STUDIES OF GALLBLADDER FUNCTION. XV. CHOLESTEROL IN HUMAN LIVER BILE

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The subject of bile drainage in the human has been very thoroughly reviewed by Fox (1) in 1928. Numerous papers have appeared, among which may be mentioned those of Walters, Green and Frederickson (2), Ravdin, Johnston, Riegel and Wright (3), and Elman and Graham (4), describing the changes occurring in hepatic bile obtained from patients with surgical drainage after the release of biliary obstruction in a varying number of cases. The data include, in addition to measurement of volume output, analyses for pigment, bile acids, chlorides and urea. Analyses for content of cholesterol, admittedly an important constituent of bile in its relation to stone formation, are few in number and usually absent in most of the papers cited. The present paper is a report of the daily variation in cholesterol concentration in hepatic bile of patients after some type of external biliary drainage.

METHODS

Thirty-two patients with external biliary drainage following operation are included in this study. The types of external drainage were as follows.

1. *Cholecystostomy.* Tube inserted into gallbladder through the fundus. The tip of the tube in some instances rested in the lumen of the gallbladder nearer the fundus than the cystic duct and in other instances the tip of the tube was pushed down into the cystic duct. Six cases of Type I (Figure 1) and 7 cases of Type II (Figure 2) are included.

2. *Choledochostomy and cholecystectomy*—Eight cases. The gallbladder was removed, and a T tube inserted into the common duct, the tip resting just below the junction of cystic duct and common duct (Type III, Figure 3).

3. *Combination of choledochostomy and cholecystostomy*—Seven cases (Type IV, Figure 4).

4. *Cholecystectomy and cholecystodochostomy.* In two instances the tube was inserted through the remaining stump of the cystic duct (Type V, Figure 5).

5. *Cholecystodochostomy and choledochostomy* —Two cases (Type VI, Figure 6). The bile obtained from Types II, III, V, VI and the common duct tube of IV, can be considered to be similar as in these cases the bile obtained does not enter the gallbladder. There is a possibility that in Type I and in the gallbladder tube of Type IV the bile may remain in the gallbladder for a time and be altered in its composition.

It was, of course, impossible in all instances to obtain the complete twenty-four hour output, as some bile passes down the common duct into the intestine in all cases where there is not complete

FIGS. 1 TO 6. METHODS OF INTUBATING THE EXTRA HEPATIC BILE PASSAGES

TABLE I

Cholesterol concentration, fluid intake and amount of drainage

Patient	Days after operation	Type of drainage	Cholesterol	Fluid intake	Drainage
			mgm. per cent	*cc.*	*cc.*
H. L.		Gallbladder			
	1		34	4760	100
	2			2060	30
	3			2240	50
	4		29	2200	50
	5			2300	150
	6		75	2550	75
	7			2320	100
	8		60	2750	100
	9		70	2230	75
	10			1920	50
	11		73	1840	75
	12		51	3250	
R. C.		Common duct			
	2		61	5210	
	3		57	5630	200
	4		96	4910	250
	6		86	2640	125
	7		103	2810	10
	8		67	2810	80
	9		93	2110	30
	10		61	1540	180
	11		83	2140	180
	12		86	1830	275
	13		83	1470	550
	14		90	1600	300

obstruction of the lower end of that duct. Furthermore, for twenty-four to forty-eight hours after common duct intubation there may be some leakage of bile. In only two of the cases here reported was the common duct completely obstructed, and the bile drainage in these must closely approximate the complete daily twenty-four hour excretion. In all other instances only concentration of cholesterol could be determined. In a number of instances the first 2 or 3 specimens were contaminated with blood. Where this was the case the results were not considered in the following discussion.

In many instances the daily fluid intake of the patient was recorded, in order to determine its effect upon the concentration of cholesterol in the bile excreted. In some patients a portion of the collected bile was re-introduced through a Jutte tube, into the stomach. A record of this was kept and its effect on cholesterol concentration studied. Determinations of bile salt were made by the Gregory and Pascoe method (5). Cholesterol determinations were made as described by Riegel and Rose (6).

RESULTS

Daily analyses of cholesterol concentration in drainage bile show not only that there is considerable variation between different patients but also that in the same patient the concentration may vary widely from day to day. Attempts to correlate these variations with alterations in other factors such as fluid intake, amount of external bile drainage, etc., were unsuccessful. The only correlation which appeared significant was with the amount of liver damage demonstrable at the operation.

