THE FILLING AND EMPTYING OF THE GALL BLADDER.

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PLATE 3.

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The discovery of a means of visualizing the gall bladder by the Roentgen ray after intravenous injection of certain halogen derivatives of phenolphthalein by Graham and Cole (1) has given a new means of studying the physiology of the biliary tract. This article belongs to a series of experimental and clinical reports (2) relating to that subject and will be particularly concerned with the filling and the emptying of the gall bladder. The experimental work has been done by both cholecystography and other laboratory methods.

A resistance to the outflow of bile from the common duct was found by cholecystography to be necessary for the collection of bile by the gall bladder (3). This resistance to the outflow of bile from the common duct into the duodenum was later found to be largely due to tonus and movements of the duodenum (4). As a result of this regulatory mechanism at the distal end of the common duct there are considerable changes of pressure in the gall bladder and the rest of the biliary tract which not only aid in the filling of the gall bladder but are a factor in its emptying. In this article we shall refer to this mechanism for the regulation of the flow of bile at the distal end of the common duct as the common duct sphincter.

The pressure changes that are reflected over the rest of the biliary tract by the opening and closing of the common duct sphincter have been demonstrated in the etherized dog in the following way.

A cannula which was inserted into the middle hepatic duct was connected with a supply of physiological saline solution for making pressure in the system. The continuous flow of bile in the hepatic ducts from the liver of man and dogs is under secretory pressure. A tambour connected by a T-tube with the cannula was used to record changes of pressure in the hepatic duct on a smoked drum. Records of changes of pressure were also made by tambours connected with the gall bladder and with the common duct. Lateral hepatic ducts were ligated. When the common duct is closed, as if by the action of a sphincter, the pressure in the duct quickly rises. After a short delay, the pressure in the gall bladder rises. The pressure in the hepatic duct rises simultaneously with that in the gall bladder. If the common duct is opened, there is an immediate fall of pressure in it which is followed shortly and consecutively by a fall of pressure in the gall bladder and hepatic duct. We have recorded a drop of pressure in the gall bladder occurring at the same time with the relaxation phase of a peristaltic movement in the duodenum. This experiment was performed by ligating the hepatic ducts and simultaneously recording the pressure in the gall bladder and peristalsis in the duodenum.

These changes of pressure in the biliary tract are exactly similar to the changes of pressure that have been demonstrated by one of us (5) in a model designed to show the changes of pressure which normally take place in the biliary tract.

The control of the contents of the gall bladder by the common duct sphincter is further demonstrated by cholecystography.

The stomach or duodenum of man or animal must be free from food in order to secure a cholecystogram after administration of sodium tetraiodophenolphthalein. If digestion is in progress, bile is permitted to enter the duodenum too freely by the common duct sphincter; and the iodine in the bile will not enter the gall bladder to produce a shadow. Likewise, a cholecystogram is not obtained if the common duct sphincter of the dog is kept open by the insertion of a cannula into the distal end of the common duct. The bile laden with the halogen passes directly through the hepatic and common duct to the duodenum. A cholecystogram may be obtained, however, after the ligation of the hepatic duct of a middle lobe of the liver of a dog. The bile from the other lobes, containing the iodine, enters the common duct from the lateral hepatic ducts, which, in the dog, enter the common duct distal to the cystic duct, and is dammed back into the gall bladder by the closure of the common duct sphincter.

A factor in the prevention of the overdistension of the gall bladder by continuous accessions of bile is the S-shaped portion of the neck of the ampulla and cystic duct. Attention has been called to this fact by Jacobson and Gydesen (6). When there is considerable pressure in the fundus of the gall bladder, the S-shaped portion kinks upon itself and tends to prevent the exit or the entrance of more bile. The valves of Heister in the cystic duct do not normally seem to offer much resistance to the entrance or exit of bile. They are doubtless more efficient as a control when the kink of the cystic duct is present. The ampulla and cystic duct are of great clinical importance.

