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SECRETION OF BILE IN RESPONSE TO RECTAL INSTILLATIONS*

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Various studies in connection with the physiology of the secretion of bile have clearly shown that bile is being secreted constantly. The passage of bile into the intestines, however, occurs at intervals; for the liver, unlike every other gland except the kidney, has in connection with it a reservoir, the gallbladder, in which the bile accumulates and from which it is only expelled periodically.

One must, therefore, clearly understand and distinguish the bile-secreting from the bile-expelling mechanism. Heretofore, investigators attempting to study these two phases of secretion and expulsion have limited themselves to the response obtained after oral administration of different foods and chemicals. With the aid of the dye method, which visualizes the gallbladder, one is able to demonstrate the rate of filling and emptying of this reservoir following the intake of various foods and drugs. It is difficult to tell, however, whether the flow of bile thus obtained is simply a result of the secretion from the liver alone or whether it is associated with the emptying of the gallbladder; naturally, both factors may play a rôle.

Of the direct influence of nerves either on the secretion of bile or its expulsion, we have little definite knowledge. It is true that the secretion of bile or its expulsion may be distinctly affected by the section and stimulation of nerves which control the blood supply to the stomach, intestines and spleen, for the quantity of blood passing through these organs and the rate of secretion are diminished when the blood supply is greatly lessened. In this way, stimulation of the medulla oblongata, the spinal cord or the splanchnic nerves stops or slows the secretion of the bile by constricting the abdominal vessels, and the same effect can be reflexly produced by the excitation of afferent nerves.

Just what effect the instillation of various solutions high up in the lower bowel would have on the secretion and expulsion of bile was a question which presented itself during investigations in connection with another problem. In every instance we noted that shortly after the intro-

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duction of different solutions high up into the rectum, a flow of bile was obtained from the duodenal tube. This occurred within fifteen minutes after the rectal instillation and lasted from thirty to forty-five minutes. The bile was always light yellow at the onset and occasionally became darker as the drainage continued. Our next object was to determine whether this flow of bile was actually initiated by the instillation of these various liquids, and if so, what was the source of the bile? Did it come from the gallbladder or from the liver? Was it a phenomenon of liver secretion or of contraction of the gallbladder or of both?

A group of patients apparently free from disease was selected for investigation. Each patient was given a cleansing high enema at night, and after that the duodenal tube was passed. The next morning the proper position of the duodenal tube was ascertained, and aspiration was attempted to determine whether there was a spontaneous flow of bile through the tube. A large size rectal tube was then introduced as high up into the bowels as possible without causing the patient too much discomfort, usually about 12 inches (30.4 cm.). One hundred fifty cubic centimeters of one of various solutions was next injected through the tube. The tube was then clamped at the end and left in place. At short intervals thereafter, aspiration of the duodenal tube was practiced, and the time of onset and cessation of the flow of bile was determined. In some cases the flow of bile started without aspiration. Chemical examinations of the blood and white blood cell counts and differential counts were made at varying intervals during the drainage of the bile.

The solutions employed for the instillations were (1) physiologic solution of sodium chloride; (2) indigo carmine (40 cc., 4 per cent); (3) dextrose (100 Gm.); (4) phenolphthalein (2 cc. standard alkaline solution to 150 cc. physiologic solution of sodium chloride); (5) methylene blue (methylethionime chloride, U.S.P.) (2 cc. 5 per cent solution to 150 cc. distilled water); (6) peptonized milk (150 cc.).

REPORT OF CASES

GROUP 1: CASE 1.—A man, aged 53, was admitted to the hospital with a diagnosis of chronic arthritis. On the evening of Feb. 12, 1928, the duodenal tube was passed, and a high cleansing enema was given. On February 13, 150 cc. of phenolphthalein solution was injected through the rectal tube at 8:50 a. m., and a flow of bile was noted at 9 a. m., which continued until 9:45 a. m. A specimen of urine collected at 10 a. m. showed the presence of phenolphthalein. The two hour urinary excretion of phenolphthalein, following the rectal injection, was 11 per cent. No kidney lesion was present. On February 15, the procedure was repeated, but this time physiologic solution of sodium chloride was introduced at 9:10 a. m. At 9:21 a. m. a flow of bile was obtained, which continued until 9:45 a. m.

