

THE REGULATION OF THE FLOW OF BILE

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The physiology of the gall bladder and the so-called resistance of the sphincter of Oddi have attracted considerable attention largely from a surgical point of view. Because of the pathology often encountered in the gall bladder and ducts, surgeons have been forced to make decisions regarding the functional significance of these structures and perhaps necessarily to draw conclusions with respect to the mechanism involved in the flow of bile into the intestine. The most recent reviews of the literature are those by Mann (1924a) and Chiray and Pavel (1925). I shall only mention here a few papers that embody the more or less common findings.

The anatomy of the biliary tract has been studied by Oddi, Hendrickson, Mann, and Auster and Crohn. Oddi (1887) found in the dog near the mouth of the duct a muscular ring which after separation from the fibers that join the intestinal musculature could be considered as an independent sphincter. Hendrickson (1898) found some muscle fibers running around the end of the duct but for the most part the fibers along the duct were continuous with the intestinal musculature. Mann (1920), who studied several species of animals, was able to make out a definite arrangement of muscle fibers which might function as a sphincter. Auster and Crohn (1922) did not see a muscular bundle formation that might be called a sphincter. Microscopic observations upon preparations made from dogs and man indicated that the muscle fibers at the mouth of the common duct were "scanty, widely separated and diffuse and at no time continuous." They gained the impression that the muscular apparatus of the papilla is made up of a fusion of the fibers of the intestinal musculature with the corresponding layer of the duct.

Oddi (1888) found this sphincter offered a resistance of 50 mm. Hg to fluids entering the lumen of the intestine. A resistance has been estimated and attributed to the sphincter by many observers since Oddi's work. Archibald (1919) reported similar findings. Mann (1919) recorded a minimal resistance in six species of animals possessing a gall bladder of 75 to 100 mm. water. Jacobsen and Gydesen (1922) found a resistance in dogs of 90 to 210 mm. water. Cole (1925) encountered 40 to 100 mm. water resistance in dogs.

These findings vary widely and would seem to attribute to the sphincter a physiological significance out of proportion to the anatomical structure described. The presence of an uncontrolled factor is indicated. An attempt has been made, therefore, to re-study this resistance under conditions where the tonus of the intestine might be observed and considered in interpreting the results.

In the dog and for that matter in most animals including man the duct passes through the intestine in a most oblique manner. The mouth of the duct in dogs lies 1 to 1½ inches below where it makes initial entrance into the wall of the intestine. As a physical arrangement this would constitute an efficient sphincter-like mechanism depending upon the tonicity of the intestine. The duct within the intestinal wall is subject to collapse and consequently would offer a resistance to the passage of fluid in proportion to the state of tonicity of the intestinal musculature.

Dogs under ether anesthesia were used for all experiments. An attempt

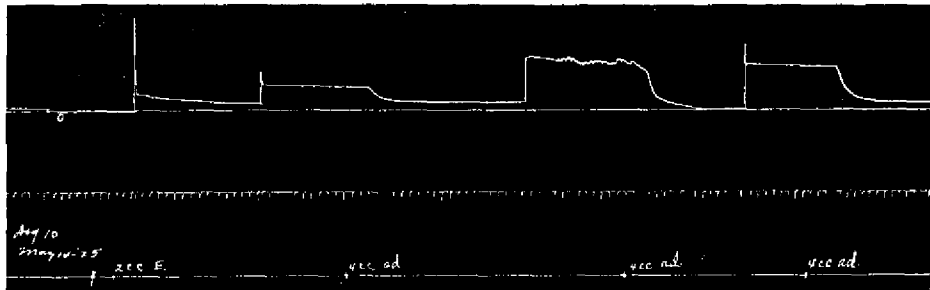


Fig. 1. Effect of adrenalin upon pressure in the common bile duct. The tonus of the intestine was increased by giving 2 cc. of 0.1 per cent eserin intravenously.

was made to insert a slender balloon through a slit in the duct into that part of the duct within the intestinal wall so that when filled with water and properly connected with a manometer the tonicity of the duct including the sphincter might be recorded. Practically, this did not work well because it was necessary to use too small a balloon. The usual technic was then utilized of placing a cannula in the duct a little distance from the intestine and pointed toward the lumen of the duct. The animal was kept under light anesthesia and the intestine well protected. The tonicity of the intestine could be observed at any time with the least amount of exposure. The cannula was connected with a manometer and pressure bottle containing water. The pressure withstood or held by the duct in a series of twenty dogs varied from 2 to 12 mm. Hg, depending upon the general condition of the animal and the degree of anesthesia.

