13547

Inhibition of Gastric and Cecal Peristalsis in Rabbit by $CO_2 + O_2$ Inhalations.

JOHN AUER AND HUGO KRUEGER.

From the Department of Pharmacology, St. Louis University School of Medicine, St. Louis, Mo.

The effect of carbon dioxide gas upon the motility of the gastro-intestinal canal has been studied chiefly on excised sections of the gut[1-4] or by the ingestion of water saturated with CO_2 or by the intragastric injection of the gas itself.[5] As far as we know the effect of $CO_2 + O_2$ inhalations upon gastric and cecal motility induced by the intragastric injection of air or by the subcutaneous injection of pilocarpine or physostigmine has not been reported. Furthermore, it may be emphasized that the results to be reported were obtained without opening the peritoneal cavity or the use of balloons but simply by inspection of the intact abdomen.

The method is a slight modification of one described sometime ago:[6] preliminary narcotization to reduce or abolish the inhibitory effects of external stimuli; to accomplish this 150 mg sodium barbital per kilo were injected subcutaneously about 30 minutes before the test; after cutting the abdominal hair, which is readily done with a blunt-pointed scissors curved on the flat, both the cecum and most of the stomach including the preantrum may be easily observed through the intact abdominal wall; the antrum itself is not visible, but its contraction is readily indicated by a bulging of the preantrum. If the stomach was not well-filled, 60-120 cc air were injected into this viscus through a hypodermic needle plunged through the abdominal wall. The gas mixtures were 50% each CO_2 and O_2 delivered from tanks at a rate of 150-300 cc per minute each; this gas mixture was administered to the rabbit through a funnel held at such a distance over the nose or the tracheal tube that the respirations were definitely deepened. All observations were 5 minutes long: before, during and after the gas administration. Gastric and cecal peristalsis was stimulated by the subcutaneous injection of physostigmine sulfate

1 Rona, P., and Neukirch, P., *Pflüger's Arch.*, 1912, **146**, 371.

2 Hooker, D. R., *Am. J. Physiol.*, 1912-13, **31**, 47.

3 Mansfeld, G., *Pflüger's Arch.*, 1921, **188**, 241.

4 Guggenheim, M., and Löffler, W., *Biochem. Z.*, 1916, **72**, 322.

5 Carlson, A. J., *Am. J. Physiol.*, 1913, **32**, 389.

6 Auer, J., PROC. SOC. EXP. BIOL. AND MED., 1906, **4**, 8.

or pilocarpine hydrochloride in doses of 0.5-1 mg per kilo; occasionally this dose was repeated after 30 minutes.

A few experiments were made on barbitalized, intact rabbits to see whether mere distension of the stomach with air would suffice to bring about good basal peristaltic activity of both stomach and cecum. In 3 rabbits, gastric peristalsis was developed and this was definitely reduced by $CO_2 + O_2$; cecal peristalsis, however, was absent in 2 and only moderate in the remaining rabbit; in this last rabbit, $CO_2 + O_2$ produced a definite decrease. Mere distension of the stomach with air, therefore, did not suffice for our purposes.

Interference with respiration in the normal rabbit by increased salivation after pilocarpine was largely if not entirely abolished by gauze drainage wicks placed in each angle of the mouth and by elevating the foot of the operating board to 35° to facilitate drainage; in the operated animals, a tracheotomy tube prevented this interference. To rule out effects from the central nervous system, the vagi were cut in the neck after tracheotomy, the spinal cord transected at the 4th to the 7th thoracic level, and then the peripheral section of the cord was pithed; the site of transection and the extent of pithing was always verified by autopsy. For all spinal cord operations the barbitalized rabbits were fully anesthetized with ether; after pithing, the ether was stopped and the animal allowed to recover. Biopsies were made on all operated animals and the lungs were found to collapse practically normally on opening the chest and excising them. In numbers of these animals the abdomen was opened at the end of an experiment and the visible effects of $CO_2 + O_2$ inhalations observed: the small arteries of the gut remained bright red and the veins and venules were only slightly darkened. The rabbits weighed from 1500 to 3000 g; both males and females were used, but no female was pregnant; some rabbits were used twice, once without operative interference and then, 5-10 days later, for pithing of the cord; 27 experiments were carried out.

Results. In normal, non-operated rabbits the subcutaneous injection of physostigmine or pilocarpine generally caused good gastric and cecal peristalsis and the inhalation of $CO_2 + O_2$ definitely reduced this peristalsis in strength and rate, though at times only the strength of the waves was reduced, the rate remaining practically unaltered; for example in the stomach, under the influence of CO_2, the visible waves started at the middle line of the abdomen and faded away at the preantrum, while before the CO_2 they started 1 to 2 cm to the left of the middle line, were deeper and progressed through the preantrum.

