

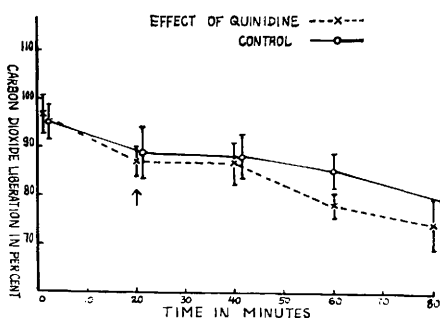


FIG. 4. Effect of quinidine (1:10000) on anaerobic glycolysis of heart slices (9 exp.).

tion does not exclude the possibility that quinidine may specifically inhibit the metabolic system required to maintain the functional integrity of the cellular membrane. This possibility, however, implies the assumption that the cellular membrane and cell itself derive their energy from different sources.

Conclusion. 1. Quinidine was found to have

a profound inhibitory effect on contractility but only a slight effect on oxygen uptake of contracting cat papillary muscle. 2. Oxygen consumption and anaerobic glycolysis of the heart slices were not significantly inhibited by quinidine.

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Effect of Adrenalectomy on Wound Healing in Normal and in Stressed Rats.* (21127)

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That non-specific stress of sufficient magnitude results in depression of the bursting pressure of standard laparotomy incisions in rats has been reported by the authors(1). In each case stress, associated with depression of healing, was observed to have resulted in some degree of adrenal hypertrophy. It was postulated that the stress-induced inhibition of healing might be due to an accelerated rate of endogenous adrenal cortical secretion, sufficient in magnitude to inhibit the healing process. The hypothesis is compatible with the fact that ACTH itself inhibits the rate of healing(1-3), presumably due to increased cortico-adrenal secretion.

In order to test this hypothesis, healing was

studied in adrenalectomized rats. Laparotomy wounds, made 15 days after bilateral adrenalectomy, showed bursting pressures equal to or greater than those of normal control rats. When stress was applied to adrenalectomized animals, the mortality rate became prohibitive. Therefore, the effect of stress upon healing was studied in adrenalectomized rats, which were given a small fixed daily maintenance dosage of adrenal cortex extract.

Methods. Young adult male rats of the Wistar strain, weighing about 175 g were used. Bilateral adrenalectomy was performed under ether anesthesia by the posterior approach. In sham-operated animals the operation was identical except that the adrenal glands were not removed. The animals were maintained in individual cages on Purina Laboratory Chow. After adrenalectomy, a 1% solution of sodium chloride was substituted for drink-

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TABLE I.
Effect of Adrenalectomy on Mean Bursting Pressure of Fifth Day Laparotomy Wounds.

	Days post-laparotomy			
	4	5	7*	10
Normal control	49 $\pm$ 2.3 (10)†	75.4 $\pm$ 2.2 (27)	108.9 $\pm$.6 (19)	122.7 $\pm$ 2.6 (28)
Sham-adrenalectomy		71.8 $\pm$.8 (12)		
Adrenalectomy (15 days pre-laparotomy)	52.3 $\pm$ 1.0 (10)	82.1 $\pm$ 3.2 (18)	118.9 $\pm$ 2.9 (15)	121.1 $\pm$ 4.4 (14)

* Difference in bursting pressures between the normal control and the adrenalectomized rats was significant only on the 7th day post-laparotomy ($P < .01$).

† Figures in parentheses indicate the No. of animals in each experiment.

ing water. Environmental temperature was $75 \pm 5^\circ\text{F}$.

Laparotomy incision was made according to a standard technic(1) 15 days after adrenalectomy. The bursting pressure of the incision was tested 4, 5, 7, and 10 days post-operatively in groups of 10 or more animals, respectively, as previously described(1). These results were compared with similar incisions in normal control animals and in some cases with sham-adrenalectomized control rats. The stress employed consisted of excision of a patch of skin measuring 6 x 3 cm from the backs of the animals under ether anesthesia. No dressing was applied. This was done 4 days prior to laparotomy. Injections of Beef Adrenal Cortex Extract Aqueous (Upjohn)† were begun immediately prior to initiation of stress in a series of adrenalectomized rats. A dosage of 2 ml twice daily was injected subcutaneously. This is equivalent to 0.8 glycogenic unit. It is estimated to constitute an average maintenance dose for the rat(4). In one experiment desoxycorticosterone in sesame oil (5 mg daily, subcutaneously) was substituted for adrenal cortex extract. In order to rule out the possibility that these hormones themselves might affect the rate of healing, the effect of the same doses of cortex extract and of DOCA was tested in groups of stressed nonadrenalectomized animals.