4 or 5 hours after the intravenous injection of sodium tetraiodophenolphthalein, sufficient iodine will enter the normal gall bladder of a fasting man or dog to cast a shadow on a film by the Roentgen ray. The shadow in 4 or 5 hours becomes smaller and is densest between 16 and 24 hours after injection. The shadow tends to come to a minimum size and gradually fades away by the end of 30 to 40 hours.

We found when investigating the appearance and disappearance of the shadow of the gall bladder that the halogen in the bile is concentrated two to four times by the gall bladder (3). This fact confirmed the work of Rous and McMaster (7) who demonstrated the concentration of bile pigment by the absorptive power of the gall bladder. It was further found that the greater part of the contents of the gall bladder leaves its lumen by way of the cystic duct (3). This latter fact has also been demonstrated by Whitaker (8). However, this conclusion is in contradistinction to the opinions of Sweet (9), Halpert (10), and Demel and Brummelkamp (11), who believe that whatever enters the gall bladder through the cystic duct does not normally pass out of it by way of the cystic duct.

Factors of dilution seem of great importance in the appearance and disappearance of the shadow of the gall bladder. If all of the hepatic ducts are ligated, leaving the common duct intact, after a dense shadow of the gall bladder has been secured from tetraiodophenolphthalein, the shadow will be found to persist for many days even while food is being taken. It is inferred from this experiment that dilution of the bile in the gall bladder by bile entering from the hepatic ducts is an important factor in the filling and emptying of the gall bladder. Ordinarily, during a cholecystographic examination, the course of events is somewhat as follows:

The tetraiodophenolphthalein is excreted in the bile shortly after injection. The sphincter of the common duct diverts a considerable portion of the bile into the gall bladder. The amount of bile secreted is probably not large, comparatively, since the animal is fasting. The addition of iodine to the bile in the gall bladder proceeds. The gall bladder becomes distended. At this time we may obtain our first shadow of the gall bladder. It is a large and faintly visible one.

The amount of iodine in the gall bladder increases by new additions of bile as the concentrating activity of the gall bladder proceeds simultaneously. The iodine content becomes great enough to cast the densest shadow in 16 to 20 hours after injection of the dye. During this same period, the iodine has probably been entirely excreted by the liver. Since iodine is no longer present in the bile coming from the liver, the shadow gradually disappears as dilution of the iodine in the gall bladder progresses. In the meantime, food has been given to the patient and the disappearance of the shadow is hastened by an increased secretion of bile and a relaxed common duct sphincter. The backing up of dilute bile from the liver into the gall bladder mechanically aids in the expulsion of the concentrated bile from the gall bladder.

Changes of density of the cycle of the shadows of a gall bladder that normally occur after administration of tetraiodophenolphthalein may be duplicated outside of the body by the use of a rubber bag containing sodium iodide. A small thin rubber bag approximately the size of a gall bladder is attached to the arm of a T-tube. The changes in the shadows of a gall bladder can be duplicated by varying the size of the bag and by the dilution of its content of sodium iodide.

It was suggested by the preceding experiments of ligating the hepatic ducts and by other facts that the gall bladder is never entirely empty. Such was found to be true. The shadow of the gall bladder of a dog will always be present if he is given a daily dose of tetraiodophenolphthalein and films made at intervals. It persists even though he is fed regularly and allowed normal freedom of action. The shadows vary in size but tend to reach a minimum size.

The finding that the gall bladder is never empty is consistent with pressure changes in the biliary tract. The pressure in the gall bladder tends to come to an equilibrium with the rest of the system though it is not necessarily the same. Bile will pass out from a distended gall bladder if the common duct sphincter is open. Also, if the sphincter is open, bile coming from the hepatic ducts may assist in the emptying of the gall bladder both by dilution and by tending to produce a negative pressure in the gall bladder in its passage down the ducts through the open sphincter into the duodenum, in a manner similar to the action of the filter pump. When its content is at a minimum pressure the gall bladder will not discharge bile even though it is not entirely empty.

