ministrations of pilocarpine (the duration of this antagonism varied from 9 minutes in one instance to 30 minutes in another); (b) causing relaxation of a uterus already contracted under the influence of pilocarpine. It was repeatedly observed that at the time pilocarpine was inhibited by atropine the uterus responded to epinephrine (0.5-1 cc., 1:50,000) and posterior pituitary extract (0.1-0.5 cc., Parke, Davis).

The present results differ from those which Cushny[6] obtained on anesthetized (paraldehyde) rabbits and cats in that when we observed a feeble sustained contraction of the quiescent uterus following pilocarpine, atropine had no antagonistic action on such a contraction, whereas it did in the experiments described by him. It is suggestive in our experiments, therefore, that the contraction of the quiescent uterus seen by us is only secondarily related to the injection of pilocarpine. Certainly, without concomitant pulmonary distress pilocarpine has not, in our experience, elicited a contraction of the quiescent uterus.

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Oxygen and Carbon Dioxide Dissociation Studies on Blood Drawn after Intravenous Injection of Pitressin.*

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In previous communications[1, 2, 3] it was pointed out that certain well defined circulatory and respiratory changes are elicited by the intravenous injection of moderate doses of pituitrin or pitressin into unanesthetized human beings or dogs. For a brief period (5 to 10 minutes) immediately following the administration of the drugs, the venous blood draining the limbs becomes arterial in

[6] Cushny, A. R., *J. Physiol.*, 1906, **35**, 1.

* This work was aided by a grant from the Hartley Corporation.

[1] Geiling, E. M. K., and DeLawder, A. M., *Bull. Johns Hopkins Hosp.*, 1932, **51**, 1.

[2] Geiling, E. M. K., and DeLawder, A. M., *Bull. Johns Hopkins Hosp.*, 1932, **51**, 335.

[3] Grollman, Arthur, and Geiling, E. M. K., *J. Pharmacol. and Exp. Therap.*, 1932, **46**, 447.

color and shows a high oxygen content, a rapidly rising lactic acid concentration, and a concomitantly lowered carbon dioxide content. There is at the same time a precipitous decrease in total oxygen consumption and a lowering of the cardiac output. In the immediately ensuing recovery period, which persists for 1½ to 2 hours after the injection, the physiological picture is reversed. An abnormally dark venous blood is found, indicating increased oxygen utilization by the "starved" tissues; a further rise in lactic acid is followed by a gradual return to the pre-injection level; the carbon dioxide content returns slowly to a slightly sub-basal value. Total oxygen consumption and cardiac output show parallel increases above their pre-injection values and then gradually return to the basal level.

A temporary inability of the blood to give up its oxygen is one cause which might account for the arterial character of the venous blood drawn from the leg 5 to 10 minutes after the intravenous injection of pitressin. To ascertain whether such a factor comes into play, oxygen and carbon dioxide dissociation studies were made on this blood and the results obtained are recorded in the present communication.

Methods. The technique followed was essentially that described by Dill,[4] with minor modifications, the most important of which was the storage of the equilibrated blood in a closed tube over mercury instead of under oil. The carbon dioxide and oxygen contents of the blood were determined by the Van Slyke and Neill method in an apparatus of the portable manometric type, and the gaseous mixtures in the tonometers were analyzed in the Haldane apparatus. The formula used for calculating the gas tensions in the tonometers during equilibration was that recommended by Dill.[4]

Results. Fig. 1 shows the oxygen dissociation curves of normal venous dog's blood, arterial-like venous blood drawn 6 to 8 minutes after the intravenous injection of 0.6 cc. of pitressin, and dark venous blood of the recovery period. It may be seen that the intravenous administration of pitressin to unanesthetized dogs has little effect upon the oxygen dissociation curve of the blood. The only noticeable deviation from the normal is a slight shift of the curve to the right, more marked in the blood obtained during the recovery period. This slight alteration in the pitressinized blood is to be expected from the fact that its lactic acid content is high, being particularly ele-

[4] Dill, D. B., Appendix to Henderson, L. J., Blood, A Study in General Physiology, Yale University Press, New Haven, 1928.

