

## THE COMPOSITION OF THE BILE FOLLOWING THE RELIEF OF BILIARY OBSTRUCTION<sup>1</sup>

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The significance of the liver, as the largest glandular organ in the body, and its paramount importance in certain phases of intermediary metabolism, contrasts strangely with the paucity of knowledge, at least in man, concerning its secretion, the bile. The characteristic biliary constituents, bilirubin, the bile acids and cholesterol have been isolated and identified chemically. Experimental work on animals, especially on dogs with permanent biliary fistulas, has indicated the multiplicity of factors, such as diet, climate, fasting, various chemical poisons, infections and exercise, which may affect either the volume or composition of the bile. In this connection, the earlier work of Bidder and Schmidt (1852), and of Stadelmann (1891, 1896) and, in recent years, that of Whipple (1922) and Rous (1925) and their collaborators has been of fundamental significance.

As a result of these studies it is now recognized that there may be great variations in the flow of bile from day to day. The secretion of bile pigment, on the other hand, continues at a fairly constant rate except for changes due to hemorrhage, anemia or other disturbances in the metabolism of the blood pigments. In consequence, the concentrations of the bile pigments tends to vary inversely with the volume of the bile, and McMaster, Broun and Rous (1923), and Greene and Snell (1928) have emphasized the extreme variations in concentration which occasionally may be found. The intimate relation between the diet and the excretion of cholesterol in the bile has recently been

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commented on by McNee (1914) and by McMaster (1924). Several factors combine to determine the excretion of bile acids: (1) an endogenous factor responsible for the relatively constant excretion of bile acids in the fasting dog which may possibly be related to the metabolism of body protein; (2) an exogenous factor, determined by the diet and especially concerned with the amount and character of the protein therein, and (3) an intestinal factor as a result of the absorption of bile acids from the bowel, with the resultant establishment of the enterohepatic circulation originally postulated by Schiff (1870); this intestinal factor is further modified as a result of changes in the intestinal flora and variations in the destruction of bile acids by bacterial action. The functional state of the hepatic cells must also be taken into consideration, for changes in the functional efficiency of the liver as a result of the production of an Eck fistula, cholangitis, or the administration of hepatic toxins, such as chloroform or phosphorus have a profound influence on the excretion of the bile acids. Greene and Snell (1928) found the variation in the attainable concentration of bile acids in the bile to be relatively slight, at least when compared to the observed variations in the concentration of bilirubin. Under some conditions, therefore, the volume of the biliary output may be determined by the excretion of the bile acids, although this relation does not always hold and the two may be entirely independent the one of the other.

Direct evidence regarding the secretion of bile in normal men, and the modifications accompanying disease, is lacking. The greater part of the available data is concerned with the composition of bile from the gallbladder but because of the concentrating action of that viscus such analyses do not indicate the composition of the bile as initially formed in the liver. Similar criticisms apply to the studies of Rosenthal and von Falkenhausen (1923), and of McClure (1925) and his associates, who used the material obtained by duodenal drainage. Apart from the uncertainty, as to how far the duodenal content is representative of the hepatic secretion, there is further difficulty in that only the concentration, and not the total amount of the different biliary constituents, is determinable. Numerous studies have been made of bile obtained from patients with permanent biliary fistulas. Unfortunately, the majority of such investigations was made before

the development of adequate analytic methods and so were concerned chiefly with the changes in the volume and total solids present in the bile.

More recently von Czyhlarz, Fuchs and von Fürth (1913), Chabrol, Bénard and Bariéty (1926), and Rosenthal, von Falkenhausen and Freund (1926) have reported single cases or small groups of cases in which the composition of the bile has been carefully studied during the first few days after cholecystectomy and drainage of the common bile duct. We wish to report the changes in an additional series of nine cases. Such cases afford an opportunity to study the effect of biliary obstruction on the secretion of bile and the return toward normal following relief of the obstruction. It is possible, in consequence, to compare the changes observed clinically in patients with those in dogs reported by McMaster, Broun and Rous (1923) following temporary occlusion of a permanent biliary fistula. Furthermore, the differences in the response of the different cases afford additional light on the disturbances in the functional activity of the liver as a result of biliary obstruction or infection.

