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.

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

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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

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intrahepatic vascular system possesses an active vasoconstrictor or an active vasodilator mechanism or both.

The literature on the subject discloses a number of different views held by investigators who employed various methods for determining the effect of stimulation of the autonomic nerves on the vascular ramifications within the liver. Bayliss and Starling[1] obtained a rise in portal pressure by electric stimulation of the splanchnic nerves. Cavazzani and Manca[2] produced constriction of the portal radicles by asphyxia after sectioning the vagus nerves, but not after sectioning the splanchnic nerves. They stated that the vagus nerves cause direct and not reflex dilation of the portal radicles within the liver. In another publication they reported that the intrahepatic branches of the hepatic artery constrict during vagal stimulation and dilate during stimulation of the celiac plexus. François-Franck and Hallion[3] obtained a decrease of hepatic volume and a rise of portal pressure in the dog when the splanchnic nerves were stimulated. The same results were obtained after ligation of the hepatic artery. Thompson[4] reported immediate decrease of hepatic volume during stimulation of the splanchnic nerves. Schmid[5] obtained a decrease of inflow through the portal vein and a rise of portal pressure by stimulation of either the splanchnic nerves or the hepatic plexus. Burton-Opitz[6] produced total cessation of inflow of blood through the hepatic artery by tetanic stimulation of the whole hepatic plexus. In another publication he concluded that stimulation of the distal end of the hepatic plexus during perfusion as well as in the normal portal circulation proved that the portal radicles have vasomotor fibres from the hepatic plexus. Neubauer[7] recorded an increase of hepatic volume during stimulation of the central end of the vagus and also during stimulation of the central end of the splanchnic nerves. Stimulation of the peripheral end of the vagus caused a decrease of hepatic volume which was attributed to constriction of the intrahepatic vessels. Macleod and Pearce[8] expressed the opinion that stimulation of the hepatic plexus causes a greater constriction of

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[5] Schmid, Julius, *Arch. f. d. ges. Physiol.*, 1909, **126**, 165.

[6] Burton-Opitz, Russell, *Quart. J. Exp. Physiol.*, 1911, **4**, 103; 1914, **7**, 57.

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[8] Macleod, J. J. R., and Pearce, R. G., *Am. J. Physiol.*, 1914, **35**, 87.

the branches of the hepatic artery than of those of the portal vein. Edmunds[9] explained the increase of hepatic volume during splanchnic stimulation as due to the constriction of the muscle fibers around the sublobular veins. He also stated that vasomotor nerves are present on the portal branches in the liver. Carnot, Gayet and Merklen[10] obtained a rise of portal pressure during stimulation of the peripheral end of the vagus or of the splanchnic nerves. This rise was attributed to constriction of the hepatic vessels. Griffith and Emery[11] obtained a decrease of hepatic volume during stimulation of the preganglionic or postganglionic nerve fibers which supply the liver. Since stimulation of the peripheral end of the vagus did not cause any change of hepatic volume, they concluded that the vagus nerves do not carry vasomotor fibers to the liver. Bauer, Dale, Poulsson and Richards[12] produced a decrease of hepatic volume, increase of outflow, increase of portal flow and arteriolar constriction within the liver by stimulation of the hepatic plexus or of the right or left splanchnic nerves, while stimulation of the vagus did not give any perceptible change. Eckardt[13] concluded that during splanchnic stimulation an outpouring of blood from the liver takes place and that the amount of blood leaving the liver is greater than that entering it. McMichael[14] stated that there was no evidence indicating parasympathetic dilator action on the portal or hepatic venules.

Methods. A modification of the quartz-rod transillumination technic as described by Knisely[15] was employed in this study on anesthetized frogs, and albino rats. The frogs were studied at room temperature, but the rats were kept at body temperature during observation by the use of a constant temperature platform. The hepatic plexus was dissected out carefully and, with the vessels of the porta hepatis, was placed in the trough of specially made shielded electrodes, and stimulated by tetanizing current when desired. In the rat, the vagi were separated from the esophagus at its exit from

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10 Carnot, Paul, Gayet, René, and Merklen, F. P., *Compt. rend. Soc. de biol.*, 1930, **104**, 1260.

11 Griffith, F. R., Jr., and Emery, F. E., *Am. J. Physiol.*, 1930, **95**, 20; Emery, F. E., and Griffith, F. R., Jr., *J. Pharm. and Exp. Therap.*, 1931, **42**, 233.

12 Bauer, W., Dale, H. H., Poulsson, L. T., and Richards, D. W., *J. Physiol.*, 1932, **74**, 343.

13 Eckardt, P., *Arch. f. d. ges. Physiol.*, 1935, **236**, 361.

14 McMichael, John, *Quart. J. Exp. Physiol.*, 1937, **27**, 73.

15 Knisely, M. H., *Anat. Rec.*, 1936, **64**, 499; 1938, **71**, 503.

the esophageal hiatus in the diaphragm and were ligated tightly and placed in the trough of the electrodes distad to the ligature.

Results. Observations on the Amphibian Liver. Stimulation of hepatic plexus. Stimulation of the nerve plexuses in the porta hepatis and around the hepatic artery by weak or strong tetanizing current caused constriction of the active sinusoids, some of which contracted. For instance, fourteen active sinusoids were counted in a region immediately before stimulation. During stimulation only six of the fourteen sinusoids remained patent but these were constricted to such an extent that the corpuscles were compressed into single file as they coursed through the narrow lumen. The other 8 sinusoids contracted to disappearance during stimulation. The constriction of the sinusoids appeared within two seconds after the beginning of stimulation and lasted for 4 to 5 seconds after discontinuance of the stimulation. On several occasions when an arteriovenous anastomosis was present in the field under observation, the anastomosis disappeared during stimulation and continuity between the two vessels no longer could be seen.

Effect of Pithing. Pithing the animal, or any severe damage to the central nervous system, led to a marked reduction in the number of active sinusoids. In fact, immediately after pithing, inactivity in the lobules becomes so extensive that one would be inclined to believe the animal is dead were it not for the continuous activity of a regularly beating heart. This inactivity may result in either a constrictor effect, leading to very narrow sinusoids containing hardly any corpuscles, or more commonly in stasis with the sinusoids packed full of corpuscles lying motionless in their lumina. However, after about 15 minutes, the circulation begins to recover in the inactive lobules and one gradually can observe the same type of rhythmic activity alternating asynchronously in the various lobules. Many more inactive sinusoids packed full of erythrocytes are seen in the liver of a pithed frog than in an intact anesthetized one.

Observations on the Mammalian Liver. Stimulation of hepatic plexus. Stimulation of the plexus of nerves in the porta hepatis and around the hepatic artery by tetanizing current produced moderate blanching of the region under observation and constriction of the sinusoids. When weak current was used, it took more than 5 seconds of latency before the sinusoids contracted and blanching was observed. After cessation of the stimulus, more than 10 seconds passed before the sinusoids resumed activity. In some lobules several sinusoids that were very active prior to strong stimulation contracted to disappearance and remained so for several seconds after