of BSP from the liver by India ink would appear plausible if India ink contained some substance which diminished the BSP-concentrating ability of the liver cells.

Our observations that the effect of India ink on BSP clearance is not produced by gelatin stabilized carbon particles and that doses of India ink sufficient to inhibit BSP excretion do not influence the phagocytic process(5) indicate that BSP clearance is not a suitable index of Kupffer cell activity.

Summary. The administration of a gelatin-stabilized carbon suspension did not affect bromsulfalein (BSP) clearance in dogs. However, a carbon-free filtrate of Higgins India ink markedly inhibited BSP uptake and effected the release of previously stored BSP from the liver. It appears that the effect of India ink on BSP excretion is not due to reticuloendothelial blockade but rather to a toxic effect of some soluble component of the ink on the liver. It is suggested that in dogs BSP clearance is not a suitable index of Kupffer cell activity.

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1. Zilversmit, D. B., Shore, M. L., and Gantt, C. H., *Fed. Proc.*, 1954, v13, 170.
2. Jaffé, R. H., *Physiol. Rev.*, 1931, v11, 277.
3. Mills, M. A., and Dragstedt, C. A., PROC. SOC. EXP. BIOL. AND MED., 1936, v34, 228.
4. Brauer, R. W., and Pessotti, R. L., *J. Pharmacol. and Exp. Therap.*, 1949, v97, 358.
5. Shore, M. L., and Zilversmit, D. B., *Am. J. Physiol.*, 1954, v177, 436.
6. Victor, J., Van Buren, J. R., and Smith, H. P., *J. Exp. Med.*, 1930, v51, 531.
7. Gaebler, O. H., *Am. J. Clin. Path.*, 1945, v15, 452.

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Effect of Quinidine on Papillary Muscle.* (21126)

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The effect of quinidine on the excitability of heart muscle has been studied in experimental animals as well as in man(1). The inhibition by quinidine is manifested by a depression of contraction and an increased refractory period. Although evidence is scanty it is generally believed that the effect of quinidine on the heart is due to a slowing of recovery processes resulting from impaired metabolism. In the present work simultaneous changes in contraction and oxygen uptake of the isolated cat papillary muscle following the administration of quinidine were observed. The results were further analyzed in the light of the effects of quinidine on the metabolism of heart slices.

Method. The method described previously (2) was used for the simultaneous observation of contraction and oxygen consumption of the muscle. The oxygen consumption and anaerobic glycolysis of cat heart slices were determined manometrically by a conventional Warburg method. The thickness of the slices

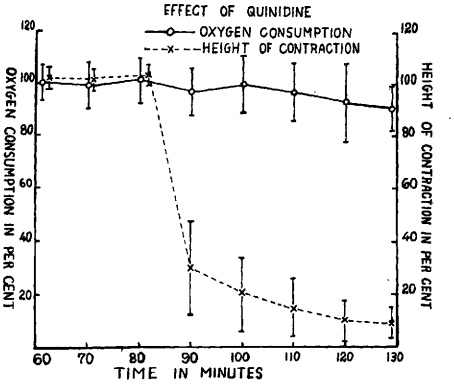

FIG. 1. Effect of quinidine (1:10000) on oxygen consumption and height of contraction of papillary muscles (7 exp.). In this and following figures, the 99% confidence limits of each mean are presented graphically by the vertical lines.

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was about 0.3 mm. The mediums used in the experiments for measurement of oxygen consumption and anaerobic glycolysis were Krebs-Ringer-phosphate and Krebs-Ringer-bicarbonate, respectively(3). Papillary muscles were prepared from the right ventricle of the cat heart according to the method of Cattell and Gold(4). Quinidine sulfate, U.S.P. (Merck) was used in these experiments.

Results. Effect of quinidine on the oxygen consumption and contraction of heart muscle. Muscles were stimulated at a rate of one per second throughout experiment. Results are summarized in Fig. 1. At the arrow, quinidine was added to make a final concentration of 1:10000. Immediately following addition of the drug, a rapid decrease in the height of contraction occurred while there was no significant change in oxygen consumption.

To compare this decline in contraction with that produced by anoxia, the system was equilibrated with an atmosphere of 95% nitrogen and 5% carbon dioxide for about 30 minutes. Muscles from oxygenated Krebs-Ringer-phosphate solution were then suddenly introduced into the anaerobic system and contractions recorded during stimulation at a rate of one per second. Results are shown in Fig. 2. The decrease in height of contraction following quinidine was included in the figure for comparison. Under an anaerobic condition, height of contraction of the muscle declined rapidly, reaching about 10% of original level in 20 minutes. Deterioration of muscular contractions induced by anoxia was thus similar to that produced by 1:10000 quinidine both in rapidity and in intensity.