A. Variations in concentration in the same patient. In Table I and Figures 7 and 8 are given the concentrations of cholesterol and fluid intake and amount of external bile drainage in two pa-

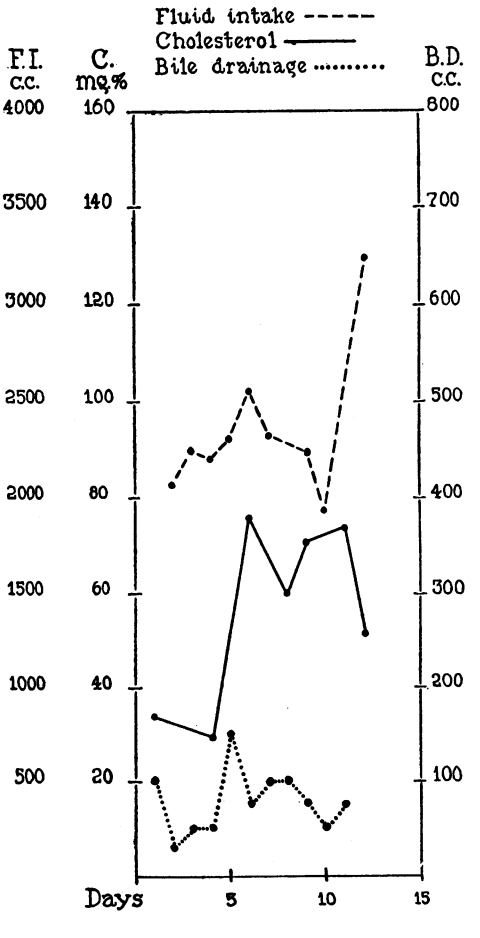

FIG. 7. FLUID INTAKE, CHOLESTEROL CONCENTRATION AND BILE DRAINAGE IN PATIENT H. L.

TABLE II

Variations in cholesterol concentration with extent of liver damage

Daily concentration of cholesterol (*mgm. per cent*)														
Slightly damaged				Moderately damaged				Badly damaged						
Patient E. P.	Patient C. W.	Patient F. B.	Patient B. G.	Patient B. D.	Patient M. F.	Patient D. C.	Patient F. M.	Patient R. G.	Patient H. I.	Patient W. R.	Patient N. A.	Patient B. M.	Patient R. S.	Patient W. W.
126	133	61	8	40	86	180	59	27	26	10	30	39	67	38
58	118	158	30	43	17	61	47	35	12	14	13	41	36	35
76	99	153	19	133	37	57	200		13	9	13	35	32	26
101	115	144	15	150	87	96	108		19	12	14	47	38	20
114	83	123	21	106	133	86	119		22	16	13	29	29	11
132	158	137	67	92	112	103	218		23	16	9	30	30	29
96	172	21	85	84	155	67			29	15	13	30	31	23
82	127	126	77	174	136	93			34	6	11	30	35	50
83	70	98	90	154	126	61			49	14	20	33	35	35
	200	62	133	108	146	83			53	9	11	39	23	
	225		71	90	159	86			53		25	47	50	
	240		47	133	154	83			47		9	62	39	
	211		154	198	170	90			54		5	72	36	
	139		57		152	169			48		14	48	19	
	152				123	110			70			80	14	
	214				76	123			65			63	27	
	82											49		
	128											47		
												45		
												51		
												51		
												58		
												62		
												42		
												28		

tients studied. In the first patient, cholesterol concentration varied from 29 to 75 milligrams per cent, and in the second, from 57 to 103. One might expect that with greater fluid intake the volume of the collected bile would be greater, and the concentration of the bile constituents lower. No such relationship was found in these patients.

There is considerable daily variation in the amount of bile drainage through the collecting tube, but no relationship between this and the cholesterol concentration could be demonstrated.

The daily variations in cholesterol concentration agree with the data reported by Elman and Taussig (7) in the two patients they studied, and the data obtained by McMaster (8) from the dog.

There is a suggestion of correlation between the condition of the liver and its ability to function, and the concentration of cholesterol. In most of the patients the samples of bile collected in the first two or three days after operation, before the liver had begun to recover from the effects of obstruction, were lower in cholesterol concentration than subsequent samples obtained at a time when hepatic function was improving.

