2. The most consistent response of the circular muscle of the duodenum to morphine was an increase in the many phases of muscular activity. This includes elevation of the tonus level with increased frequency and amplitude of the normal spontaneous tonic contractions.

3. The most frequent though not completely consistent response of the longitudinal muscle was found to be either a decrease or an abolition of the many phases of the muscle activity. This includes a depression of the tonus level with a decreased frequency and amplitude of the normal spontaneous tonic contractions.

4. The type of response of the duodenum to morphine was independent of the original state of tonus and independent of the dose over the range of 0.01 mg to 1.0 mg per kg.

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Protective Action of Dibenamine After Hemorrhage and After Muscle Trauma.*

J. W. REMINGTON, N. C. WHEELER, G. H. BOYD, JR., AND H. M. CADDELL.

From the Department of Physiology, University of Georgia School of Medicine, Augusta, Ga.

Wiggers and associates[1,2] have demonstrated that dogs given the sympatholytic substance Dibenamine showed a higher survival rate than controls from shock produced by hemorrhage. The inference made is that abolition of a severe vasoconstriction normally following hemorrhage protects the life of the animal.

In a series of dogs under morphine-nembutal anesthesia, 6 arterial hemorrhages of 5 cc/kg b.w. each, were performed at 10 minute intervals. Aortic pressure pulse contours were recorded during the hemorrhage period, and for an additional hour. All wounds were then closed, and the animals returned to their cages. Cardiac outputs were calculated from the pressure pulse contours,[3] and in a selected series by the dye injection method,[4] and vasomotor resistance (Rv) calculated as the mean aortic pressure less 20 mm Hg divided by the flow per second.[5] Specific gravity values of plasma and whole blood were determined at 10 minute intervals by the falling drop technic.

This experiment was done during the summer months, so that an expectedly sub-lethal hemorrhage proved fatal in 13 of 14 dogs, with an average survival of the 13 dogs of 4 hours. Ten more dogs were given 10-20 mg/kg Dibenamine,† in 50 cc saline, *i.v.*, one hour before the hemorrhage was begun. The completeness of the sympathetic block was demonstrated by the injection of epinephrine 5 minutes before the first bleeding. Nine of these animals survived. To rule out the possible effect of the salt solution itself, the last 5 of the control series received 50 cc saline one hour before the hemorrhage. All of these dogs died.

Systolic and diastolic pressure values for

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1 Wiggers, H. C., Roemhild, F., Goldberg, H., and Ingraham, R. C., *Fed. Proc.*, 1947, **6**, 226.

2 Ingraham, R. C., Roemhild, F., and Goldberg, H., *Fed. Proc.*, 1948, **7**, 60.

3 Hamilton, W. F., and Remington, J. W., *Am. J. Physiol.*, 1947, **148**, 14.

4 Hamilton, W. F., Riley, R. L., Attyah, A. M., Cournand, A., Fowell, D. M., Himmelstein, A., Noble, R. P., Remington, J. W., Richards, D. W., Wheeler, N. C., and Witham, A. C., *Am. J. Physiol.*, 1948, **153**, 309.

5 Hamilton, W. F., and Remington, J. W., *Am. J. Physiol.*, 1948, **153**, 287.

† We are indebted to Dr. W. Gump of Givaudan-Delawanna, Inc., for the Dibenamine Hydrochloride used in this study.

the two groups were not significantly different The Dibenamine treated animals showed slightly higher blood flow values throughout, with faster pulse rates. Vasomotor resistance values, while showing roughly parallel changes in the two groups, were consistently lower in the treated dogs. There was no demonstrable correlation between the dilution of the blood and the survival period. In fact, as a group, the treated animals showed less dilution than the controls.

It has been shown that animals subjected to contusion of the muscles of both hind legs, by multiple blows with a light mallet, show higher resistance values than after hemorrhage,[6] and die after a smaller blood volume loss than would be required by hemorrhage.[7] This higher resistance is presumably brought about by afferent nervous discharge from the traumatized limbs.[8] Nine control animals, under morphine-nembutal anesthesia, were given 80 blows/kg b.w. to each hind leg. All these dogs died, with the average survival of 3½ hours. Nine more dogs were given Dibenamine, as above, 1 hour before the trauma. Eight of these recovered, the ninth dog surviving 15 hours. As with the hemorrhage experiment, pressure values were not different in the two series. Pulse rates of the Dibenamine-treated animals were greater, and flows were maintained at higher levels. They therefore showed a lower vasomotor resistance.

A limited number of blood volumes, determined by T-1824 injection, indicated that the blood volume loss in these animals was sufficient in itself to have caused death. The blood volume loss was of similar magnitude in treated and untreated dogs. Peripheral resistance was definitely higher than after hemorrhage. The treated dogs did not show this rise in resistance, but rather a vasodilation. Death in the control series may be preceded by the appearance of cardiac irregularity, which developed while the peripheral resistance was still high. Both groups showed a hemoconcentration. In the control series, however, this developed not during the trauma but after its completion.

Summary. A hemorrhage of 30 cc/kg proved fatal in 93% of the cases. Pretreatment with Dibenamine reduced this mortality to 10%. Pulse rate and blood flow per second were consistently greater in the second series. Administration of 80 blows/kg to each hind leg with a light mallet produced fatal shock in 100% of the cases. Pretreatment with Dibenamine reduced the mortality to 11%. Control animals showed vasoconstriction, treated animals vasodilation.

[6] Root, W. S., Walcott, W. W., and Gregerson, M. I., *Am. J. Physiol.*, 1947, **151**, 34.

[7] Wang, S. C., Overman, R. R., Fertig, J. W., Root, W. S., and Gregerson, M. I., *Am. J. Physiol.*, 1947, **148**, 164.

[8] Swingle, W. W., Kleinberg, W., Remington, J. W., Eversole, W. J., and Overman, R. R., *Am. J. Physiol.*, 1944, **141**, 53.