CASE 2.—A man, aged 27, was admitted to the hospital with a diagnosis of malnutrition. On Feb. 18, 1928, 150 cc. of peptonized milk was instilled into the rectum at 9:12 a. m. At 9:19 a. m., a flow of bile was obtained from the duodenal tube; it was extremely profuse and continued until 10:20 a. m. On February 22,

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this procedure was repeated and 150 cc. of a solution of phenolphthalein was introduced through the rectal tube at 8:55 a. m. The flow of bile commenced at 9:01 a. m. and continued until 9:35 a. m. At 10:15 a. m. a specimen of urine showed the presence of phenolphthalein. The total amount of phenolphthalein recovered in the urine at the end of two hours was 18 per cent. The subsequent functional tests of the kidney in this patient showed a normal excretion of phenolsulphonphthalein and failed to reveal any kidney insufficiency.

CASE 3.—F. B., a man, aged 46, was admitted to the hospital for observation, but no pathologic condition was discovered.

On Feb. 24, 1928, 150 cc. of physiologic solution of sodium chloride was injected through the rectal tube at 9:05 a. m. A flow of bile was obtained from the duodenal tube at 9:12 a. m., and it continued until 9:45 a. m. On February 26, this procedure was repeated, peptonized milk being used. The milk was injected through the rectal tube at 9:12 a. m., and a flow of bile was obtained at 9:17 a. m.; this continued until 9:54 a. m.

CASE 4.—E. M., a man, aged 21, who was convalescing from a lobar pneumonia, was admitted to the hospital for observation.

On March 6, 1928, 150 cc. of physiologic solution of sodium chloride was instilled into the rectum at 9:15 a. m. At 9:18 a. m., a flow of bile was obtained which was profuse and continued until 10 a. m. On March 8, at 8:45 a. m., this procedure was repeated, 150 cc. of an indigo carmine solution being used. A flow of bile started at 8:53 a. m. and continued until 9:15 a. m. On March 9, we attempted to see what effect simple inflation of the bowel with air would have on the flow of bile. At 9:05 a. m., the lower bowel was distended to a moderate degree. No bile was obtained from the duodenal tube in spite of repeated aspirations for a period of one hour.

CASE 5.—J. L., a man, aged 45, was admitted with a diagnosis of ulcer of the stomach.

On March 11, 1928, 150 cc. of physiologic solution of sodium chloride was introduced into the rectum at 8:45 a. m. At 8:48 a. m., a flow of bile began spontaneously from the duodenal tube and continued until 9:20 a. m.

CASE 6.—S. G., a man, aged 37, was admitted to the hospital with a diagnosis of gastric ulcer.

On March 12, 1928, the duodenal tube was passed at 9 p. m. On March 13, at 9 a. m., 150 cc. of peptonized milk was injected through the rectal tube. At 9:12 a. m., bile began to flow and continued to flow until 10 a. m.

The white blood cell count and differential count and the results of chemical examination of the blood in this case are recorded in the accompanying table.

CASE 7.—C. P., a man, aged 22, was admitted to the hospital for observation, but no pathologic process was discovered.

On March 26, 1928, 150 cc. of a solution of methylene blue was injected into the rectum at 9:05 a. m. At 9:17 a. m., bile started to flow from the duodenal tube and continued until 9:55 a. m. Methylene blue made its appearance in the urine at 10:30 a. m.

CASE 8.—J. F., a man, aged 67, was admitted to the hospital with a diagnosis of mild diabetes.

