duced coefficient of elasticity associated with the lower diastolic pressure both would have the effect of reducing the P. P. produced by a given stroke volume, and both would, therefore, tend to put the mean of the recumbent reading to the left of the line passing through the mean standing and exercise readings.

The scattering of the points and the fact that the lines drawn through the mean of the standing and exercise determinations do not pass through zero must be attributed to the influence of systolic time and arterial elasticity upon the relation to P. P. to S. V. It so happens that these modifying factors do not, in our observations, materially obscure the linear relationship of P. P. to S. V. The scattering of the points around their respective means is in part explained by experimental error, and in part again by the influence of systolic time and arterial elasticity. Thus the determinations in which the pulse rate is relatively rapid all tend to fall to right of the line.

Obviously when the product P. P. $\times$ P. R. is used as an index to the C. R. the modifying influence of the systolic time on the relation of P. P. to S. V. will have to be taken into consideration. In every case save two, the means of the P. P. $\times$ P. R. and of the C. R. change in the same direction. The two exceptions occur in the change from the recumbent to the standing posture and in these two cases the pulse has the largest rate.

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The action of adrenalin on the pyloric sphincter.

J. E. THOMAS.

[*From the Department of Physiology, St. Louis University School of Medicine, St. Louis, Mo.*]

Because of the lack of consistent data bearing on the action of adrenalin on the pyloric sphincter, a further investigation of the problem has been undertaken. The results so far obtained have been sufficiently constant that a preliminary report, indicating their general character, seems justified. The investigation has been confined to a study of the immediate effects of the drug administered intravenously to anesthetized dogs. Several methods

have been employed to observe the reactions of the sphincter muscle without significant differences in the results.

In dogs that have been anesthetized with morphin and ether, and allowed an hour or more for recovery from operative procedures, adrenalin produces regularly a prompt relaxation of the sphincter muscle. After a variable interval, the duration of which depends on the dosage, the tonus recovers and may temporarily reach a level slightly higher than before the drug was given. On the other hand, if observations are made immediately after operating on the animal or if ether alone is used for anesthesia, the administration of adrenalin usually causes, immediately, a slight increase in the tonus of the sphincter.

No very pronounced changes in the tonus of the sphincter have been observed as a result of administering adrenalin. The greatest increase in tonus obtained with adrenalin was much less than that which results from morphin, or from vagus stimulation. When a decrease in tonus is obtained it is generally somewhat more pronounced, but is decidedly less than is seen in the small intestine when adrenalin is given.

Although Gruber[1] and others have found that adrenalin may contract or relax gastrointestinal muscle, depending on the dosage, no such influence of dosage is apparent in the results of these experiments so far, but further study of this point seems desirable. Under the experimental conditions that have obtained in this work up to the present, identical doses produce opposite effects in the same animal at different times, and under certain conditions, qualitatively similar results are obtained with a wide range of dosage. Larger doses (*e. g.,* 0.05 mg. per kilo) produce a somewhat more prolonged effect than smaller ones, (*e. g.,* 0.005 mg. per kilo) but an inhibitory response was not observed to change to motor, or vice versa, as a result of change of dosage.

On the other hand, a sphincter muscle which is responding constantly to adrenalin with an increase in tonus can be made to change its response to relaxation by procedures which increase the tonus of the muscle, *e. g.,* the administration of morphin or stimulation of the vagus, the adrenalin being given during the period of stimulation. This fact suggests an explanation for the different responses obtained under different conditions. In animals under ether anesthesia without morphin, and in animals

[1] Gruber, Charles M., *J. Pharm. and Exp. Therap.,* 1922, xx, 321.

recently subjected to operative procedures the tonus of the sphincter is found to be comparatively low. It is under such conditions that motor effects are obtained. On the other hand the records indicate a gradual recovery of tonus in the sphincter muscle after operation if the animal is not disturbed, and a sudden and permanent increase in tonus if morphin is administered. When these conditions are established the response to adrenalin is characteristically inhibitory.

It appears, therefore, that adrenalin increases the tonus of the pyloric sphincter when the muscle is relaxed and decreases it when the muscle is contracted. It will be recalled that these results correspond to those described by Carlson and Litt[2] as following stimulation of the sympathetic nerve supply.

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The conjugation of benzoic acid in rabbits.

WENDELL H. GRIFFITH.

[*From the Department of Biological Chemistry, St. Louis University School of Medicine, St. Louis, Mo.*]

A study has been made of the excretion of free benzoic acid, hippuric acid, and total combined benzoic acid in the urine of normal adult rabbits following the administration of sodium benzoate. The maximum rate of synthesis of hippuric acid occurred after the ingestion of 0.5 gm. of benzoic acid per kilo. Larger doses of benzoic acid increased the rate of excretion of combined benzoic acid but not that of hippuric acid. In the 24 hour period following the administration of 1.0 gm. of benzoic acid per kilo, the average excretion of hippuric acid in six rabbits was 82 per cent of the combined benzoic acid, the individual variations ranging from 65 to 90 per cent. These urines contained an ether-soluble, non-fermentable reducing substance which gave a positive naphtho-resorcin test. Therefore, it was concluded that 10 to 35 per cent of the combined benzoic acid excreted by the six rabbits was benzoyl glycuronic acid. It has

[2] Carlson, A. J., and Litt, S., *Arch. Int. Med.*, 1924, xxxiii, 281.