THE LIVER LIPIDS AND THEIR DISTRIBUTION IN DISEASE. AN ANALYSIS OF 60 HUMAN LIVERS[1]

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The lipid distribution in normal human livers and in cases of cirrhosis and fatty infiltration of the liver was reported in a previous study (1). As a corollary to these observations, the livers of patients dying from other diseases were analyzed for their lipid content and distribution. The question as to whether diseases other than those directly affecting the liver may alter the lipid content and its distribution in the liver is of interest because the functions of the liver are so varied that it tends to be involved in almost any profound disturbance in the body.

The clinical methods available for determining the function of the liver in relation to fat are limited. At present, the most satisfactory index of a lipid disturbance is the ratio of free to total cholesterol in the plasma. This is altered in cirrhosis, fatty infiltration of the liver, and in parenchymatous liver disease (2), but this ratio does not give information as to the total lipid content of the liver, or the other lipid fractions.

The determinations that we are reporting were made to ascertain the changes that might occur in the liver lipids in diseases other than those directly affecting the liver. These values are compared to the normal liver lipid values obtained by analysis from a group of 25 normal subjects reported in the previous study (1). The average total liver lipid for this group of normals was 4.98 grams per 100 grams of wet liver. The range was from 2.42 to 8.41 grams per cent. The average fatty acids were 3.50 grams per cent, the average phospholipids 2.08 grams per cent, and the average neutral fat 2.26 grams per cent; the average total cholesterol was 283 mgm. per cent and the average free cholesterol 204 mgm. per cent.

Liver samples were obtained in almost all of the cases within 24 hours after death. As reported previously (1), the fraction which is most subject to change as a result of standing is the phospholipid fraction, which tends to decrease after about 5 hours. There seems to be no further decrease after 24 hours. Lipids and their fractions were done by the methods previously described from this laboratory (3).

Samples of liver were obtained from patients dying of the following diseases: (*1*) Acute infections, such as meningitis, pneumonia, peritonitis, and septicemia; (*2*) chronic infections, including tuberculosis, subacute bacterial endocarditis, syphilis and osteomyelitis; (*3*) malignancy; (*4*) metabolic diseases; and (*5*) cardiovascular diseases. The diseases of 4 of the patients in the metabolic group were complicated by an acute infection (Numbers 3, 7, 54, 88), and 2 (Numbers 10 and 92) cases in this group also had some form of heart disease. The liver values for these 6 cases are entered in both pathological groups. The acute infections were subdivided into two groups, as 5 of these patients were diagnosed pathologically as having fatty infiltration or cirrhosis of the liver.

RESULTS

In Table I are the findings in 21 cases in whom death was due to some acute infection. Of these 21 cases, 16 had no evidence of cirrhosis or fatty infiltration of the liver. The average weight of the livers in this group was 1760 grams. The lowest weight was 1400 grams and the greatest was 2900 grams. The average total liver lipid was 4.72 grams per cent. In one liver the total lipid was 9 grams per cent, but in the majority of the group the total lipid was 5 grams per cent or less. The lowest lipid value in the group was 2.3 grams per cent. The average phospholipid was 1.89 grams per cent and the average of the neutral fat was 2.41 grams per cent. The total cholesterol averaged 269 mgm. per cent. These