McWhorter (1921) found that adrenalin increased the tension of the sphincter slightly. Schafer (1924) states that adrenalin causes constriction

of the bile ducts. This is in accord with Meltzer's (1917) law of contrary innervation of the gall bladder and sphincter. Figure 1 shows the typical effect of adrenalin upon duct pressure. The tonicity of the intestine has been increased by physostigmine. Adrenalin caused temporary relaxation of the intestine and the duct pressure fell to almost zero.

Atropin was used in some experiments and the atony of the intestine produced by it was effective in reducing the duct pressure as may be seen in figure 2. The recovery was less certain and consequently it did not



Fig. 2. Effect of atropin upon pressure in the common duct.

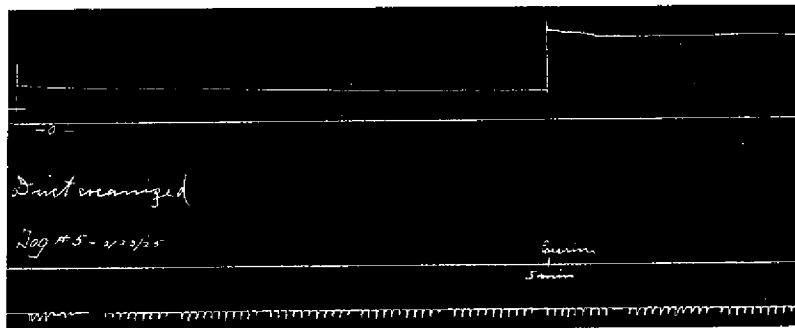


Fig. 3. After cocainizing the duct and sphincter of Oddi a resistance of 8 mm. Hg was obtained. Following the intravenous injection of eserine the resistance was greatly increased.

lend itself well when repeated trials were desired on one animal. Cole (1925) says that intravenous injections of atropin, pilocarpine and physostigmine have no effects on this resistance. His observations were made with the duodenum laid open which perhaps accounts for his results. Haberland (1924) who has recently made an extensive study of the function of the gall bladder says that atropin dilates the sphincter. However, he states that he believes that the importance of the sphincter has been over-emphasized. In the dog he thinks its action dependent upon the movements of the duodenum.

In attempting to further eliminate the possibility of a sphincter action the duct was cocainized. Cotton was twisted about a small wire and saturated with a 4 per cent cocaine solution. This was inserted into the duct far enough that the end entered the lumen of the intestine. A second application was made and ample time allowed for the drug to become effective. The cannula was then inserted and resistance measured. Figure 3, for example, shows 8 mm. Hg pressure withstood. Following an intravenous injection of physostigmine the resistance was increased as in previous experiments where the duct was not cocainized.

Increased tonus of the duodenum brought about by mechanical irritation increases the amount of pressure that may be held by the duct. Some observers (Cole, 1925) have reported that mechanical irritation of the papilla causes a spasm visible to the naked eye. I have observed a swelling of the papilla when similarly tested but feel that it may be accounted for in part at least by contraction of the muscle fibers of the intestinal wall.

In discussing an hypothesis of the function of the gall bladder, Mann (1924b) states that the acid chyme causes a relaxation of the sphincter of Oddi and allows a flow of bile. The only observations made in this connection were upon the effect of a 0.4 per cent solution of HCl introduced into the duodenum above the entrance of the common duct. In most instances there followed a series of peristaltic waves in the duodenum. These reduced the pressure in the duct by a milking action. It seems probable that this would be an important factor in the flow of bile in digestion.

DISCUSSION. The fact that strong inhibition brought about by adrenalin and that brought about by paralysis of the parasympathetic by atropin result equally well in lowering the resistance in the duct would indicate that if there is a reciprocal activity between the gall bladder and the sphincter such a mechanism probably does not play a major rôle in the regulation of bile flow.

All investigators agree that while $MgSO_4$ paralyzes the sphincter it also causes relaxation of the intestinal musculature.

Archibald (1919) seldom found a sphincter in dogs that was overcome by less than 600 mm. water. Thinking a tonic sphincter might cause bile to be forced back into the pancreatic duct and cause pancreatitis, he "abolished" the sphincter in dogs and found the resistance reduced to 70 mm. water or less for as long as eight weeks after the operation. McWhorter (1921) attempted to bring about the same end by dilating the sphincter. He says the sphincter was paralyzed by a quite severe dilatation (a small hemostat was used). The resistance was reduced from 180 to 200 mm. water to 25 to 50 mm. water. Of course in such experiments severe damage must have been done to the duodenum and the duct within

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its walls. The extent of injury and the time element would be important factors to be considered in determining the cause of the reduced resistance.

