Cinefluorographic Observations of Common Bile Duct Physiology *

RICHARD N. MYERS, M.D., GEORGE J. HAUPT, M.D., NEWTON C. BIRKHEAD, M.D.,
J. MONTGOMERY DEAVER, M.D.

*From Surgical Service "A" and the Division of Research,
Lankenau Hospital, Philadelphia, Pennsylvania*

THE PHYSIOLOGY of the common bile duct has been studied by many investigators since the classic work of Oddi, in 1887.[15] Most conclusions regarding its function have been based upon indirect evidence, for until recently no method was available to clearly observe the common bile duct under various conditions, and to record these observations permanently.[5, 17] It has generally been agreed that common bile duct size and pressure are related to the volume rate of bile production by the liver and to the tone of the sphincter of Oddi.[1, 2, 3, 13, 14, 16] There also have been sporadic reports, one recently, describing peristaltic activity of the common bile duct.[6] The effects of various drugs on the sphincter of Oddi with secondary changes in common bile duct size and pressure have also been reported.[4, 7-9, 10, 12, 19] In the present study, by combining cinefluorography with simultaneous measurements of intraductal pressure, an attempt has been made to correlate previous observations and to resolve some of the conflicting viewpoints.

Material and Methods

Twenty-eight studies were performed upon sixteen patients within the three-week period following cholecystectomy with choledochotomy and T-tube drainage. Ages ranged from 29 to 74 years. Approximately two-thirds of the patients were receiving a cholegogue (Decholin **) at the time of their studies.

The studies were made with the patient supine on the fluoroscopic table. The T-tube was attached to a system in which the common duct pressure was measured by a Sanborn strain gauge and recorded photographically by a multi-channel oscillograph. The zero pressure reference point for calibration of the gauge was set midway between the level of the third anterior interspace and the back. The patient's electrocardiographic tracing and respiratory excursions were also simultaneously recorded. After calibrations and baseline records were made, either 50 per cent hypaque *** or renographin † was introduced from a reservoir into the system at body temperature by means of a T-connection (Fig. 1). The biliary tree was visualized using a pulsed fluoroscopic image intensifier and television read-out. Choledochocinefluorograms were made on 16 mm. film at appropriate intervals.

It was observed that common duct pressure could be increased by changing the volume of the system with the introduction of the radio-opaque media at a rapid rate. When the infusion was stopped, the pressure would gradually return to normal. These variations in pressure could be avoided if the dye was introduced at a slow constant rate (Fig. 2). After obtaining a record of the normal resting common duct pressure, the dye was continuously infused at a rate of 15 drops per minute.

* Presented before the American Surgical Association, Washington, D. C., May 9–11, 1962.

** Dehydrocholic acid, Ames.

*** Hypaque Sodium, brand of diatrizoate sodium, Winthrop.

† Methylglucamine diatrizoate, 76%, Squibb.

All subsequent pressures were obtained under these circumstances. The mean difference between the control or resting intraductal pressure and the intraductal pressure during infusion of dye at 15 drops per minute was 2.0 cm. of water (range 1.0 to 4.0 cm.). This method, therefore, allowed continuous opacification of the biliary system for subsequent studies without significant alteration of the intraductal pressures due to introduction of the dye.

The following drugs were administered and their effects observed:

Nitrites. In 25 of the studies patients were intially given either nitroglycerin 0.32 mg. sublingually or amyl nitrite by inhalation (crushed pearl) after stabilization of the intraductal pressure.

Opiates. In 28 of the studies an opiate, either morphine sulfate intravenously (0.15 mg./kg.) or demerol †† intravenously (0.9 mg./kg.), was administered. In 25 studies, the opiate was given when there was no further discernible effect of the nitrite. In the other three studies an opiate was administered as the initial agent.

Repeat Nitrites. In 18 studies either nitroglycerin 0.32 mg. sublingually or amyl nitrite by inhalation (crushed pearl) was repeated at the time of maximal opiate effect.