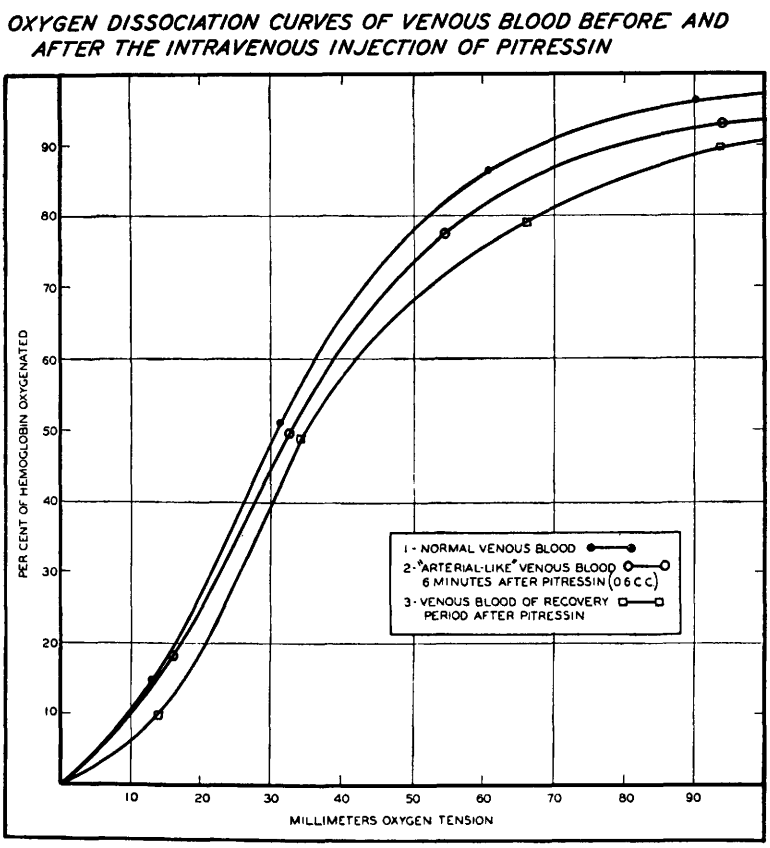

FIG. 1.

vated during the recovery period.[1] Accordingly, any effect of pitressin upon the oxygen dissociation curve of the blood is in the direction of a decreased rather than an increased oxygen affinity. Our curve for normal dog's blood is in close agreement with that reported by Dill, Edwards, Florkin and Campbell.[5]

Results which are essentially similar to those shown in Fig. 1 were obtained when the same procedure was carried out on 2 other unanesthetized dogs.

Fig. 2 represents a comparative study of the carbon dioxide dissociation curves of normal and post-pitressin bloods. The only outstanding variation is a change in the level of the curves of the post-pitressin bloods, with no alteration in the slope. This change, like those noted in the oxygen dissociation studies, is apparently

[5] Dill, D. B., Edwards, H. T., Florkin, M., and Campbell, R. W., *J. Biol. Chem.*, 1932, **95**, 143.

CARBON DIOXIDE DISSOCIATION CURVES BEFORE AND AFTER THE INTRAVENOUS INJECTION OF PITRESSIN

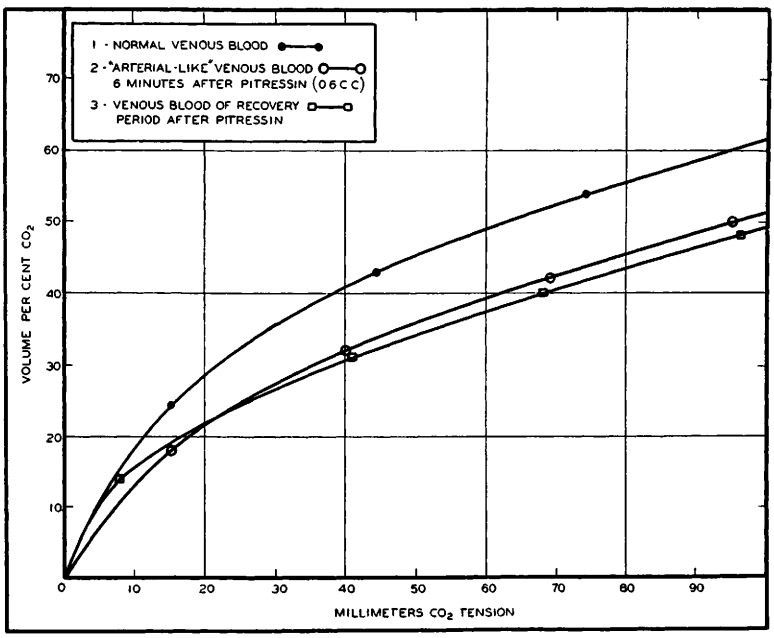

FIG. 2.

due to the presence of lactic acid, which has been shown to increase to a value 3 times the basal level after the injection of pitressin.

From the above findings it seems justifiable to conclude that the high percentage of oxy-hemoglobin in venous blood after the injection of pitressin cannot be attributed to any interference with the power of the blood to yield its oxygen at a given tension.

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Effect of Pitressin and Pitocin on Oxygen Consumption of Excised Tissue.

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A direct action of pituitrin and pitressin on the tissue cells so as to render them incapable of taking up oxygen was one of the possible explanations suggested by Geiling and DeLawder for the sig-