B. Variations in concentration in different patients. When the patients were grouped according to extent of liver damage, as observed at operation, the seven patients known to have badly damaged livers had extremely low concentrations of cholesterol in the bile, while in the moderately or slightly damaged groups the concentrations on the whole were considerably higher. In Table II are given the data from the seven patients with a badly damaged liver, together with the data from four patients with a moderately damaged liver and four patients with a slightly damaged liver.

Table III shows that refeeding bile to the patients has little effect on cholesterol concentration, although Whipple (9) has shown that feeding bile salts to dogs increases cholesterol output.

One must take into account the fact that the bile which was refed, the patient's own bile, was not normal and almost certainly contained at least

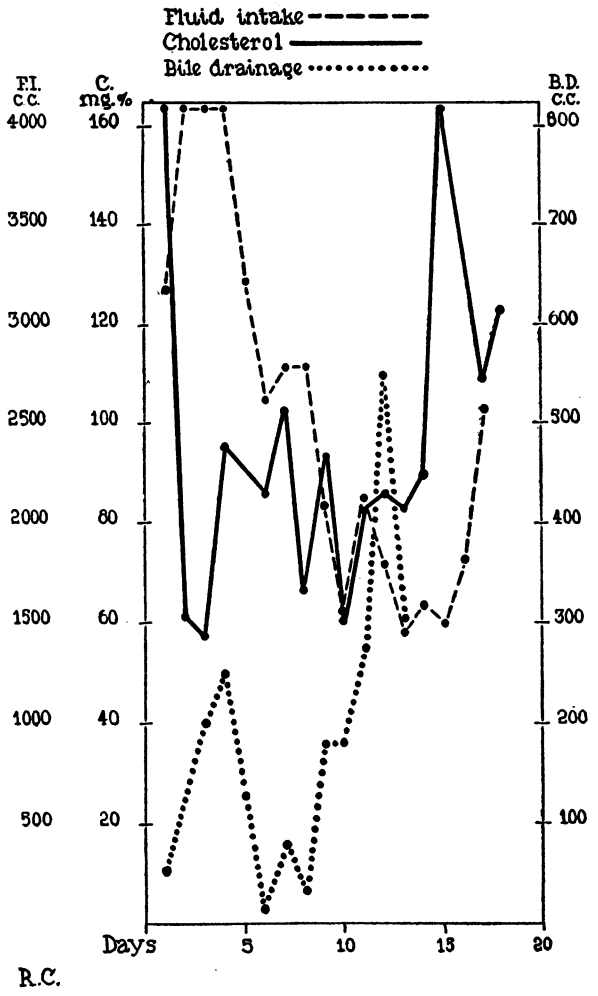

FIG. 8. FLUID INTAKE, CHOLESTEROL CONCENTRATION AND BILE DRAINAGE IN PATIENT R. C.

for a time, little or no bile salt. In fact, at all times during these experiments it contained considerably less than the normal amount of bile salt (3). The feeding of a bile high in bile salt concentration would perhaps have caused an increase in concentration of cholesterol, such as Whipple (9) reported in dogs.

This viewpoint is strengthened by the comparison of the concentrations of bile salt and cholesterol (Figure 9). In general, the concentrations of bile salt and cholesterol in the same patient varied directly with each other, the patients with the higher cholesterol concentrations having higher bile salt concentrations. There is, however, no correlation between the absolute amounts

TABLE III

Effect of feeding patient's bile on cholesterol concentration

Patient	Liver	Days after operation	Cholesterol	Bile refed
				cc.
B. D.	Moderate damage	5	43	0
		8	133	0
		9	150	0
		11	106	100
		12		50
		13	92	200
		14		200
		15		200
		16		200
		17	84	200
		18		200
		19	174	200
		20		200
		21	154	200
		22		200
		23	108	200
		26	90	0
		28	133	0
		29	198	0
				Feeding continued for three weeks
W. R.	Badly damaged	4	38	850
		5		800
		6	35	500
		10	26	500
		12	20	500
		15	11	500
		18	29	500
		21	23	500
		26	50	500
		29	35	500

TABLE IV

Twenty-four hour output of cholesterol in total liver bile

Days after operation	Drainage	Cholesterol concentration	Cholesterol per 24 hours
	cc.	*mgm. per cent*	*mgm.*
	PATIENT W		
4	400	38	152
6	900	35	315
10	1100	26	286
12	1600	20	320
15	2700	11	297
18	1500	29	435
21	3500	23	805
26	3000	50	1500
	PATIENT M		
5	350	39	137
7	350	41	144
9	450	35	158
11	300	47	141
13	500	29	145