#### DETAILS OF INVESTIGATION

The drainage of bile from the gallbladder or common bile duct, subsequent to the relief of biliary obstruction, was studied in nine cases. Details regarding the clinical histories of certain of these cases are given elsewhere (26). The methods of analysis were those used in previous studies of this series: the method of Greene, Snell and Walters (1925) for bilirubin; of Aldrich and Bledsoe (1928) for bile acids; of Van Slyke (10) for chlorides, and of Van Slyke and Cullen (10) for urea. The data obtained in the different cases are given in the accompanying tables. It is recognized that the collection of bile from a drainage tube inserted in the gallbladder or common bile duct is not always complete. In the present series the analysis of bile was continued during the whole period of observation but the tables include only the data obtained during the period when the collection was apparently complete. For purposes of study the cases have been divided into three groups.

*Group 1.* Tables 1, 2 and 3, and figure 1A comprise three cases of chronic cholecystitis with stone in the common bile duct. In these

cases, the histories were of typical, intermittent biliary obstruction, with mild degrees of jaundice. The liver was apparently normal at the time of operation. Cholecystectomy, choledocholithotomy and choledochostomy were performed in all, and the postoperative course was uneventful.

*Group 2.* Tables 4, 5 and 6 and figure 1*B* contain three cases. One patient had chronic cholangitis, biliary obstruction and a consequent obstructive type of biliary cirrhosis; a T-tube was inserted in the common bile duct. Another patient had chronic cholecystitis with stones, a stone in the common bile duct, and considerable biliary cirrhosis; a T-tube was inserted in the common bile duct after removal of the stone. The third patient had complete biliary obstruction due to carcinoma of the head of the pancreas, but also had cirrhotic changes in the liver in consequence of the obstruction; cholecystostomy, as a preliminary to cholecystenterostomy, was performed.

*Group 3.* Increase in the biliary drainage, with paling and thinning of the bile, is one of the symptoms of postoperative hepatic insufficiency in cases of obstructive jaundice. Walters and Parham (1922) have pointed out the serious prognostic importance of cholerrhagia. This condition was present in the three cases in group 3 (tables 7, 8 and 9 and figures 1*C* and *D*). The patients gave a history of marked and painless jaundice of from two to six months' duration. In two cases there was a carcinoma of the head of the pancreas and cholecystostomy was done, preliminary to cholecystenterostomy. In the third patient there was a carcinoma of the common and hepatic bile ducts, and only choledochostomy could be done.

#### COMMENT

McMaster, Broun and Rous (1923) have described in detail the changes, in dogs, produced in the character of the bile as a result of obstruction to a permanent biliary fistula and the response to the relief of such an obstruction. They pointed out that with partial biliary obstruction there was a reduction in the output of pigments, of bile acids and of cholesterol, and to a much greater degree than that in the volume of bile, so that the fluid elaborated by the liver became progressively poorer in the typical biliary constituents. Because of the analogy with changes in the renal secretion incident to the develop-