Parasympatholytic Agents. In 12 studies either intravenous atropine (0.2 mg.) or intravenous probanthine ††† (15 mg.) was administered after the transient effect of the second dose of nitrite was no longer apparent. In four studies the parasympatholytic agent was administered directly at the time of maximal opiate effect.

Biopsies of the common bile duct were taken from eight patients at the time of operation. These were compared with normal duct sections taken from 24 postmortem examinations. All specimens were stained with hematoxylin and eosin, Masson Trichrome stain for muscle, and Verhoeff–Van Gieson stain for elastic fibers.

Results

Control Studies. Common duct pressures before and during perfusion of dye at 15 drops per minute are shown in Table

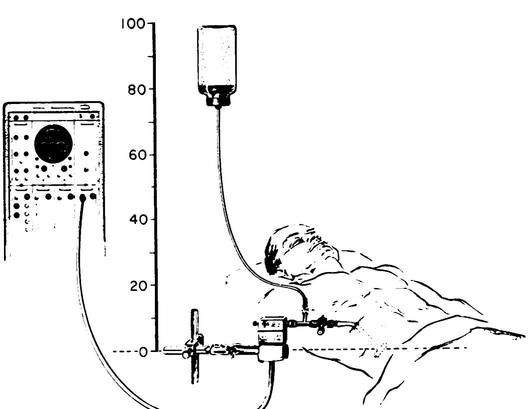

FIG. 1. Illustration of the method of recording common duct pressure and infusion of radio-opaque media.

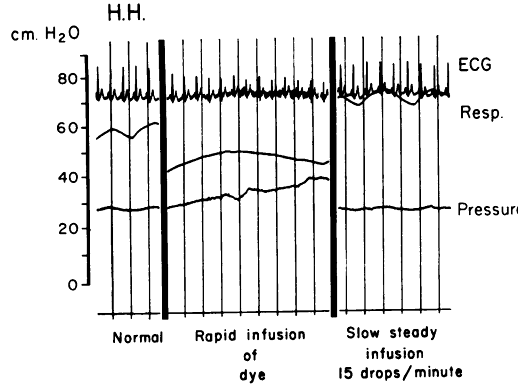

FIG. 2. Photographic record of oscillographic data. On this and subsequent illustrations, from above down are shown the electrocardiographic tracing, respiratory excursions, and common duct pressure. The calibration scale to the left refers to common duct pressure only. Time lines are in one second intervals. In this patient rapid infusion of the dye resulted in an increase of pressure of 12 cm. of water in 8 seconds. A slow infusion of dye at 15 drops per minute results in a steady near-control pressure.

†† Meperidine hydrochloride, Winthrop.

††† Pro-Banthine Bromide, brand of Propentheline Bromide, Searle.

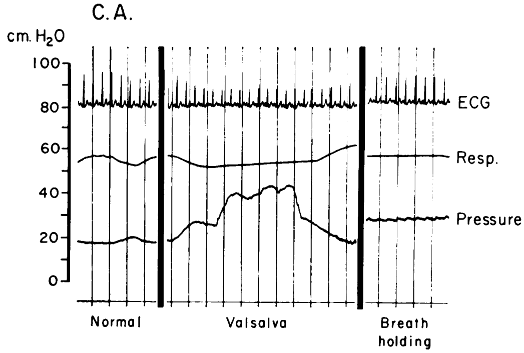

FIG. 3. The normal or resting common duct pressure, fluctuating with respiratory cycle, is shown on the left. During the Valsalva maneuver, intraductal pressure increases. With breath-holding, small pressure changes synchronous with the heart beat are clearly seen.

1. The resting pressures ranged from 12 to 29 cm. of water in those patients studied. Rhythmical fluctuations in common duct pressure synchronous with respiration were observed. These disappeared with breath holding. It was further noted that there were also small regular pressure changes synchronous with the heart beat. These presumably represent a *fluid wave* or *ballisto* effect. In order to demonstrate more clearly the effect of intra-abdominal pressure on common duct pressure, the Valsalva maneuver was performed on all patients. The intraductal pressure rose consistently during the maneuver, confirming the fact that common duct pressure reflects alterations in intra-abdominal pressure (Fig. 3). There were no pressure changes which could be interpreted as peristaltic activity of the common bile duct. There was no recordable pressure change under resting conditions as the sphincter of Oddi opened and closed. No evidence of peristalsis was seen cinefluoroscopically or on the cinefluorograms.