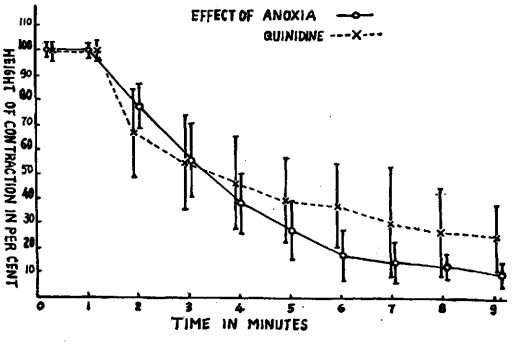

FIG. 2. Effects of anoxia and quinidine (1:10000) on height of contraction of papillary muscles (8 exp.).

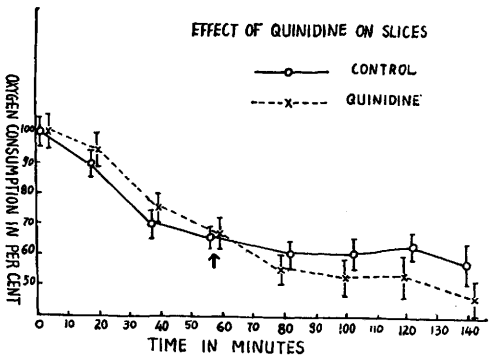

FIG. 3. Effect of quinidine (1:10000) on oxygen consumption of heart slices (12 exp.).

Effects of quinidine on the oxygen consumption and anaerobic glycolysis of heart slices. Fig. 3 represents results obtained in experiments on oxygen consumption. In comparison to control tests there was a little less oxygen consumption following addition of quinidine (1:10000) but the magnitude of this difference was not statistically significant. The effect of the drug on anaerobic glycolysis of slices is shown in Fig. 4. Here again, there appeared to be slight inhibition of glycolysis following addition of the drug but this was not statistically significant.

Discussion. Decrease in oxygen consumption and in glycolysis of heart slices treated with quinidine have been previously reported (5,6). In the present experiments with heart slices, decreases in these 2 functions appeared to follow administration of 1:10000 quinidine, but these effects were of doubtful significance. Quinidine in this concentration exerted no significant effect on oxygen consumption of stimulated papillary muscles. On the other hand, 1:10000 quinidine had a profoundly depressant effect on contraction of stimulated muscle which almost equalled the effect of complete anoxia in its intensity and rapidity.

The effect of complete blockade of glycolysis by iodoacetate on contractility of papillary muscle is very much slower than that produced by complete anoxia(7). These data suggest that inhibition of glycolysis or oxygen uptake *per se* by quinidine, does not satisfactorily explain the profound depressant action of the drug on contraction. This interpreta-

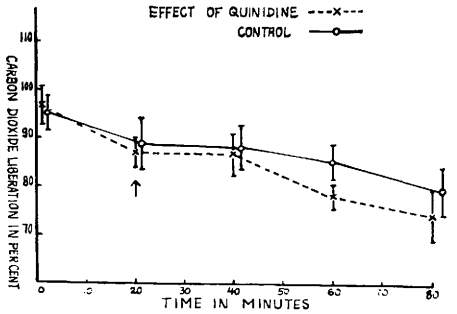

FIG. 4. Effect of quinidine (1.10000) on anaerobic glycolysis of heart slices (9 exp.).

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.

1. Dipalma, J. R., and Mascatello, A. V., *J. Pharm. Exp. Therap.*, 1951, v101, 243.

2. Lee, K. S., *ibid.*, 1953, v109, 313.

3. Umbreit, W. W., Burris, R. H., Stauffer, J. F., *Manometric techniques and related methods for the study of tissue metabolism.* Burgess Publishing Co., 1948, p194.

4. Cattell, McK., and Gold, H., *J. Pharm. Exp. Therap.*, 1938, v62, 115.

5. Speck, J. F., and Evans, E. A., Jr., *J. Biol. Chem.*, 1945, v159, 83.

6. Webb, J. L., Saunders, R., and Nakamura, K. J., *J. Pharm. Exp. Therap.*, 1951, v101, 287.

7. Lee, K. S., unpublished data.

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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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