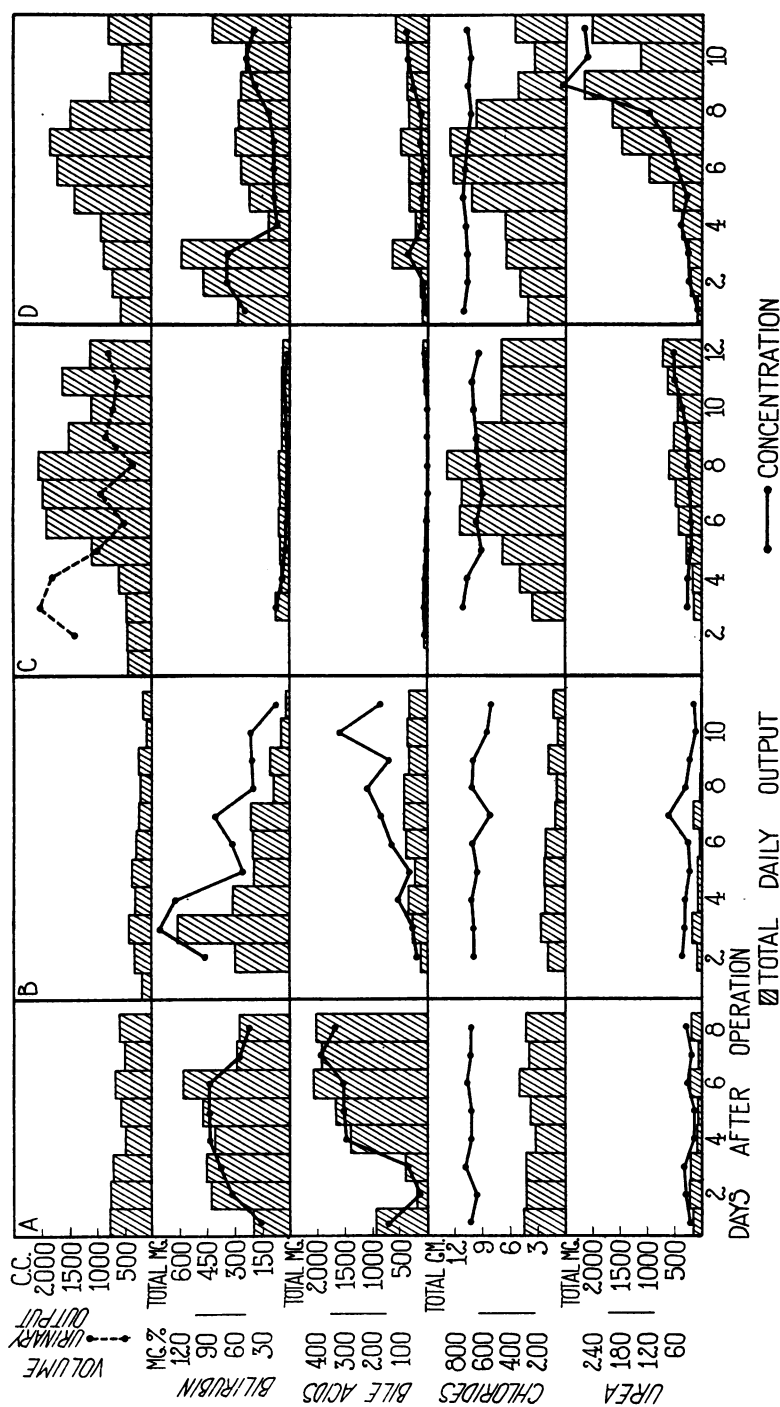


FIG. 1. THE COMPOSITION OF THE BILE FOLLOWING THE RELIEF OF BILIARY OBSTRUCTION

A, case of chronic cholecystitis with stone, illustrating group 1; B, case of chronic cholangitis with obstructive biliary cirrhosis, illustrating group 2; C, case of carcinoma of the pancreas with obstructive jaundice, illustrating cholerrhagia; the urinary output is shown; D, carcinoma of the common bile duct with obstructive jaundice, illustrating group 3 and the development of cholerrhagia and uremia.

ment of hydronephrosis, they used the term hydrohepatosis to designate the changes in the liver. They also pointed out that in the presence of complete biliary obstruction, the concentrating activity of the gallbladder may mask these changes either in whole or in part. Following relief of the biliary obstruction, a copious amount of bile was elaborated by the liver and the flow persisted until the greater part of the retained biliary constituents had been eliminated. This bile was more dilute than normal although the increase in volume was

TABLE 1  
*Summary of data in case 1 (group 1)*

Days after operation	Bile									Blood serum*		
	Volume	Bilirubin		Bile acids as glycocholic acid		Urea		Chlorides as sodium chloride		Bilirubin	Urea	Sodium chloride
		Concentration	Total	Concentration	Total	Concentration	Total	Concentration	Total			
		mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	grams			
1	650	31	200	145	940	25	162	693	4.50			
2	655	64	425	26	170	36	236	645	4.23			
3	600	75	450	70	420	39	234	723	4.35			
4	475	87	414	296	1,410	18	85	681	3.24		38	585
5	550	87	478	308	1,690	18	99	681	3.75			
6	675	87	587	308	2,080	32	216	708	4.77			
7	500	56	280	387	1,930	24	120	692	3.46			
8	600	45	270	339	2,040	36	216	687	4.13			

\* Before operation the following values in milligrams in each 100 cc. were determined: serum bilirubin, 2.8; blood urea, 24; serum chlorides as sodium chloride, 613.

such that the total output of pigment was increased during the period of choleresis.

