

of the mesenteric nerve, yet cocaine depressed several such poisoned muscles.

*Colon.* Five segments of rabbit colon were contracted by cocaine, 1:10,000. This action of cocaine was in no way influenced by nicotine or atropine, 1:20,000.

*Uterus.* Four segments of excised uterus of the rabbit were contracted by cocaine, 1:10,000 both before and after ergotamine reversal of epinephrine action.†

*Conclusions.* Since the drugs which are known to paralyze ganglia and nerve terminations of the autonomic nervous system failed to prevent either the augmentor or depressant effects of cocaine on the small intestine, colon and uterus of the rabbit, it seems reasonable to conclude that this alkaloid acts on the muscle, rather than the nerves of the organs studied.

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#### Studies on Cyanide-Stable Respiration.

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The opinion has long been held that the respiration of animal tissues is completely inhibited by cyanides.<sup>1</sup> However, Dixon and Elliott<sup>2</sup> have shown that in most tissues there is an appreciable oxygen consumption in the presence of the cyanide radical.

We have found that the cyanide-stable fraction of the respiration of the liver of the frog, *Rana pipiens*, is quite appreciable. The frogs were pithed and the liver promptly removed. The tissue was then minced with a razor moistened with Ringer's solution into slices 0.5 mm. or less in thickness, under which conditions Warburg<sup>3</sup> has shown that oxygen and cyanide have free access to the several cells. The minced liver, suspended in phosphate Ringer's,<sup>4</sup> was placed in the respiration chamber of a Warburg manometer. A cup containing 7% KOH removed the CO<sub>2</sub> produced. All the mano-

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<sup>1</sup> Macleod, J. J. R., "Physiology and Biochemistry in Modern Medicine." 1930, 622.

<sup>2</sup> Dixon, M., and Elliott, K. A. C., *Biochem. J.*, 1929, **23**, 872.

<sup>3</sup> Warburg, O., *Biochem. Z.*, 1923, **142**, 317.

<sup>4</sup> Dickens, F., and Simer, F., *Biochem. J.*, 1930, **24**, 1301.

meters were calibrated according to the method of Warburg.<sup>5</sup> The respiration chamber was placed in a water thermostat at 21.5°C., and shaken 70 times per minute.

The cyanide-stable fraction of the respiration was measured by placing a weighed portion of a given liver prepared as described in each of 2 respiration chambers, so that all comparisons were made between portions of one liver. One of the chambers contained phosphate-Ringer's, the other phosphate-Ringer's which was M/210 with respect to KCN. Dixon and Elliott<sup>2</sup> have shown that M/300 KCN produces maximal inhibition in most tissues, and we have found no appreciable difference between the effects of M/210 and M/21 KCN. In every case the cyanide was neutralized.<sup>2</sup>

The oxygen consumption of a given suspension of tissue was determined over a period of at least 2 hours, after previous soaking in the solutions for 15 to 45 minutes. Only those experiments in which the oxygen consumption is approximately linear with respect to time are reported. The ratio  $\frac{\text{cyanide-stable respiration}}{\text{total respiration}} \times 100$  in 8 experiments varied between 15.62 and 57.9%, average 35.3.

Urethane is known to interfere with cytochrome reduction. If this is quantitative, one might assess the importance of the cytochrome b system in the cyanide-stable moiety of the respiration by treating with both cyanide and urethane. Liver tissue, prepared as before was divided into 2 portions, which were suspended in phosphate-Ringer's (a) including M/210 KCN; (b) M/210 KCN and 5% ethyl urethane. The  $\frac{\text{Respiration in cyanide + urethane}}{\text{Respiration in cyanide}} \times 100$  was 71.0, 61.9, 71.2, 59.5, 39.0% respectively.

It is clear that a portion of the cyanide-stable respiration is not inhibited by ethyl urethane, and it is possible that we are here dealing with a new type of respiratory system. Further experiments on the properties of cyanide-stable and cyanide-urethane-stable respiration are under way in this laboratory.

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<sup>5</sup> Warburg, O., "Über den Stoffwechsel der Tumoren," 1926.