Effects of Drugs. The first group of drugs studied were the nitrites, which have been reported to have a relaxing effect on the sphincter of Oddi with subsequent reduction in common duct pressure.[4, 9, 10] In this study, however, no significant pressure change occurred in the resting common bile duct after administering either nitroglycerin sublingually or amyl nitrite by inhalation (Fig. 4, Table 1). Fluoroscopically, and on the cinefluorograms, there was no change in common duct size or in sphincter tone.

Following the administration of either morphine intravenously or demerol intravenously, all patients exhibited a marked increase in common duct pressure, confirming previous reports.[9,11,13,18] The rise in pressure was always greater with morphine than with demerol. Morphine increased the intraductal pressure an average of 110 per cent; demerol caused an average increase of only 62 per cent (Fig. 5, Table 1). A

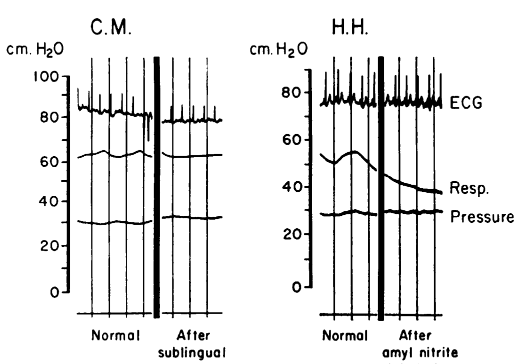

FIG. 4. The lack of a significant effect of the nitrites on the normal or resting common duct pressure is illustrated in these two patients.

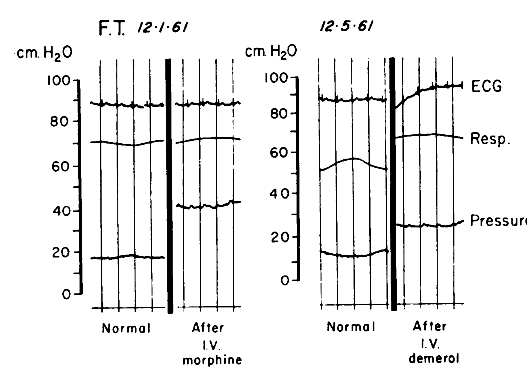

FIG. 5. The marked increase in intraductal pressure following morphine is shown on the left; the lesser increase with demerol is shown on the right.

TABLE 1

Patient	Date	Resting Press. cm.H_2O	Resting Press. Dye Infusion cm.H_2O	Max. Press. After Nitrite * cm.H_2O	Max. Press. After Opiate ** cm.H_2O	Press. After Nitrite * Given at Max. Opiate Response cm.H_2O	Press. After Parasympatholytic Agent *** at Max. Opiate Response, After Transient Nitrite Effect cm.H_2O
1. B. L.	10-30-61	12	14	14[n]	46[m]		
	11- 1-61	14	15	15[n]	30[d]		
2. F. C.	11-10-61	18	19	19[n]	40[m]		
3. A. N.	11-20-61	16	18	18[n]	38[m]		
	11-22-61	17	19	20[n]	29[d]		
4. R. S.	11-28-61	12	15	16[n]	34[m]		
5. A. M.	11-27-61	15	16	15[n]	36[m]	32[n]	
	11-30-61	14	16	16[a]	28[d]	25[a]	
6. M. D.	11-29-61	19	20	21[a]	39[m]	36[a]	
	12- 1-61	17	19	20[n]	26[d]	24[n]	
7. F. T.	12- 1-61	17	20	20[n]	41[m]	38[n]	
	12- 5-61	14	17	16[n]	26[d]	24[n]	
8. C. A.	12-14-61	19	22	23[n]	37[m]	36[n]	20[p]
	12-15-61	20	23	24[n]	34[d]	32[n]	25[p]
9. W. K.	12-30-61	18	19	20[n]	38[m]	35[n]	21[p]
	1- 8-62	16	17	17[a]	27[d]	24[a]	20[at]
10. C. M.	1- 5-62	24	26	26[n]	47[m]	43[n]	29[p]
	1- 9-62	20	22	21[n]	39[d]	38[n]	22[p]
11. K. S.	1-22-62	17	19	19[n]	31[m]	30[n]	18[p]
12. P. D.	2- 5-62	16	18	18[a]	42[m]		32[at]
	2- 7-62	17	20	21[a]	32[d]		25[at]
13. H. H.	2- 9-62	29	32	31[a]	53[m]	47[a]	36[at]
14. A. D.	2-16-62	22	25	27[a]	57[m]	49[a]	38[at]
	2-19-62	26	30	29[a]	42[d]	36[a]	30[at]
15. E. S.	3-26-62	19	22		43[m]		25[p]
	3-29-62	18	21		33[d]	26[a]	20[p]
16. J. B.	4- 4-62	23	24	22[n]	55[m]	52[n]	35[p]
	4- 6-62	21	22		40[d]		28[at]