Similar changes are found in many cases following the relief of biliary obstruction. The initial changes depend on the character of the bile present in the biliary tract at the time of operation. If it is thick and viscid as a result of the concentrating action of the gallbladder, there is an initial decrease in the concentration of the biliary drainage as this retained "stasis" bile is washed out (tables 1 and 2). If, on the other hand, "white" bile is present in the bile ducts, the fluid initially obtained may contain only minimal quantities of bili-

TABLE 2  
Summary of data in case 2 (group 1)

Days after operation	Bile									Blood serum*		
	Vol- ume	Bilirubin		Bile acids as glycocholic acid		Urea		Chlorides as sodium chloride				
		Concen- tration	Total	Concen- tration	Total	Concen- tration	Total	Concen- tration	Total			
		cc.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	grams	mgm. per 100 cc.	mgm. per 100 cc.
1	130											
2	190	128	244	138	262	50	95	689	1.31	1.3	25	511
3	250	97	243	134	335	37	92	617	1.54			
4	175	71	124	333	583	24	41	675	1.18			
5	215	51	110	397	855	20	43	675	1.45			
6	200	77	154	513	1,026	13	26	648	1.29			
7	175	101	177	545	955	21	37	611	1.07			
8	150	112	168	450	675	16	24	619	0.93			
9	150	103	155	800	1,200	13	20	628	0.94		24	549
10	145	62	90	1,064	1,540	8	12	539	0.78			

\* Before operation the following values in milligrams in each 100 cc. were determined: serum bilirubin, 1.5; blood urea, 25; serum chlorides as sodium chloride, 519.

TABLE 3  
Summary of data in case 3 (group 1)

Days after operation	Bile									Blood serum*		
	Vol- ume	Bilirubin		Bile acids as glycocholic acid		Urea		Chlorides as sodium chloride				
		Concen- tration	Total	Concen- tration	Total	Concen- tration	Total	Concen- tration	Total	Bili- rubin	Urea	Sodium chloride
	cc.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	grams	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.
1	200											
2	350											
3	365	44	160	66	240	50	183	619	2.26			
4	700	19	133	62	434	55	385	460	3.32	3.6	24	507
5	600	79	474	387	2,320	92	550	723	4.34			

\* Before operation the following values in milligrams in each 100 cc. were determined: serum bilirubin, 3.8; blood urea, 15; serum chlorides as sodium chloride, 1.

rubin or bile acids. The changes reported by Rosenthal, von Falkenhäusen and Freund (1926), and by Chabrol, Bénard and Bariéty (1926)

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TABLE 4  
Summary of data in case 4 (group 2)

Days after operation	Bile								Blood serum*			
	Vol- ume	Bilirubin		Bile acids as glycocholic acid		Urea		Chlorides as sodium chloride				
		Concen- tration	Total	Concen- tration	Total	Concen- tration	Total	Concen- tration	Total			
		cc.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	Bili- rubin	Urea
1	200											
2	320	94	300	40	128	51	163	663	2.12			
3	425	143	607	60	255	47	200	673	2.86			
4	325	98	319	106	345	46	150	691	2.25	3.7	36	519
5	365	51	186	68	248	30	110	645	2.35			
6	290	68	197	137	400	35	101	677	1.96			
7	250	83	208	174	435	78	195	575	1.44			
8	200	42	82	222	444	40	80	688	1.37			
9	250	46	115	141	353	30	75	680	1.70			
10	120	49	59	321	386	17	20	572	0.69			
11	200	16	32	173	346	20	40	541	1.08			

\* Before operation the following values in milligrams in each 100 cc. were determined: serum bilirubin, 2.1; blood urea, 24.