In the non-operated physostigmine series, 4 out of 7 rabbits showed a definite reduction in *gastric* peristalsis during $CO_2 + O_2$ inhalation; 2 showed no definite peristalsis of the stomach at any time during the experiment; and in one the gas mixture exerted no appreciable effect upon the rate and strength of the gastric waves. All the *ceca* of this series exhibited a definite decrease in the rate and strength of peristaltic and antiperistaltic waves during the gas inhalation.

In the non-operated pilocarpine series of 6 rabbits, comparable effects to those described for physostigmine were obtained. In this series also, one stomach with active peristalsis was refractory to the action of $CO_2 + O_2$.

In the operated physostigmine series (vagotomy, spinal transection and pithing) a striking difference became observable: 5 out of 6 rabbits developed no *gastric* peristalsis at all, while in the 6th rabbit good gastric waves were present but remained practically unaffected by $CO_2 + O_2$ inhalations; *cecal* peristalsis, however, was good and the gas mixture definitely decreased its rate and strength in 5 out of the 6 rabbits.

In the operated pilocarpine series a similar effect to that described above was obtained: 3 out of 5 rabbits showed no visible *gastric* peristalsis throughout the entire experiment, the remaining 2, however, showed good gastric peristalsis that was definitely decreased by $CO_2 + O_2$ inhalation. All rabbits of this series also showed *cecal* peristalsis and this was decreased by $CO_2 + O_2$. In both of these series the stomach had been distended with air about 10 minutes after pithing.

Summary and Conclusion. In the normal rabbit, gastric and cecal peristalsis caused by the subcutaneous injection of physostigmine or pilocarpine (0.5 to 1 mg per kg) is definitely reduced by the inhalation of non-asphyctic doses of $CO_2 + O_2$ gas (50% each).

When the stomach and cecum are deprived of their central innervation by double vagotomy, spinal transection and pithing, both physostigmine and pilocarpine in normally effective doses, become largely ineffective in provoking *gastric* peristalsis; *cecal* peristalsis, however, persists with both drugs in these operated animals and this cecal activity is reduced by $CO_2 + O_2$ inhalation.

As far as the *cecum* is concerned, the experimental findings indicate clearly that $CO_2 + O_2$ inhalations exert a *peripheral,* inhibitory action upon cecal peristalsis produced by the subcutaneous injection of physostigmine or pilocarpine in the pithed rabbit, for cecal peristalsis developed in the pithed rabbits after the injection of the drugs and this cecal peristalsis was definitely reduced by the gas inhalation.

Furthermore, it may be concluded that vascular shock in these pithed animals did not prevent the occurrence of cecal peristalsis after physostigmine and pilocarpine nor did shock prevent the inhibitory action of $CO_2 + O_2$ inhalations upon this cecal peristalsis.

With regard to the *stomach*, however, the experimental data do not permit a similar conclusion, for normally effective doses of the drugs generally caused little or no apparent gastric peristalsis in the pithed animals, thus preventing a study of the inhibitory action of the gas mixture. This difference between the cecum and stomach might possibly be caused by a difference in sensitivity to the drugs employed, the cecum responding to smaller doses of the drugs than the stomach, for the drugs were always injected after pithing when the blood pressure was low and the speed of circulation probably decreased. In addition, this low blood pressure itself might be assumed to be a factor in preventing or reducing *gastric* peristalsis, though low blood pressure is definitely not an important factor in *cecal* peristalsis under the experimental conditions described.

It may perhaps be suggested that inhalations of $CO_2 + O_2$ mixtures might be of some value in the human subject under conditions of gastric and perhaps colonic unrest.

13548

Effect of Stimulation of Autonomic Nerves on Intrahepatic Circulation of Blood in Intact Animal.*

KHALIL G. WAKIM. (Introduced by F. C. Mann.)

From the Mayo Foundation, Rochester, Minn.

The influence of the sympathetic and parasympathetic nerves on the intrahepatic vascular system has been deduced mainly from indirect evidence based on data obtained from plethysmographic changes in volume of the liver and from changes in hepatic inflow or outflow, as well as from variations in portal pressure during stimulation of the nerves. The object of this study was to observe directly, by transillumination of the intact liver in the anesthetized animal the effect of stimulation of the sympathetic and parasympathetic nerves on the intrahepatic vessels and to determine whether or not the

* Abridgment of part of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Ph.D. in Physiology.