* n—nitroglycerin,
a—amyl nitrite.
** —morphine sulfate,
d—demerol (Meperidine hydrochloride, Winthrop).

*** p—Pro-Banthine Bromide, brand of Propentheline Bromide, Searle,
at—atropine sulfate.

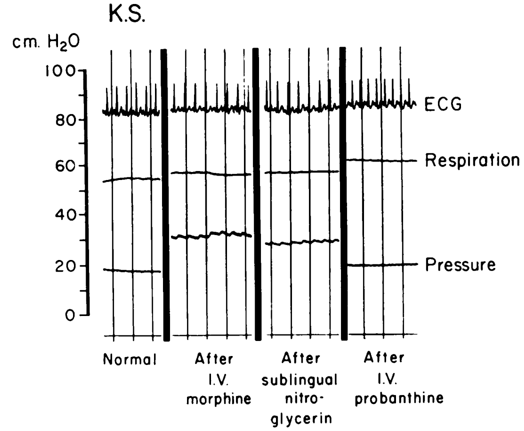

FIG. 6. This illustrates an example of the rise in common duct pressure after morphine, the slight drop in pressure after nitroglycerin, and the return to nearly normal pressure with probanthine.

striking increase in duct size was seen cinefluoroscopically after the administration of the opiates. This was consistently more marked after morphine than demerol. Dilatation of the common duct and biliary radicals as seen cinefluoroscopically was proportional to the rise in intraductal pressure. Despite the marked increase in intraductal pressure no dye was seen to flow into the duodenum. This was interpreted as the result of prolonged contraction of the sphincter of Oddi. Again no peristaltic activity of the duct was noted.

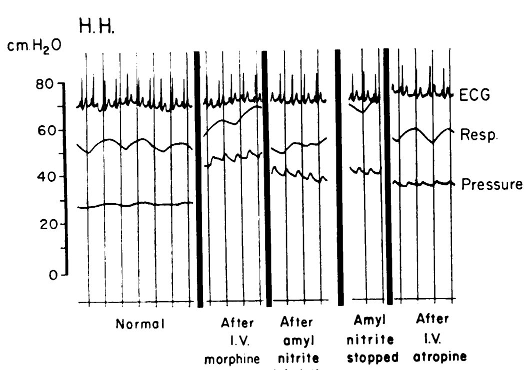

FIG. 7. The transient fall in intraductal pressure with amyl nitrite administered after morphine is well demonstrated. A further fall in pressure is seen with atropine, but to a lesser extent than with probanthine, as seen in Fig. 6.

While the opiates were exerting a maximal effect with the sphincter of Oddi still contracted, the nitrites were again administered. Under these circumstances both nitroglycerin and amyl nitrite caused a slight transient drop in intraductal pressure, and a small amount of dye was seen to flow into the duodenum. A more profound and prolonged drop could be produced, however, by the intravenous administration of a parasympathetic blocking agent such as atropine or probanthine (Fig. 6, 7, Table 1). Probanthine was much more effective in this regard than atropine. Measurements of duct size from the cinefluorograms showed no change following administration of the nitrites. However, a decrease in size to normal or near normal was seen in all patients following administration of the parasympathetic blocking agent.

