1 single wound:		21.6 ± 1.1	

* Stand. dev. of the mean.

(1,2). In order to assess the time during which the assumed inhibitory substance was effective, 3 other sets of experiments under the same conditions were undertaken, producing 2 equal wounds in one animal. 2) The second wound 10 days after the first one (8 animals). 3) The second wound 14 days after the first one (8 animals). 4) In the fourth experiment the second wound was produced 3-6 days before the first wound closed, *i.e.*, 18-23 days after the wound had been produced (14 animals). Control experiments with one single wound (36 animals) and with 2 equal wounds produced simultaneously in one animal (15 animals) were made so as to obtain the normal curve of the wound healing process. If a marked difference between the size of the 2 wounds occurred unintentionally, these experimental animals were discarded, as mathematical evaluation of all experiments clearly showed that the greater the difference between the initial wound surfaces the smaller became the difference of the respective healing times. These results are in accordance with those of Carrel and Hartmann(3). In case of infection the experiment was also discarded.

Results: (See tabulation above).

In Exp. 1 in which the second wound was produced 6-7 days after the first wound, a marked inhibition of the wound healing process of the second wound appeared during the last 7-10 days before the first wound was closed, *i.e.*, 15-20 days after the production of the first wound. While the healing process of the first wound ran its normal course(2) to the very end, the second wound for several days showed a diminished tendency to heal, so that the healing process was completed only after a considerable delay of 12 days. (See Fig. 1, one of the characteristic curves). The healing time of the second wound was also considerably extended as compared with the control experiments with one single wound (21.6 days) and with 2 wounds produced simultaneously in one animal (22.2 days).

The other 3 experimental series (2-4) showed only a short inhibition in the healing of the second wound.

It should be noted that the healing of the first wound in Exp. 1 to 4 was also delayed in comparison with the controls.

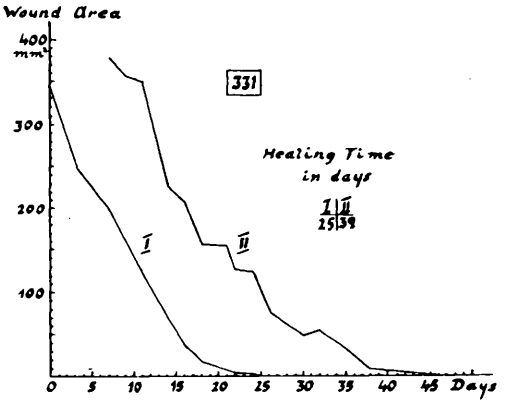

FIG. 1. Healing curves of 2 wounds produced 7 days apart, demonstrating inhibition of healing in the second wound during the last phase of the first.

The weight of the animals remained approximately at a constant level during the whole experiment.

Discussion. The most striking outcome of these experiments was the delay of 12 days of the time of healing in a second wound produced 6-7 days after the first one (Exp. 1). This interval is judged in comparison with the time of healing of the first wound. Compared to the 2 control groups, the interval would be even greater. This, however, is due to a fact I cannot explain, namely that the healing times of the first wounds in experiments 1-4 were consistently later, by about 4 days, than those of the controls.

It seems to follow from the experiments described, that an inhibiting effect appears during a limited period of the wound healing process, which has its influence on another healing process in the same organism. This effect may indicate the existence of an inhibiting factor appearing during this period. There is normally an inhibition during the last 7 days before closure in the first wound. In Exp. 1 a further inhibition in the second wound was observed which occurred within 1-3 days after the former. This inhibition in the second wound occurred much earlier in the wound healing process than usual, making its appearance during the phase of active proliferation of the granulation-tissue.

This inhibitory influence was not present or was too weak to become clearly visible in the Exp. 2-4, where the inhibiting period of the first wound coincided with an earlier and more active stage of the proliferation of the granulation-tissue of the second wound or with the stage immediately after the production of the second wound.

Summary. 1. Experiments were carried out in which the last phase of the healing process of a primary wound was made to coincide either with the phase of active proliferation of the granulation-tissue in a second wound in the same animal or with the stage of the very beginning of this proliferation. 2. The results obtained show the appearance of an inhibiting effect during a limited period of normal wound healing. This finding may suggest the existence of an inhibiting factor.

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Effect of Age upon Hepatic Synthesis of Cholesterol in Rat.* (19855)

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Although *in vitro* studies have been done on the effect of age on the hepatic synthesis of cholesterol in the rat, no similar study has been done on intact rats. Recently, however, a means was found(1) by which the hepatic synthesis of cholesterol might be gauged in the living unanesthetized rat. It consisted of collection of the daily bile output of a rat and determination of its cholesterol concentration. Other studies(2-4) have confirmed the validity of this technic, in that an increase or decrease of the biliary cholesterol concentration parallels an induced respective increase or decrease in the hepatic synthesis of cholesterol as determined by tracer studies. Accordingly, groups of rats at various ages were subjected to a study in which bile was collected and analyzed for its cholesterol concentration.

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