On April 2, 1928, 150 Gm. of dextrose was given per rectum at 9:20 a. m. At 9:27 a. m., bile began to flow from the duodenal tube and continued to do so until 10:15 a. m. The blood sugar determination made at 9:10 a. m. just before the instillation, showed 180 mg.; at 10:10 a. m., it was 192 mg.; at 12:15 p. m., 200 mg.

Thus, it is noted from this group of cases that flow of bile was stimulated by simple instillation of various fluids into the rectum.

The results obtained in all of the cases are recorded in the accompanying table.

After these experiments were completed, a second group of apparently normal persons was selected for study in order to establish whether the flow of bile came from the liver or from the gallbladder and

A Review of Eight Cases in Group 1, Showing the Effect of Rectal Injections on the Flow of Bile

Case	Date	Solution Used for Rectal Injection	Time	Time of Appearance of Bile from Duodenal Tube	Time of Cessation of Bile Flow	Remarks
2	2/13/23	150 cc. phenolphthalein	9:30 a. m.	9:50 a. m.	9:40 a. m.	At 10 a. m. phenolphthalein was detected in urine
	2/15/23	150 cc. physiologic solution of sodium chloride	9:10 a. m.	9:21 a. m.	9:45 a. m.	
2	2/18/23	150 cc. peptonized milk	9:12 a. m.	9:19 a. m.	10:20 a. m.	
	2/22/23	150 cc. phenolphthalein	8:56 a. m.	9:01 a. m.	9:35 a. m.	At 10:15 a. m. phenolphthalein was detected in urine
3	2/24/23	150 cc. physiologic solution of sodium chloride	9:06 a. m.	9:17 a. m.	9:43 a. m.	
	2/25/23	150 cc. peptonized milk	9:12 a. m.	9:17 a. m.	9:54 a. m.	
6	3/ 6/23	150 cc. physiologic solution of sodium chloride	9:15 a. m.	9:13 a. m.	10:00 a. m.	
	3/ 8/23	150 cc. indigo carmine	8:45 a. m.	8:53 a. m.	9:15 a. m.	At 10 a. m. indigo carmine appeared in urine
	3/ 9/23	Inflation of air into lower bowel	9:06 a. m.	None appeared as late as 1 hr. thereafter		
5	3/11/23	150 cc. physiologic solution of sodium chloride	8:45 a. m.	8:48 a. m.	9:20 a. m.	
6	3/13/23	150 cc. peptonized milk	9:00 a. m.	9:12 a. m.	10:00 a. m.	
7	3/24/23	150 cc. methylene blue	9:06 a. m.	9:17 a. m.	9:35 a. m.	At 10:30 a. m. methylene blue made its appearance in urine
8	4/ 2/23	150 Gm. dextrose.....	9:20 a. m.	9:27 a. m.	10:15 a. m.	Blood sugar determination: 9:10 a. m., 150 mg. 10:10 a. m., 192 mg. 12:15 p. m., 200 mg.

whether the mechanism was one of secretion or expulsion. To do this we employed the dye method of visualization of the gallbladder. The sodium salt of tetraiodophenolphthalein was given to the patient in capsule form at the time of passing the duodenal tube (i.e., the night before), and x-ray plates were made the next day at twelve and sixteen hour intervals after ingestion of the dye. Directly after the sixteen hour plates were taken, one of the various aforementioned solutions was instilled into the rectum and the time of flow of bile and its duration were

recorded. One hour after the rectal instillation, when the flow of bile had already ceased (which was seventeen hours after the administration of the dye capsules), another plate of the gallbladder was taken, and this was repeated at the eighteenth hour. At the nineteenth hour the usual fatty meal was given, and at the twentieth and thirty-sixth hours, plates were again made of the region of the gallbladder.

GROUP 2: CASE 1.—F. X, a man, aged 65, was admitted to the hospital for observation of the condition of the gallbladder.