Microscopy. Histologic studies were made of 24 normal common bile ducts obtained at postmortem examination. These were compared with biopsy specimens from eight patients. Normally, the wall of the common duct is composed of a homogeneous collagenous-appearing tissue. There are a few fibroblastic nuclei scattered throughout the substance (Fig. 8). A Masson Trichrome stain for muscle shows that most of the material in the wall stains green, indicating that it is collagen with dispersed reddish-staining nuclei and no smooth muscle (Fig. 9). A Verhoeff–Van Gieson elastic stain shows many black-stained elastic fibers throughout the collagenous tissue of the wall (Fig. 10). There was no evidence of muscle fibers in the wall of the common bile duct in any of the specimens. The wall of the common bile duct, then, is made up of three coats: an inner mucosal coat, a middle collagen and elastica layer, and an outer loose collagenous layer. Since no muscle is present, inherent contractility is not possible. Changes in the size of the common bile duct are, therefore, entirely passive.

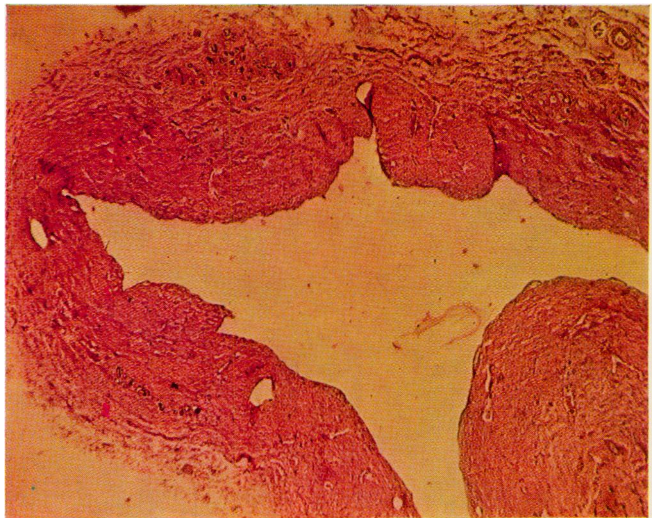

FIG. 8. Cross-section of a normal common bile duct taken from postmortem examination. Note the autolysis of the mucous membrane. The wall of the duct is composed of a homogeneous collagenous-appearing tissue. Hematoxylin and eosin stain (30 ×).

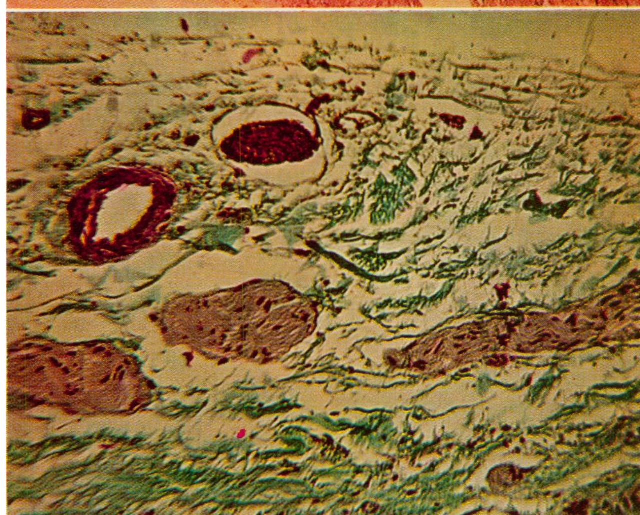

FIG. 9. Cross-section through wall of common bile duct. The Masson Trichrome technic stains muscle fibers red, collagen green and collagenous nuclei red. Muscle fibers can be seen in the arteriolar wall but nowhere else in the common duct (200 ×).