The fact that the gall bladder is never entirely empty coincides with the well known clinical fact that the gall bladder is never found empty on abdominal exploration. The physiological importance of this fact may be explained by the suggestion of Boyden (12) that the capillary network of the rugæ of the gall bladder of the cat is greater in collapse than when pressed out by distension. He believes that the most rapid absorption takes place when the gall bladder is partially collapsed. It is during partial collapse of the gall bladder that the density of the shadow of a cholecystogram is maximum. The gall bladder is in this state of partial collapse for the longest period of time during its visibility by Roentgen ray.

We have noted that the shadow of the normal gall bladder varies in size, denoting that other factors than dilution or interchange of bile may play a part in the slow emptying of the gall bladder. The importance of changes of intraabdominal pressures, especially due to respiration, has been lately stressed by Winkelstein (13). The effect of respiration on the intravesical pressure may be demonstrated by placing a manometer in the gall bladder and closing the abdominal wall about it as was done in the anesthetized dog. There may be a variation as high as 60 mm. of bile during respiration, vomiting, and other changes of intraabdominal pressure. The changes of pressure in the ducts with respiration are not so large as those in the gall bladder. Bile in some instances may be seen to be expelled from the duodenal papilla with forced respiration. Furthermore, the shadow of a gall bladder in a dog may be decreased in size by deep palpation of the abdominal wall over the region of the gall bladder.

We believe with Boyden (12) that, as regards emptying, the gall bladder is largely a passive organ, except for the elasticity of its walls. It is influenced by pressure changes which we have described. The anatomy of the walls of the gall bladder are ideal for such an elastic or contractile mechanism. Its tonus varies in response to pressure changes. The smooth muscle fibers and connective tissue aid in preventing overdistension and prevent complete collapse of the walls. The distensible walls equalize extremes of pressure due to the variation of the rate of secretion of bile, to the variable state of contraction of the common duct sphincter, and to changes of intraabdominal pressure. The elasticity of the walls is also a mechanism for the expulsion of bile through the cystic duct. The maximal pressure which the wall of the gall bladder can exert is difficult to determine *in situ*. It is probably great enough to expel bile from a distended gall bladder when the common duct sphincter is relaxed. Though the gall bladder has an elastic or contractile mechanism which exerts pressure on its contents until it has reached a minimum pressure, we have not been able to demonstrate an actively contracting movement due to its intrinsic musculature. Direct fluoroscopic examinations of visualized gall bladders have uniformly failed to show any evidence of a peristaltic wave; and more important still, direct electrical stimulation of the wall of the gall bladder of an anesthetized dog has never resulted in a contraction wave, although a similar stimulation of the intestine induced violent peristaltic contractions. This agrees with a previous observation made by Boyden (12) and Whitaker. Rhythmic changes of pressure of the content of the gall bladder have been recorded by us by various means in the anesthetized dog. However, no curves have been obtained from the gall bladder that have not been duplicated by a rubber bag of like size placed in the upper part of the abdominal cavity of the etherized dog. The rhythmic changes which were recorded, corresponded to changes of intraabdominal pressure largely due to respiration.

The same experiment as the preceding one was conducted on dogs after operation under ether anesthesia.

A rubber tube was connected to a small rubber bag which was placed in the fundus of the gall bladder. A similar bag was placed alongside the viscera of the upper abdomen. The rubber tubes were brought out of the abdominal wall through different incisions. The dogs were allowed to recover from their operations. The bags were distended with air and simultaneous readings made of the changes of pressure after feeding, alteration of position of the dog, etc. The records from each bag corresponded essentially. This experiment confirms the finding in the preceding one that the so called rhythmic contractions were independent of peristaltic or other active muscular contractions of the wall of the gall bladder.

There has not been an indication of an actively effective contraction of the gall bladder, such as a peristaltic movement of the intestine or evacuation of the urinary bladder, in the thousands of cholecystograms that have been made by this department in man and animals. All of the changes in size and shape of the shadows are referable to an expansile organ. It is not necessary in any instance to explain the emptying of the gall bladder on the basis of an active muscular contraction of its wall.