TABLE 5  
Summary of data in case 5 (group 2)

Days after operation	Bile									Blood serum*		
	Vol- ume	Bilirubin		Bile acids as glycocholic acid		Urea		Chlorides as sodium chloride				
		Concen- tration	Total	Concen- tration	Total	Concen- tration	Total	Concen- tration	Total			
	cc.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	Bili- rubin	Urea	Sodium chloride
1	450											
2	300	56	168	13	39	49	147	705	2.11	5.6	48	551
3	425	34	145	29	123	51	217	843	3.58			
4	350	57	200	71	248	26	87	723	2.53			
5	400	8	32	111	444	29	116	739	2.95			
6	615	11	68	45	277	20	123	600	3.69			
7	390	37	144	119	465	17	66	711	2.77			
8	320	12	38	88	281	35	112	751	2.40			
9	200	20	40			49	98	789	1.58			
10	325	22	71	112	364	27	88	702	2.28		42	592

\* Before operation the following values in milligrams in each 100 cc. were determined: serum bilirubin, 5.6; blood urea, 26.



were similar to those observed in group 1 in this series. In all (tables 1, 2 and 3, and figure 1A), there was a secretion of a moderate amount of bile of good color. There was a rapid increase in both the concentration and total output of bilirubin during the greater part of the first week with a subsequent decrease to the apparent normal level. This initial increase may be interpreted as evidence of a washing out of retained bile pigment, although it is recognized that some of the

TABLE 6  
*Summary of data in case 6 (group 2)*

Days after operation	Bile									Blood serum*		
	Vol- ume	Bilirubin		Bile acids as glycocholic acid		Urea		Chlorides as sodium chloride		Bili- rubin	Urea	Sodium chloride
		Concen- tration	Total	Concen- tration	Total	Concen- tration	Total	Concen- tration	Total			
		mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.			
1	250											
2	300	14	42	58	174	29	87	767	2.3			
3	325	20	65	57	185	15	50	767	2.5	11.0	19	
4	250	20	50	40	100	7	18	797	2.0			
5	270	29	80	36	96	15	40	787	2.1	10.0	19	559
6	300	6	78	29	90	14	42	781	2.3			
7	300	22	66	32	93	17	51	725	2.2			
8	270	17	47	36	98	14	38	741	2.0			
9	240	17	40	33	79	15	36	743	1.8			
10	280	13	35	37	103	19	53	760	2.1	8.2		
11	350	20	50	36	117	19	66	720	1.8			
12	300	29	89			28	81	761	2.2			

\* Before operation the following values in milligrams in each 100 cc. were determined: serum bilirubin, 16.2.

increase in bilirubin may be explained by hemorrhage and trauma at the time of operation. Both the concentration and the total output of bile salts were reduced in the bile first formed after the relief of the obstruction. Recovery was rapid, however, and within a week the concentration in the bile compared favorably with that seen in hepatic bile from normal dogs (tables 1, 2 and 3, and figure 1A). This concentration and the total output of bile would seem to be well maintained thereafter. These changes would seem to be typical of the

response when the obstruction to the biliary passages had not been sufficiently long continued or complete to produce permanent hepatic injury. Smyth and Whipple (1924) pointed out that in dogs a reduction in the excretion of bile acids is produced by a dose of chloroform so small as to be incapable of causing any recognizable structural change in the hepatic epithelium. Similarly, reduction or cessation in the production of bile acids would seem to be a characteristic effect

TABLE 7  
*Summary of data in case 7 (group 3)*

Days after operation	Urine in twenty-four hours*	Bile										Blood serum*		
		Volume	Bilirubin		Bile acids as glycocholic acid		Urea		Chlorides as sodium chloride					
			Concentration	Total	Concentration	Total	Concentration	Total	Concentration	Total				
	cc.	cc.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.
1		450												
2	1,425	475			13	62								
3	2,025	480	16	77	17	82	35	168	752	3.62	16.5	41		
4	1,800	650	9	58	11	71	35	227	711	4.62				519
5	1,000	1,100	5	55	4	44	25	275	609	6.70				
6	500	1,825	4	73	3	55	22	402	649	11.84				
7	950	1,950	3	59	1	19	26	506	601	11.70	13.5			
8	350	2,050	3	61	2	41	31	635	637	13.05				
9	850	1,550	3	46	1	16	33	512	641	9.95				
10	700	1,100	3	33	1	11	45	495	667	7.34	13.7	33		
11	650	1,650	4	46	6	69	60	690	685	7.87				
12	800	1,240	3	37	7	87	63	781	633	7.85	14.3	38	639	

\* Before operation the following values were determined: urine, cc. in 24 hours, 606; serum bilirubin, mgm. in each 100 cc., 25; serum urea, mgm. in each 100 cc., 15.

of biliary obstruction, and confirmation of this view is furnished by the experiments of Brakefield and Schmidt (1926) and of Snell, Greene and Rowntree (1927). If the injury to the liver in consequence of the obstruction is not too great, recovery is rapid and the concentration and total amount of bile acids in the bile rapidly return toward normal. In no case was there evidence for the washing out of any appreciable quantity of retained bile acids.