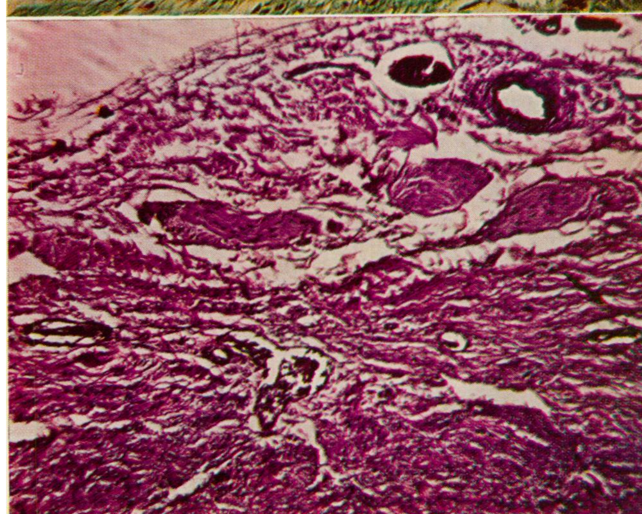

FIG. 10. Cross-section through wall of common bile duct. Elastic fibers appear black with the Verhoeff-Van Gieson elastica stain. The nerves and collagen stain red. Many black-stained elastic fibers are seen throughout the collagenous tissue of the wall (90 ×).

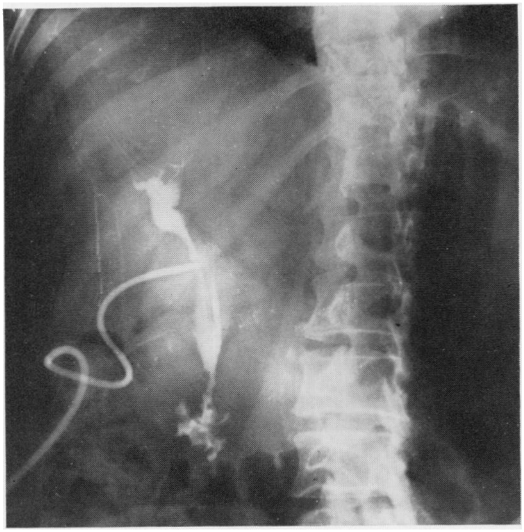

FIG. 11. A postoperative x-ray cholangiogram in which there is a questionable filling defect in the distal common duct. Cinefluorographically, this defect was only seen intermittently and interpreted as action of the sphincter of Oddi in combination with duodenal peristalsis.

Discussion

The technic of cinefluorography has made continuous visualization of the biliary tree possible. The dye can be followed from the time of injection through the T-tube into the biliary system and thence into the duodenum through the sphincter of Oddi. This not only permits measurement of the common duct under various conditions, but also gives a dynamic visualization of the action of the sphincter of Oddi with its surrounding duodenal musculature.

Recently Daniels *et al.*,[6] using a cinefluorographic technic, reported what they interpreted as peristaltic activity in the common duct, and show histologic evidence for the presence of muscle fibers in the wall of the common duct with hematoxylin and eosin stained sections. In the present study similar minor fluctuations in common duct pressure were found to be related to respiration and heart beat. In addition, acute changes in intra-abdominal pressure were, as expected, reflected in common duct pressure. Since it is frequently difficult to differentiate smooth muscle and collagen fibers on routine hematoxylin and eosin stained sections, we believed that special staining technics were indicated for definitive study. Our own histologic studies of sections of the common duct from these patients and from normal controls, including Masson Trichrome and Verhoeff–Van Gieson stains, revealed the wall of the common duct to consist of mucosal, collagen, and elastic tissue. No muscle fibers were seen. These findings indicate, then, that fluctuations in common duct pressure under these circumstances are not peristaltic but appear to reflect changes in intra-abdominal pressure with

FIG. 12. Postoperative x-ray cholangiogram showing a suspicious distal common duct defect, which on cinefluorography was again seen to be only transitory. Retained common duct stones could be excluded by this technic.

respiration and rhythmical changes with heart beat.