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TABLE I

Acute infections with and without cirrhosis or fatty infiltration of the liver

Number case	Age	Sex	Nutrition of patient	Weight of liver	Total lipid	Unsaponified	Fatty acid	Cholesterol		Phospholipids	Neutral fat	Pathological findings and diagnoses
								Free	Total			
				grams	*grams per cent*	*grams per cent*	*grams per cent*	*mgm. per cent*		*grams per cent*	*grams per cent*	
ACUTE INFECTIONS WITHOUT CIRRHOSIS OF THE LIVER												
3	50	M	Fair	1770	4.96	0.62	4.46	189	259	1.65	3.48	Meningococcus meningitis, diabetes mellitus
9	65	M	Poor	1650	2.44	0.80	1.92	231	232	1.11	1.24	Streptococcus hemolyticus endocarditis, chronic passive congestion of liver
19	18	F	Good	1780	7.00	0.14	5.51		415	3.61	2.98	Staphylococcus aureus septicemia
59	32	M	Fair	1860	4.51	0.66	3.16		208	1.75	2.13	Bronchopneumonia, tetanus, normal liver
42		M	Good	1750	5.52	0.60	4.40		298	1.86	3.29	Lobar pneumonia
51	35	M		1800	5.60	0.65	4.87		210	1.46	4.10	Post-operative peritonitis
86	40	M	Good	1450	9.05	0.82	7.33					Pneumonia, normal liver
54	45	F	Obese	2900	3.39	0.54	2.26		232	1.87	1.07	Liver abscesses, enlarged liver, chronic cholecystitis
29	45	M		2050	3.15	0.72	2.17		263	1.22	1.46	Staphylococcus aureus septicemia, abscesses and areas of infarction in liver
23	50	M	Poor	2740	3.63	0.64	2.70		287	2.80	0.92	Lobar pneumonia, CPC of liver
88	67	F	Obese	1400	3.92	0.78	2.69					Bronchopneumonia, normal liver
67	50	M	Fair	1640	4.86	0.69	3.43			2.08	2.12	Generalized peritonitis, rupture of ileum
70	50	M	Good	1370	4.75	0.67	3.59			1.15	2.93	Pneumonia
93	78	M	Fair	1350	3.48	0.78	2.08					Lobar pneumonia, cardiac failure, normal liver
18	53	M	Good	1440	6.91	0.71	4.45		287	2.06	3.20	Purulent meningitis, fracture of skull, normal liver
105	71	M	Poor	1300	2.35							Acute cystitis, purulent
Average	50			1760	4.72	0.65	3.67	210	269	1.89	2.41	
ACUTE INFECTIONS WITH CIRRHOSIS OR FATTY INFILTRATION OF THE LIVER												
56	35	F	Poor	2450	11.50	0.84	10.20.		337	1.99	9.28	Streptococcus meningitis, fatty and cirrhotic liver
31	38	M	Good	1650	7.68	0.74	6.72		338	1.80	5.71	Lobar pneumonia, cirrhosis of the liver
75	41	M	Poor	1910	16.10	0.39	14.90					Chronic alcoholism, lobar pneumonia, fatty liver
58	50	M	Poor	1950	28.10	1.00	25.50		389	1.97	25.30	Alcoholism, lobular pneumonia, fatty and cirrhotic liver
30	65	F	Poor	1170	14.05	0.97	13.60		238	2.53	12.50	Lobular pneumonia, fatty liver, Paget's disease
Average	43			1835	15.48	0.79	14.18		326	2.07	13.20	

figures are almost identical to the average of the values obtained in the 25 normal subjects. In the 5 cases in whom there was cirrhosis or fatty infiltration of the liver there was a definite increase in the total lipid and fatty acids. The average total liver lipid for the group was 15.48 grams per cent. The phospholipids were a trifle higher than in the other patients dying of acute infections, and the neutral fat was, of course, increased, since any increase in total lipid is due outstandingly to the increase in the neutral fat fraction. The average of the total cholesterol was increased.

These figures correspond with the liver lipid values obtained in the 25 alcoholic patients reported previously, with the exception that the phospholipid fraction is somewhat higher in this group of 5 cases. Free cholesterol determinations were not done in these 5 cases but any increase in the total cholesterol is probably due to an increase in the esterified fraction.

