after removal of the liver. Fourteen minutes later there was profuse salivation and after a latency of 47 minutes it almost vomited; at the end of 2 hours it died in a vomiting-like convulsion. The fourth cat, in apparently good condition, received 0.25 mg. per kg. by muscle 7 hr., 45 min., after liver removal. Although the dose was repeated twice a half-hour or so after the first injection no emesis resulted; however, there was marked tachypnoea.

From the results of the denervation work it is probable that if actual complete denervation of the liver in the cat could be attained strophanthidin would still cause emesis; the dehepatization experiments lend support to the conclusion. Although each of the 2 dehepatized cats which vomited received double the normal minimal emetic dose, in order to increase the probability of response, it does not necessarily follow that the operated cats were greatly depressed. Nevertheless, the negative results in the fourth cat suggest that the abnormal metabolic state had lowered the reactivity, as one would expect.

Conclusion. Strophanthidin can induce emesis in cats after very extensive denervation of the liver, and also after dehepatization, thus confirming the results Hanzlik and Wood obtained with pigeons. How the vomiting is brought about in animals deprived of the liver, or its nerve supply, is a problem for further study.

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Presence of Cholesterol in Combined Form in Human Bile.*

CECILIA RIEGEL, I. S. RAVDIN AND HENRY J. ROSE.

From the Harrison Department of Surgical Research, Schools of Medicine, and the Hospital of the University of Pennsylvania.

Early reports of the presence of cholesterol esters in bile have been questioned because the methods used for the determination of esters were open to criticism. Later work by Thannhauser[1] indicates that human bile contains only free cholesterol. A recent paper by Wright[2] reported that the cholesterol present in dog bile is also present as free cholesterol. He was unable, using an improved method of analysis, to find any evidence of cholesterol esters. In

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1 Thannhauser, S., *D. Arch. Klin. Med.*, 1922-1923, **141**, 290.

2 Wright, A., *J. Exp. Med.*, 1934, **59**, 407.

the last 2 years, using a method which has been demonstrated to be satisfactory for determination of esters in bile,[3] we have investigated a large number of bile specimens from patients with biliary fistulae. The data reported in this paper indicate that under rare conditions cholesterol may occur in human liver bile in a combined form.

With one exception all the patients from whom bile was collected had either had a cholecystostomy or choledochostomy. These patients had either simple gallstone disease, with or without cystic duct block, common duct stone, with or without obstruction, or malignant disease of the head of the pancreas. In one instance the biliary symptoms were very mild, but exploration was advised in the hope that the cardiac symptoms from which the patient suffered were in part due to chronic gallbladder disease. The gallbladder did not appear to be diseased when examined at operation, but a cholecystostomy was done following exploration of the interior of the gall bladder wall.

A bile sample was collected almost daily from each patient, and analyzed for concentration of free and total cholesterol. The method of analysis was that described by Riegel and Rose.[3]

In Table I are given the results of analyses of bile from a number of these patients. In all, the bile from 32 patients was studied, although not all analyses are included in the table.

It will be observed that of the 10 patients listed first in the table, none showed the presence of esters of cholesterol after the first few days. In each of these the bile for from one to 4 days after operation was contaminated with blood and we believe that the small amount of ester which was frequently found during this period can be attributed to the presence of blood in the bile specimens.

However, the patient, F. B., whose bile is that reported last in the table, presents a different picture. Here, cholesterol in the combined form was present in all the specimens collected up to the time the drainage tube was removed 17 days after operation. No contamination of this bile with blood was noted at any time, except possibly the very first specimen obtained immediately after operation.

Bile removed from this patient's gall bladder at operation also presented an unusual picture. The total concentration of cholesterol was 2480 mg. %.

The case described presents an unusual finding and one which we believe has not been reported previously in the literature. The patient, who differed from the others in that she had angina pec-

[3] Riegel, C., and Rose, H. J., *J. Biol. Chem.*, 1936, **113**, 117.

TABLE I.

Patient	Bile obtained from	Days After	Cholesterol Total mg. %	Cholesterol Free mg. %	Cholesterol Ester mg. %
K.K.	Common Duct	10	128	127	0
	" "	15	109	109	0
	" "	17	107	107	0
	" "	21	102	102	0
	" "	31	179	181	0
	" "	35	130	130	0
G.S.	" "	3	31	29	0
	" "	8	79	78	0
	" "	16	81	81	0
A.S.	Gall Bladder	2	50	50	0
	" "	10	202	200	0
	" "	15	188	186	0
B.G.	" "	13	112	110	0
	" "	17	175	174	0
	" "	19	136	135	0
E.P.	Common Duct	1	126	125	0
	" "	4	58	57	0
	" "	12	114	115	0
	" "	17	96	96	0
	" "	21	83	84	0
W.W.	Gall Bladder	4	38	36	0
	" "	6	35	34	0
	" "	10	26	26	0
	" "	12	20	21	0
	" "	15	11	12	0
	" "	18	29	28	0
	" "	21	23	23	0
	" "	26	50	50	0
	" "	29	35	35	0
M.Y.	" "	6	124	126	0
	" "	9	216	216	0
	" "	12	216	220	0
	" "	13	163	163	0
D.B.	Common Duct	5	43	44	0
	" "	8	133	134	0
	" "	9	150	150	0
	" "	29	198	197	0
I.H.	" "	2	26	26	0
	" "	18	53	53	0
R.W.	" "	14	9	8	0
	" "	18	12	11	0
	" "	31	15	14	0
	" "	36	14	15	0
F.B.	Gall Bladder	6	153	124	+29
	" "	9	144	128	+16
	" "	10	123	95	+28
	" "	11	137	80	+57
	" "	12	21	13	+ 8
	" "	13	126	82	+44
	" "	15	98	32	+66
	" "	17	62	27	+35

toris, had only mild biliary symptoms, had no stones, no obstruction of the biliary tract, and had an apparently normal gall bladder and liver. The fact that bile from such a patient contained cholesterol in a combined form may indicate:

1. Patients with angina pectoris may have such an excess of cholesterol ester in the blood that the liver is unable to handle it, and hence some ester spills over into the bile. Total blood cholesterol of this patient, however, varied from 268 to 316 mg. %. While distinctly above the normal, the blood cholesterol cannot be considered excessively high. Of the 268 mg. per 100 cc. of blood, 86 mg. % was free, and 182 mg. % combined cholesterol (67% of total), which is considered a normal distribution.

2. It is possible that normal human bile may contain esters. The remainder of the bile specimens were from patients with diseased biliary tracts. Against this, is the fact that normal dog bile contains no ester. One might also expect that, as the liver began to recover from the effects of obstruction, cholesterol esters might begin to appear in the bile if they are normally present. This has never been observed in any of the patients we have studied, although specimens obtained as late as 191 days after operation have been analyzed.

3. Absence of the enzyme "cholesterolesterase" described by Thannhauser. This seems with our present knowledge the most logical deduction. Further studies of incubation of this bile with blood have a bearing on this phase of the subject and will be reported later.

Summary. In the majority of specimens of drainage bile obtained from biliary fistulae in the human patient, cholesterol is present only in the free form unless the bile is contaminated with blood. One case is reported of the occurrence of combined cholesterol in bile draining from a cholecystostomy.