Finally, in this series there were two patients in whom the usual postoperative T-tube cholangiograms showed a deformity suggestive of a retained stone at the lower end of the common duct (Figs. 11, 12). Both patients, when studied cinefluorographically, showed this apparent deformity to be due to the muscular action of the sphincter of Oddi combined with duodenal peristalsis. This deformity is present only during certain phases of sphincter activity. Cinefluorographic visualization, therefore, has proved clinically valuable in the differentiation of retained common duct stones in patients with questionable common duct deformities.

Summary and Conclusions

1. Twenty-eight studies of common bile duct pressure during cinefluorography were carried out on 16 patients within the three week period following cholecystectomy and T-tube drainage.

2. Intravenous morphine caused a marked and sustained rise in common duct pressure due to spasm of the sphincter of Oddi. The effect was less marked with demerol.

3. The administration of nitroglycerin or amyl nitrite after the opiates resulted in a slight transient drop in common duct pressure. No significant change in pressure was noted if these agents were given before the administration of opiates.

4. Intravenous probanthine and to a lesser extent, atropine, after opiates, resulted in relaxation of the sphincter of Oddi and a prolonged decrease of common duct pressure to near control levels.

5. Common duct size and pressure are dependent upon the state of tone of the sphincter of Oddi and volume flow of bile. Minor pressure fluctuations are due to respiratory cycle and heart beat. No inherent contractility of the common bile duct was observed.

6. Histologic study of normal and pathologic common bile ducts showed complete absence of muscle fibers, indicating the passive role of the common duct in bile flow.

7. The rationale of parasympathetic blocking agents in biliary tract disease and pancreatitis is confirmed by this study. The use of opiates may be hazardous. Nitrites have little beneficial effect.

Bibliography

1. Bergh, G. S.: Sphincter Mechanism of Common Bile Duct in Human Subjects. Surgery, **11**:299, 1942.
2. Bockus, H. L.: Gastroenterology, Vol. III. Philadelphia and London, W. B. Saunders Co., 1946.
3. Boyden, E. A.: Anatomy of Choledochoduodenal Junction in Man. Surg., Gynec. & Obst., **104**:641, 1957.
4. Butsch, W. L., J. M. McGowan and W. Walters: Clinical Studies on Influence of Certain Drugs in Relation to Biliary Pain and to Variations in Intrabiliary Pressure. Surg., Gynec. & Obst., **63**:451, 1936.
5. Caroli, J., P. Porcher, G. Pequignot and M. Delattre: Contribution of Cineradiography to Study of the Function of the Human Biliary Tract. Am. J. Digest. Dis., **5**:677, 1960.
6. Daniels, B. T., F. B. McGlone, H. Job and R. B. Sawyer: Changing Concepts of Common Bile Duct Anatomy and Physiology. J. A. M. A., **178**:394, 1961.
7. Doubilet, H. and R. Colp: Resistance of Sphincter of Oddi in Humans. Surg., Gynec. & Obst., **64**:622, 1937.
8. Gaensler, E. A., J. M. McGowan and F. F. Henderson: Comparative Study of Action of Demerol and Opium Alkaloids in Relation to Biliary Spasm. Surgery, **23**:211, 1948.
9. Hicken, N. F., A. J. McAllister, B. J. Franz and E. Crowder: Does Removal of Gall Bladder Produce Functional Changes of Sphincter of Oddi and Choledochus? Am. Surgeon, **17**:598, 1951.
10. Ivy, A. C.: Motor Dysfunction of the Biliary Tract. Am. J. Roentgenol., **57**:1, 1947.
11. Jonson, M.: Width of the Common Bile Duct Before and After Morphine Studied by Cholegraphy. Acta Radiol., **54**:345, 1960.
12. Kozell, D. and H. Necheles: A Study of the Mechanics of Bile Flow. Surg., Gynec. & Obst., **74**:961, 1942.