Judd and Mann (1917), in a paper on the effect of cholecystectomy, say that following the removal of the gall bladder in the dog or cat the ducts dilated within 60 days. They cite a typical experiment (expt. 469) whereby 113 days after removal of the gall bladder in a dog the common bile duct increased in diameter from 6 mm. to 1 cm. but after entering the intestinal wall the diameter was still 6 mm. They set about to study the mechanism that produced dilatation of the ducts after cholecystectomy. The part played by the sphincter was investigated by three methods: 1, by comparing the pressure withstood by the sphincter in animals before and following the removal of the gall bladder; 2, at the time of removal of the gall bladder, by dissecting the duct free from the muscle fibers of the duodenal wall; 3, by sectioning the mucosal opening and a portion of the sphincter through a duodenal incision. Regarding the first point, they always found the residual pressure after removal of the gall bladder much lower than in normal animals. No explanation is offered. Further study may throw light upon this point. Concerning the second point they say, "In those animals in which the muscle fibers were dissected free from the intramural portion of the duct at the time the gall bladder was removed, dilatation of the duct did not occur except when there was mechanical obstruction due to adhesions." This would point strongly toward the seat of the resistance lying in that portion of the duct within the duodenal wall. Judd and Mann did not see this interpretation, as we shall see later.

"Section of the mucosal opening and a portion of the sphincter through a duodenal incision after the removal of the gall bladder has given variable results in regard to the effect on the duct and positive conclusions cannot be drawn. However, in one perfect experiment the same dilatation occurred as in animals in which the gall bladder had been removed." This would again indicate the insignificance of the sphincter. They give these findings a different interpretation. In summarizing they say in part, "After the removal of the gall bladder all the ducts outside the liver dilate. The sphincter at the entrance of the common bile duct into the duodenum is the chief factor in producing this dilatation." Certainly such a conclusion is not justifiable by the experimental data presented. For the most part the results support the theory that the seat of resistance is in that portion of the duct within the wall of the duodenum.

No great tonicity of the duodenum is necessary to close the small lumen of the duct. The normal tonus is no doubt sufficient to prevent a continuous flow when the gall bladder is present. When the pressure is high enough to overcome this resistance the bile flows into the intestine. The increased mechanical pressure upon the filled gall bladder brought about

by inspiration may easily be conceived to cause bile to spurt into the intestine irrespective of considerable tonus in the duodenum. Coupled with this is the peristalsis of the duodenum in digestion that invariably causes a flow when there is a moderate pressure in the duct. This is brought about partly by a milking action on the duct and probably partly by aspiration due to reduced pressure in the duodenum following the peristaltic wave. Rost (1923) states that in cholecystectomized dogs there is a continuous flow of bile. In observing the flow in normal dogs under ether through an opening in the duodenum he observed spurts of bile absolutely synchronous with inspiration.

In emphasizing the importance of the tonicity of the intestine and intestinal peristalsis in the regulation of bile flow it is not intended to leave the impression that the author feels that the theory is entirely proven. Further evidence is necessary. It may be that the contractions of the gall bladder and the activity of the sphincter play a part. A reciprocal physiological action between the gall bladder and the sphincter has not been satisfactorily demonstrated. This study indicates that such action may not take place and suggests that intra-abdominal pressure, respiration, and tonus and peristalsis of the duodenum are the most important factors in regulating the flow of bile.

CONCLUSIONS

1. The normal tonus exhibited by the duodenum offers resistance to pressure in the common bile duct.
2. Drugs that affect the tonus of the intestinal musculature affect this resistance. Pilocarpine and physostigmine greatly increase the amount of pressure withstood in the duct while adrenalin and atropin reduce it to a minimum.
3. Peristalsis of the duodenum is an important factor in emptying the duct.
4. The function of the sphincter of Oddi has been over-emphasized and not enough attention has been given to the tonicity of the intestine in attempting to measure the resistance of this sphincter.
5. This study favors the hypothesis that bile flow is regulated by intra-abdominal pressure and tonicity and peristalsis of the duodenum rather than being dependent upon a reciprocal activity between the gall bladder and the sphincter of Oddi.

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