Further proof of this rather passive reaction of the gall bladder is offered by the results obtained from an artificial gall bladder. A thin rubber bag the size of a gall bladder may be tied into a cystic duct of a dog by means of a short glass tube after cholecystectomy. If the animal is given a dose of sodium tetraiodophenolphthalein after the surgical operation, there will be a faint shadow of the artificial gall bladder visible in 4 hours. 16 hours later the shadow is larger and denser. The shadow may persist 6 or 8 days. The cycle of shadows produced by the artificial, rubber gall bladder is quite like that obtained from the normal gall bladder of the human, except that the shadows may not be so dense and that they usually persist over a longer period of time (Fig. 1, *a* and 1, *b*). The presence of the shadow seems to indicate that a forceful contraction due to a muscular action of the gall bladder wall is not necessary for the emptying or filling of the gall bladder. While the elastic or contractile mechanism present in the gall bladder is not necessary for its filling or emptying, it is probably the lack of this factor in the artificial gall bladder which delays its emptying. In this experiment, the increase in density of the shadow obviously cannot be due to concentration of the bile in the rubber bag but more probably must be due to a greater amount of iodine which has entered the bag through the cystic duct in its process of filling. In ordinary cholecystography the increase in density of the shadow which is observed is probably due in part to the factor of concentration by absorption of water. The shadow in the artificial gall bladder appears quite as promptly as in the normal gall bladder. The disappearance of the shadow must take place by washing out of the bile in the bag by fresh liver bile and by intraabdominal pressure. The pressure in the biliary tract is not sufficient to distend the rubber bag. Also, since the artificial gall bladder is not in apposition to the liver, changes in volume of that organ are not necessary for the filling or emptying of the gall bladder, although doubtlessly they are normally a factor. Changes of blood pressure in the normal gall bladder do not seem to be essential for its activity. This experiment, furthermore, casts considerable doubt on the contrary innervation of the gall bladder described by Meltzer (14). He has concluded that there is a coordinated action of relaxation of the sphincter of Oddi and contraction of the gall bladder. Lyon (15) has based the nonsurgical drainage of the gall tract upon this hypothesis.

CONCLUSIONS.

As a result of the control of the flow of bile into the duodenum largely by tonus and movements of the duodenum, bile intermittently enters the gall bladder where it is concentrated and undergoes other changes. The gall bladder empties itself of its content through the cystic duct (1) by the washing out of its contents by bile from the liver, (2) by the elasticity or contractile mechanism of its walls, and (3) by variations of intraabdominal pressure due to respiratory movements, contiguous organs, etc. A fourth manner of emptying of the gall bladder is by absorption of a portion of its content through its walls. The gall bladder is never entirely empty but tends to come to a state of partial collapse, when its contents are under minimum pressure. We have been unable to demonstrate rhythmic contractions of the gall bladder due to its musculature. If they are present they may aid but they are not essential for its emptying or filling. Experimentally, in the dog, a rubber bag which was substituted for the gall bladder functioned in a manner very similar to that of the normal gall bladder as shown by cholecystographic studies. The concentrating function, however, was absent.

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EXPLANATION OF PLATE 3.

FIG. 1, *a*. Arrows point to the shadow produced by an artificial, rubber gall bladder, 24 hours after intravenous injection of sodium tetraiodophenolphthalein. The small dense shadow within the shadow of the gall bladder is the glass tube which connected the bag with the cystic duct. The same tube shows in Fig. 1, *b*.

FIG. 1, *b*. Roentgenogram of the same dog 6 days later. The shadow of the artificial gall bladder has disappeared.