Results. Table I summarizes the effect of adrenalectomy upon the rate of healing, when compared with normal control rats. On the

4th and the 10th postoperative days, there is essentially no difference between the adrenalectomized and the normal rats. On the 5th day the mean bursting pressure is increased in the adrenalectomized animals, but this increase is not of statistical significance ($P .05$). On the 7th postoperative day, however, the adrenalectomized group had a significantly greater mean bursting pressure than did the normal controls ($P < .01$).

From Table II it can be seen that skin-excision-stress resulted in significant depression of the mean bursting pressure. Treatment with either cortex extract or DOCA did not improve this mean bursting pressure. When the same stress was applied to adrenalectomized rats, maintained on cortex extract, there was no depression of the mean bursting pressure. These wounds are significantly stronger than those of stressed, nonadrenalectomized rats. Similar results are evident following the use of DOCA for supportive therapy, except that here the series is not large enough for statistical significance.

Discussion. Skin-excision-stress in the adrenalectomized rat, supported by small doses of cortex extract, failed to depress the mean bursting pressure of the 5th day laparotomy wound. In the normal control rat, stress did result in depressed bursting pressure in both untreated rats and in animals receiving the same dosage of cortex extract. It appears, therefore, that under the conditions of this experiment, stress-induced inhibition of healing may be attributed to an accelerated rate of cortico-adrenal secretion following stress.

If the impairment of healing following stress is due to an accelerated rate of cortical

† We are indebted to Dr. W. T. Haines of Upjohn Co. for a generous supply of this product.

TABLE II. Effect of Stress in Adrenalectomized Animals.

	No. rats	Mean bursting pressure	n	t	P
Normal control	27	75.4 $\pm$ 2.2	—	—	—
1. Skin-excision-stress	34	60.0 $\pm$ 1.5	—	—	—
2. Skin-excision-stress + A.C.E. 4d pre-lap.	8	56.8 $\pm$ 2.3	40	—	N.S.*
3. Adrenalectomy 15d pre-lap., skin-exc. and A.C.E. 4d pre-lap.	12	74.0 $\pm$ 2.1	44	3.46	<.01
4. Skin-exc.-stress and DOCA 4d pre-lap.	12	53.8 $\pm$ 2.9	44	—	N.S.*
5. Adrenalectomy 15d pre-lap., skin-exc. and DOCA 4d pre-lap.	5	69.1 $\pm$ 1.3	37	3.33	.037*

* N.S. = Not significant as compared with skin-excision-stress.

n, t and P calculated according to the t-test of Student.

A.C.E. = Adrenal cortex extract. DOCA = Desoxycorticosterone acetate. Pre-lap. = Pre-laparotomy.

secretion, this phenomenon is not in complete accord with the concept of Ingle(4) that "the increased secretory activity of the adrenal corticés during stress tends to maintain homeostasis rather than to cause hypercorticalism."

With regard to the effect of adrenalectomy upon the healing process, previous reports have been contradictory(3,5). Our results indicate that adrenalectomy does not interfere with wound healing. This fact is itself of great interest. A number of authors have hypothesized that the negative nitrogen balance which follows wounding or surgical operation represents the mobilization of protein raw materials essential to the normal healing process(6-9). Adrenalectomy prevents this increased nitrogen excretion following stress(10-12). Nevertheless, in our experiment healing was not in the least impaired.

Summary. 1. The bursting pressures of healing laparotomy wounds, made 15 days after bilateral adrenalectomy were equal to or superior to those of normal control rats. 2. In adrenalectomized rats, maintained on a small fixed dosage of aqueous adrenal cortex extract, skin-excision-stress did not result in depression of the bursting pressure of 5th day laparotomy wounds, as is the case with non-

adrenalectomized rats subjected to the same stress.

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