A report of the determinations on 10 cases dying of chronic infection is made in Table II. Of these, 3 had tuberculosis, 1 had a lung abscess, 2 had endocarditis, 1 had a bronchiectasis, 1 died of malaria, another of luetic heart disease, and 1 of chronic cholecystitis. In 3 of the patients the total lipid in the liver was increased. One of these was the case with lung abscess, and the other

TABLE II

Chronic infections

Number case	Age	Sex	Nutrition of patient	Weight of liver	Total lipid	Unsaponified	Fatty acid	Cholesterol		Lecithin	Neutral fat	Pathology of the liver and other disease processes
								Free	Total			
				grams	*grams per cent*	*grams per cent*	*grams per cent*	*mgm. per cent*		*grams per cent*	*grams per cent*	
7	57	M	Obese	1440	4.03	1.06	2.33	294	323	1.43	1.43	Bronchiectasis, cerebral arteriosclerosis
11	62	M	Poor	1370	12.05	1.32	10.80	221	312	0.87	10.70	Lung abscess
36	43	M	Poor	2000	3.24	1.20	2.29		242	1.77	1.16	Subacute bacterial endocarditis, aortic valvulitis
73	41	M	Good	1620	2.22	0.55	1.41			1.16	0.64	Malaria, liver normal
78	30	M	Good	2090	3.43	0.58	2.50					Chronic cholecystitis, emphysema, liver normal
97	27	M	Good	1550	4.44	0.74	2.96					Luetic aortitis, liver normal
82	45	M	Good	1720	15.27	0.58	14.13		265			Chronic alcoholic, pulmonary tuberculosis; fatty liver
84	38	M	Good	1850	13.30	0.59	11.91					Chronic alcoholic, pulmonary tuberculosis
95	49	M	Poor	2330	3.43	0.65	2.09					Osteomyelitis, endocarditis, slightly fatty liver
21	23	F	Good	1430	3.59	0.61	2.06			2.65	0.28	Tuberculous meningitis and peritonitis, fatty liver with perihepatitis
Average	41			1760	6.90	0.76	5.63	258	279	1.98	2.33	

2 were chronic alcoholics who had pulmonary tuberculosis. In the remaining cases, the total lipid was lower than the average for the normal livers, being about 3 grams per cent in most of the cases. The 2 patients who were chronic alcoholics also had pulmonary tuberculosis. As it was noted in the previous study that an increase in liver lipid was found in the livers of patients with a history of chronic alcoholism, it is probable that tuberculosis was not the cause of this increased lipid.

There were 7 patients dying with some form of malignancy (Table III). One of the cases, a patient with lymphosarcoma and metastatic nodules in the liver, had a total liver lipid of 15 grams per cent. It is interesting that most of these patients, several of whom had metastatic involvement of the liver, showed no change in the lipid content of the liver or its distribution. In 2 of the cases the total lipid values were somewhat lower than the usual normal values.

Table IV gives the observations on 12 patients with some metabolic disturbance. Three of these patients had diabetes, 8 were obese and had some other disease process, and 1 was a patient with Paget's disease of the bone. Interestingly enough, none of the diabetic patients had an increase in the total liver lipid. In 3 patients in this group the total liver lipids were elevated. Of these, 1 was the patient with Paget's disease, 1 was a patient with obesity, and 1 was a patient with coronary thrombosis and obesity. Four of the obese patients were killed in accidents, and no other pathological changes were found.

Table V presents the findings on 16 patients dying from some form of cardiovascular disease. Four of these had elevated total liver lipids; of these 4, 2 had coronary sclerosis (1 of whom in addition was an alcoholic), 1 had a coronary thrombosis, and 1 died of hypertensive heart disease. The last subject was also obese. The aver-