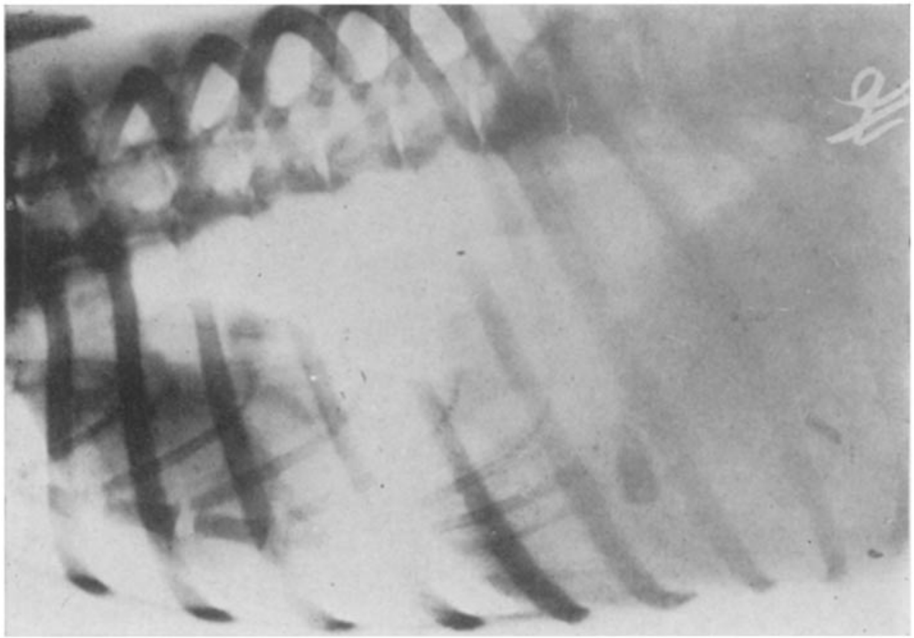

FIG. 1, *b*.

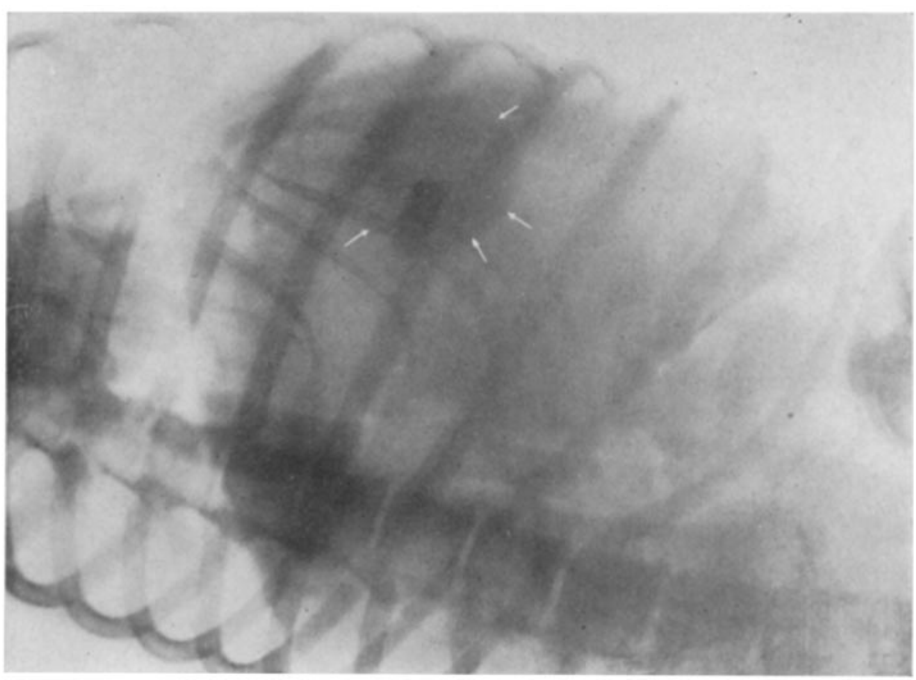

FIG. 1, *a*.

(Copher, Kodama, and Graham: Gall bladder.)