Hepatic injury and the development of obstructive biliary cirrhosis, as in the cases in group 2, modified the response of the liver to the relief of the obstruction (tables 4, 5 and 6, and figure 1*B*). The changes in the curve of excretion of bilirubin were not significantly different from those in the preceding group of cases although possibly the values were reduced slightly. Both the concentration and the total output of bile acids, on the other hand, were reduced and remained low throughout the period of observation. We believe this

TABLE 8  
*Summary of data in case 8 (group 3)*

Days after operation	Bile									Blood serum*		
	Volume	Bilirubin		Bile acids as glycocholic acid		Urea		Chlorides as sodium chloride				
		Concentration	Total	Concentration	Total	Concentration	Total	Concentration	Total	Bilirubin	Urea	Sodium chloride
		mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.
1	1,935											
2	3,025											
3	1,635	9	155			21	330			7.5	28	
4	1,540	10	155			21	320					
5	1,530	10	153	15	237	17	260	540	8.31	7.2	17	565
6	1,750	9	161	16	284	17	300	540	9.51	7.4	17	521
7	2,000	12	248	14	274	17	340	520	10.4	7.6	19	637
8	2,700	7	156	21	556	16	330	600	16.2	8.8	20	599
9	1,850	7	122	14	257	25	460	560	10.2	8.8	21	
10	2,800	6	162	20	550	26	730	560	15.6	9.2	32	563
11	2,400	6	130	7	350			580	12.2	9.8		

\* Before operation the following values in milligrams in each 100 cc. were determined: serum bilirubin, 14.2; blood urea, 13.

indicates failure of recuperation by the liver and so is further evidence of the functional disturbance produced by the combined effect of the biliary obstruction and infection present in these cases.

In the cases in which marked cholerrhagia developed, the changes in the composition of the bile were most marked (tables 7, 8 and 9, and figure 1 *C* and *D*). This supports the clinical impression that cholerrhagia is a symptom of serious hepatic dysfunction. In this condition the concentration and total output of bilirubin are somewhat reduced,

whereas the reduction in the bile acids is even more striking. Surgeons (Judd and Lyons, 1923) have recognized that the presence of white bile in the biliary tract ordinarily is evidence of the accumulation within the gallbladder and biliary passages of mucus and of the secretion of the mucous membrane lining these ducts, and this conception has been amply confirmed by the experimental studies of Rous and McMaster (1921). A second variety of white bile has been recognized, on the other hand, as occasionally appearing after the

TABLE 9  
*Summary of data in case 9 (group 3)*

Days after operation	Bile										Blood serum*		
	Vol- ume	Bilirubin		Bile acids as glycocholic acid		Urea		Chlorides as sodium chloride					
		Concen- tration	Total	Concen- tration	Total	Concen- tration	Total	Concen- tration	Total				
		cc.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm.	mgm. per 100 cc.	mgm. per 100 cc.	
1	550	50	292	14	77	15	82	757	4.17	7.0	37	589	
2	700	68	477	17	119	33	231	703	4.92				
3	875	68	595	71	622	30	263	707	6.20				
4	900	14	126	23	207	42	379	723	6.50				
5	1,400	16	224	22	308	39	546	740	10.35	5.0			
6	1,700	16	274	19	323	56	952	730	12.40				
7	1,825	16	292	27	493	80	1,460	707	12.90				
8	1,450	19	275	23	334	119	1,725	675	9.80				
9	710	36	256	50	355	304	2,160	703	5.00	5.8			
10	500	45	225	69	350	254	1,270	681	3.40				
11	760	36	374	71	540	263	2,000	707	5.38				178

\* Before operation the following values in milligrams in each 100 cc. were determined: serum bilirubin, 12.9; blood urea, 16.

institution of biliary drainage, and the data in case 7 illustrate the development of the latter condition. In this case the fluid secreted by the liver was almost completely acholic. Bile pigments were not present in as great a concentration as in the blood serum, whereas the sensitive Pettenkofer test showed the presence of but traces of bile acids. The characteristic constituents of the bile were entirely lacking, to all practical purposes, even though this deficient secretion was elaborated in considerable quantity. In this case, the development of

hydrohepatosis had apparently progressed to a stage of almost complete abolition of the biliary functions of the liver.