13. Kjellgren, K.: Persistence of Symptoms Following Biliary Surgery. Ann. Surg., **152**: 1026, 1960.
14. Mallet-Guy, P.: Value of Preoperative Manometric and Roentgenographic Examination in Diagnosis of Pathologic Changes and Functional Disturbances of Biliary Tract. Surg., Gynec. & Obst., **94**:385, 1952.
15. Oddi, R.: D'une Disposition à Sphincter Spéciale de l'ouverature du Canal Cholédoque. Arch. ital. de biol., **8**:317, 1887.
16. Richards, T. G. and J. Y. Thompson: Secretion of Bile Against Pressure. Gastroenterology, **40**:705, 1961.
17. Sandersson, S. S. and K. E. Gross: Cinecholedochography. Radiology, **76**:267, 1961.
18. Zimmerman, L. M. and R. Levine: Physiologic Principles of Surgery. Philadelphia and London, W. B. Saunders Co., 1957.
19. Zollinger, R.: Observations Following Distension of Gallbladder and Common Duct in Man. Proc. Soc. Exper. Biol. and Med., **30**: 1260, 1933.

Discussion

Dr. Frank Glenn (New York): Dr. Deaver and his group are certainly to be congratulated on this very graphic demonstration pinpointing the action of the sphincter of Oddi. In a sense this is a demonstration of the direction we are moving today with precision of diagnosis by directing observing physiological reactions with the aid of radiography.

There are many avenues for exploration that are obvious from such a study. It enables us, for example, to have a clearer concept of what drugs do when we give them, and their possible role in individuals with biliary colic.

Indeed, it provides us with an opportunity to see what can be done with diet, with variation of activity, and with drugs that are long lasting in their effect. This may help us considerably in such diseases as pancreatitis, particularly that pancreatitis that is associated with the repeated and excessive ingestion of alcohol. I hope the authors will avail themselves of the opportunity to study some of the patients who have pancreatitis, at a relatively early stage.

Dr. Elliott S. Hurwitt (New York): I should like to echo Dr. Glenn's congratulations on this addition to an understanding of the pathophysiology of the common bile duct and also to mention two ancillary procedures that we have been employing at the Montefiore Hospital in the management of such patients. One of these, the lateral cholangiogram, has enabled us frequently to demonstrate lesions that were not seen in the conventional antero-posterior plane.

Secondly, the use of the choledochoscope for direct inspection of the common bile duct during surgery has enabled us to visualize and study the appearance of suppurative, catarrhal and granulomatous cholangitis, to identify residual solitary stones high in the intrahepatic ductal system as well as the sphincter area, and in the hands of one of our residents, to pick up early carcinoma of the ampulla susceptible to a succesful Whipple procedure.

Dr. John Englebert Dunphy (Portland, Oreg.): We have been very much interested in this same problem. One of the criticisms the proponents of peristalsis will level at Dr. Deaver's paper is that he has a tube in the common duct. We have repeated the studies reported by Burnett and Shields and others. In experiments on dogs and goats, after injecting the gallbladder with dye and following it through the common duct by cineradiography we are as convinced as Dr. Deaver that there is no true peristaltic motion in the common duct. I would like to have him comment about the effect of the tube in the duct.

Dr. Richard N. Myers (closing): Dr. Glenn, there are, of course, possibilities for any number of drugs and various combinations of drugs, diets, and so forth, to be studied. In addition, we might mention that we have been looking for a patient to study in whom a sphincterotomy had been done. So far, we have not had one of those but we think it would be interesting to perform these studies on sphincterotomized patients.

We also on our regular cholangiogram take lateral as well as antero-posterior views and we agree that this view will often help us pick up deformities.

So far as the tubing in the common duct, we realize that it is a matter of question as to whether or not this is a normal or resting common duct. But this, we thought, was as close as we could get to one. We studied several patients with polyethylene tubes left in the stump of the cystic duct and measured pressures and the effects of drugs, but we believed that the pressure measurements we obtained were not valid, because, presumably, the width of the polyethylene was too small to accurately reflect true pressures, especially with the viscosity of the dye and the bile.

All the specimens were stained with the Masson stain for muscle and a Verhoeff-Van Geisson stain for elastic fibers, and in none of these were we able to demonstrate muscle fibers in any of the common ducts.