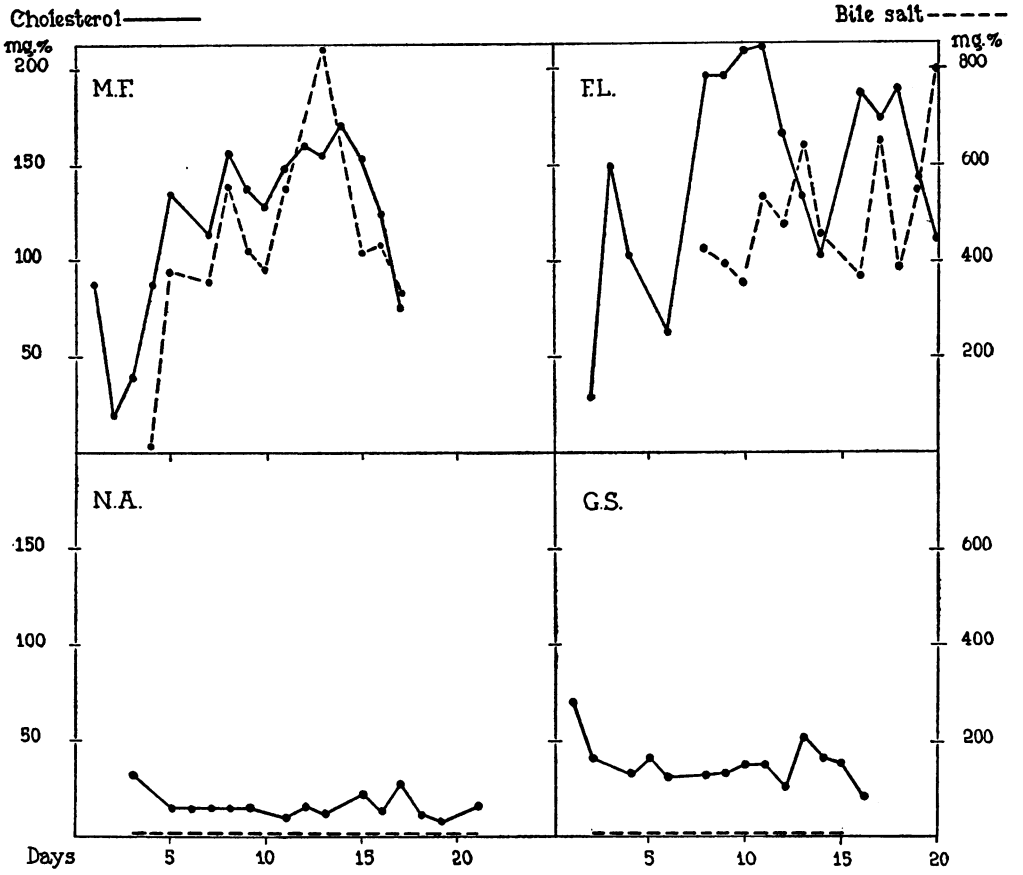

FIG. 9. COMPARISON OF CONCENTRATIONS OF CHOLESTEROL AND BILE SALT IN FOUR PATIENTS

of bile salt and cholesterol; that is, one cannot predict from a given concentration of cholesterol what the level of bile salt will be, or vice versa.

Twenty-four hour bile excretion. In two patients whom we studied there was complete obstruction of the common duct due to a lesion in the head of the pancreas, and the bile collected represents the complete twenty-four hour output of the liver. Table IV shows the concentrations and total amounts of cholesterol in the bile from these two patients.

SUMMARY

The data reported in this paper were obtained from patients who had some disease of the biliary tract with or without complete obstruction of the common bile duct prior to operation. Even in those patients whose total hepatic excretion of bile was collected the amount varied considerably from day to day. The amount of bile collected by external drainage was not directly related to the fluid intake of the patient.

Cholesterol concentration as well as total output of cholesterol in the liver bile, where this could be determined, varied in the same patient and in different patients, from day to day. In general the more severely damaged the liver, the lower was the cholesterol concentration in the liver bile, and the lower was the concentration of bile salt.

The feeding of the patients' own bile, while without doubt of value as far as the patients' clinical improvement was concerned, did not result in an elevation of the cholesterol concentration in the liver bile.

The study of the cholesterol-bile salt concentrations should prove of real value in determining the functional state of the liver when common duct drainage has been instituted.

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