In all of these cases the concentration of urea in the bile was approximately equal to that in the blood, and the daily output was, therefore, determined by the volume of the bile. In one patient (case 9, figure 1*D*) postoperative renal insufficiency developed, and the concentration of urea in the blood increased to 300 mgm. in each 100 cc. The concentration of urea in the bile was increased in a similar manner. Marked cholerrhagia developed in this case at about the same time, with the result that the output of urea was increased to approximately 2 grams a day. Such an elimination of urea in the bile ordinarily would not be significant from the standpoint of renal function because the urea would be promptly reabsorbed on the passage of the bile into the intestine. In this case, however, the external drainage of the bile permitted vicarious elimination of the urea and consequent reduction in the burden borne by the kidneys.

Foster, Hooper and Whipple (1919) reported the development of abnormalities in the bones of dogs with prolonged external drainage of the bile. Only the excretion of chlorides in the bile was studied in the present series of cases. The concentration of chlorides in the bile was the same as, or slightly greater than, that in the blood serum, and was seemingly unaffected by such factors as changes in the food, the volume of the bile, or the intake of water or salt by the patient. The total output of chlorides in the bile varied between 1 and 4 grams. This is a quantity of salt that ordinarily would not be significant, although, if no salt were provided in the food, the loss might eventually become significant. The development of cholerrhagia, on the other hand, markedly increased the loss of chlorides; a maximal excretion of 16 grams in one day was observed and one patient lost 87 grams through the biliary tract in the course of a week. This is a quantity that would quickly lead to serious depletion of chlorides in the body if continued unchecked or unless the chlorides were replaced by the administration of appropriate amounts of chlorides, as was done in these cases.

In these cases oral administration of fluids was forced and an additional 1,000 cc. of a solution containing 100 grams of glucose and 10 grams of sodium chloride was given intravenously, so that the daily

intake of fluids varied between 3,000 and 4,000 cc. Notwithstanding this liberal intake of fluids, the output of urine frequently was reduced following the onset of cholerrhagia. This is shown in table 4. Under these conditions, unless care is taken to secure an adequate intake, there is danger of serious depletion of both fluids and salt in consequence of such cholerrhagia.

It is recognized that experiments such as these are open to many criticisms. The collection of bile from a drainage tube, inserted in the gallbladder or common bile duct, is not always complete. When the drainage is through the gallbladder, possible effects of the normal concentrating action of that viscus cannot be excluded. The amount and character of the bile are not the same when there is complete external drainage as when the bile enters the intestine and the normal enterohepatic circulation is uninterrupted.

Most of these criticisms are inherent in the nature of the problem to be studied and cannot wholly be avoided. It is believed, nevertheless, that the changes reported are sufficiently distinct to indicate the response of the liver of man to the relief of biliary obstruction, and some of the modifications of that response caused by various associated conditions.

#### SUMMARY

The composition of the bile following the relief of biliary obstruction was studied in a series of nine cases.

The total daily output of bilirubin was more or less constant and was not related to the other factors studied in this series of cases. The concentration, on the other hand, varied inversely with the volume of the bile. One or two patients showed some evidence of a washing out of retained pigment, but if this occurred in all it took place so slowly as not to be apparent in observations of as short duration as these.

Biliary obstruction inhibits or stops the formation of bile acids. If the liver is not too greatly injured there is a relatively rapid return to normal; otherwise the return is greatly delayed. This was true both with regard to the concentration and total amount of bile acids.

The concentration of chlorides in the bile is slightly greater than that in the blood serum. With cholerrhagia, the resultant loss of

salts becomes so great as to be of clinical significance. The loss of fluids by this channel may also be so great as to cause diminution in the output of urine.

The concentration of urea in the bile apparently varies directly with that in the blood. Ordinarily this pathway of elimination is not significant, but in one case there was considerable loss of urea through the fistula.

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