On the evening of March 13, 1928, the patient was given a cleansing enema, and then tetraiodophenolphthalein in capsules was administered by the oral method. The duodenal tube was passed. The following morning, at the end of the twelve hour period, x-ray plates revealed the gallbladder fairly well filled out with the dye. At the sixteenth hour the x-ray picture showed the shadow to be practically of the same size but markedly increased in intensity.

The patient was then given 150 cc. of physiologic solution of sodium chloride per rectum, and within ten minutes a flow of bile was obtained from the duodenal tube. This steady drainage continued for thirty-five minutes. At the seventeenth, eighteenth and nineteenth hour periods, which corresponded to ten minutes and two hours after the rectal injection of the physiologic solution of sodium chloride, with its subsequent drainage of bile, the x-ray picture showed no reduction in the size of the gallbladder, but some intensification of the shadow. The duodenal tube was then removed, and the patient was given a fatty meal. Roentgen examination one hour after this food intake showed the gallbladder had emptied of the dye (fig.).

CASE 2.—P. D., a man, aged 66, was admitted to the hospital on account of varicose veins of the lower part of the left leg.

On the evening of March 23, 1928, the patient received the usual preparations, as in case 1. Twelve hours after the intake of the dye, no distinct shadow was visible. At the sixteenth hour, the shadow of the gallbladder could be fairly well outlined and appeared to be regular. The patient was then given a rectal injection of 150 cc. of peptonized milk, with the same result as regards the flow of bile from the duodenal tube as had been obtained in the previous cases.

Roentgen examinations were made one and two hours after the rectal injection. There was a marked concentration of the dye in the gallbladder, but no evidence of emptying. The patient was then given a meal and reexamined one hour later. The gallbladder was found markedly reduced in size. At the thirty-sixth hour, the shadow had entirely disappeared. Subsequent examination revealed no evidence of pathologic changes in the gallbladder.

CASE 3.—W. K., a boy, aged 15, was admitted to the hospital with a diagnosis of chronic nephritis.

On April 1, 1928, the procedure mentioned in the preceding two cases was repeated. X-ray plates of the gallbladder taken after the injection of the peptonized milk into the rectum showed no emptying of the gallbladder in spite of the fact that bile was obtained through the duodenal tube.

CASE 4.—L. C., a man, aged 28, was admitted to the hospital for observation.

On April 4, 1928, at the twelve hour period after the intake of the dye capsules, the gallbladder was not visible. At the sixteen-hour period, the shadow of the gallbladder was present. One hour after the injection of 150 cc. of peptonized milk into the rectum, the shadow of the gallbladder had not decreased in size

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Fig. 1.—*A*, a roentgenogram, showing the dye method of visualization of the gallbladder, taken twelve hours after the administration of tetraiodophenolphthalein by capsules. *B* shows the extent of the shadow sixteen hours after the administration of capsules of tetraiodophenolphthalein; *C*, the extent of the shadow ten minutes after the administration of a physiologic solution of sodium chloride per rectum; *D*, the extent of the shadow eighteen hours after the administration of capsules of tetraiodophenolphthalein, and one hour after injection of a physiologic solution of sodium chloride by rectum; *E*, the extent of the shadow nineteen hours after the administration of the capsules and two hours after injection of a physiologic solution of sodium chloride by rectum, and *F*, the extent of the shadow twenty hours after the administration of capsules and one hour after eating.

but had become more intensified. At the two hour period after the injection, the shadow did not show up well because the patient breathed.

CASE 5.—E. W., a man, aged 24, was admitted to the hospital for observation but no pathologic process was found.

On April 15, 1928, twelve hours after the dye had been taken by mouth, a definite shadow of the gallbladder was seen. Sixteen hours later, the shadow of the gallbladder was slightly contracted. One hour later, 150 cc. of physiologic solution of sodium chloride was injected into the rectum, and shortly thereafter a flow of bile was obtained from the duodenal tube.

At the eighteenth hour, or one hour after injection of fluid into the rectum, the shadow of the gallbladder was more intensified and slightly larger in size. At the nineteenth hour, or two hours after the injection of physiologic solution of sodium chloride, the shadow of the gallbladder was still intense and remained about the same size. The patient was then given the fatty meal by mouth, and one hour after eating, which corresponded to the twenty-hour period after the intake of the dye capsules, the gallbladder appeared contracted and half the size. Thirty-six hours after the patient had taken the capsules no shadow of the gallbladder could be made out.¹

COMMENT

In former years, irrigation of the colon was an established treatment for various types of jaundice. This paper offers the first proved experimental demonstration of the possible efficacy of this form of therapy.

In each of eight cases it was uniformly noted that within a period varying from three to twelve minutes after the instillation of various solutions high into the rectum, a flow of bile was obtained from the duodenal tube. This flow would continue for a period varying from eighteen to even as long as sixty-one minutes without any interruption. In three of the patients the rectal instillations were repeated once and in one of them twice. The solutions employed for instillation were, physiologic solution of sodium chloride, indigo carmine, peptonized milk, methylene blue, dextrose and phenolphthalein. This variety certainly precludes the possibility of any specificity in the response on the part of the liver. In one instance, case 4 (group 1) air was used to inflate the lower bowel, but no flow of bile was obtained as a result of this procedure, although the response had been obtained twice before in this patient after the use of physiologic solution of sodium chloride and a solution of indigo carmine. This fact would speak against a mechanical or nervous stimulation resulting from the mere filling of the rectum as being a cause for the secretion of bile. In the cases in which indigo carmine, methylene blue and phenolphthalein were employed, it was proved that these solutions were actually absorbed from the lower bowel, as they were detected in the urine at varying intervals after the rectal instillations. Similarly, in case 8 (group 1) a diabetic patient on whom dextrose solution was

1. Only the x-ray plates in connection with case 1 are reproduced. The x-ray pictures in association with the other cases are just as striking, but were not published on account of lack of space.



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employed, the blood sugar determinations showed a progressive rise at the one and three hour periods.

These facts thus reveal that the introduction of various solutions into the lower bowel causes a definite flow of bile into the intestines. The mechanism whereby this is brought about is either a direct stimulation of the cells of the liver from the absorption of the instilled fluids into the portal system or a reflex nervous phenomenon. The former is the more probable explanation.

Further study will be undertaken to prove this point by the use of agents which are known to have a direct stimulating effect on the liver cells and by noting the quantity of bile obtained in comparison with the agents which are not especially cholagogue in action. This method of bile drainage may prove of therapeutic importance in those cases in which bile drainage by means of Lyon's method is impossible or inadvisable.

Another group of cases was studied for the purpose of determining whether such flow of bile was the result of stimulation of the bile-secreting or bile-expelling organs. Conclusive proof is offered by means of the x-ray picture (fig.). Twelve hours after the ingestion of the tetraiodophenolphthalein, a fairly large and distinct shadow of the gallbladder is present. At the sixteen-hour period the shadow is slightly larger and more intense. At the seventeenth hour, the physiologic solution of sodium chloride is introduced rectally, and ten minutes later, when the bile commences to flow, another plate taken shows the gallbladder about the same size as that previously noted but slightly more intense. The physiologic solution of sodium chloride is given at approximately the time when the usual fatty meal is employed to stimulate the contractions of the gallbladder. After a profuse flow of bile is obtained, other plates, taken at the eighteenth hour or one hour after the introduction of the physiologic solution of sodium chloride per rectum, and at the nineteenth hour, or two hours following the rectal instillations, reveal the gallbladder to be practically the same size as at the sixteenth hour and the shadow slightly more intensified. On the other hand, the usual fatty meal then administered brings about contraction of the gallbladder so that at the twentieth hour the shadow of the gallbladder is practically absent.

CONCLUSION

The introduction of various solutions into the upper rectum produces a drainage of the bile into the duodenum. This flow comes directly from the liver without contraction of the gallbladder.