TABLE III

Malignant diseases

Number case	Age	Sex	Nutrition of patient	Weight of liver	Total lipid	Unsaponified	Fatty acid	Cholesterol		Lecithin	Neutral fat	Pathology of the liver and other disease processes
								Free	Total			
				grams	*grams per cent*	*grams per cent*	*grams per cent*	*mgm. per cent*	*mgm. per cent*	*grams per cent*	*grams per cent*	
14	67	F	Poor	920	15.03	1.27	12.55	253	301	1.79	11.90	Lymphosarcoma, metastatic nodules in the liver, fatty infiltration, early cirrhosis
40	59	F	Fair	1800	3.29	0.62	2.00		273	2.30	0.51	Leukemia with involvement of spleen, bone marrow, lymph nodes and liver
62	58	M	Poor	1600	3.22	0.73	2.02			1.63	0.95	Carcinoma of stomach with metastases to ribs and spine
64	45	M	Poor	2250	3.22	0.75	2.02			2.27	0.15	Carcinoma of larynx with metastases to lungs and liver
68	83	M	Poor	1120	4.03	0.74	2.38			2.44	1.62	Carcinoma with metastases to lungs and lymph nodes
103	55	M	Poor	2550	2.45							Hypernephroma, no metastasis to liver
109	56	M	Good	4000	2.82		2.14		247	1.04	1.53	Carcinoma of gall bladder with metastases to liver, ascites, jaundice
Average	60				4.86	0.82	3.85	253	274	1.91	2.78	

TABLE IV

Disease of metabolism

Number case	Age	Sex	Nutrition of patient	Weight of liver	Total lipid	Unsaponified	Fatty acid	Cholesterol		Lecithin	Neutral fat	Pathology of the liver and other disease processes
								Free	Total			
				grams	*grams per cent*	*grams per cent*	*grams per cent*	*mgm. per cent*	*mgm. per cent*	*grams per cent*	*grams per cent*	
2	56	F	Poor	1475	3.59	0.77	2.16	253	253	1.86	0.97	Diabetes mellitus, diabetic ketosis, normal liver, cholelithiasis
3	50	M	Fair	1770	4.96	0.62	4.46	189	259	1.65	3.48	Diabetes mellitus, meningococcus meningitis, pericentral atrophy of the liver
7	57	M	Obese	1440	4.03	1.06	2.33	294	323	1.43	1.43	Diabetes mellitus, mild obesity, lobular pneumonia, hypertensive and arterial heart disease
10	50	F	Obese	1330	7.43	0.83	6.17	259	335	1.31	5.52	Arteriosclerotic heart disease, obesity, CPC of liver
22	50	M	Obese	1875	6.06	1.33	4.57	293		2.99	2.68	Obesity, normal liver
30	65	F	Poor	1170	14.05	0.97	13.60		238	2.53	12.50	Paget's disease, lobular pneumonia, fatty liver
32	54	M	Obese	1730	6.61	0.95	4.91		201	1.40	4.21	Obesity, slightly fatty liver
48	50	F	Obese	1640	10.60	0.96	8.90		326	2.01	6.85	Obesity, normal liver
52	31	M	Obese	1660	7.72	0.77	4.22		333	2.89	2.35	Obesity, normal liver
54	45	F	Obese	2900	3.39	0.54	2.26		232	1.87	1.07	Liver abscess, chronic cholecystitis, obesity
88	67	F	Obese	1400	3.92	0.78	2.69					Bronchopneumonia, obesity, normal liver
92	50	M	Obese	2490	19.63	0.46	18.71		237			Coronary thrombosis, fatty liver, obesity
Average	52			1740	7.67	0.84	6.25	258	274	1.99	4.11	

age total cholesterol for the group was above the normal average. Otherwise, the findings did not show any very striking changes.

DISCUSSION

In 14 of the 60 cases the total liver lipids were increased. Of these 14 cases, 5 were patients dying from acute infections; of these 5, 4 were found to have some cirrhosis of the liver and 2 had previous histories of alcoholism. Three of the 14 patients died of some chronic infection, and 2 of these were alcoholics. Of the remaining 6 patients in whom the liver lipids were increased, 1 was a patient with lymphosarcoma, 1 was an obese patient with no other complication, and 4 were patients with heart disease.

In the group of patients dying of chronic infections, and in the group of patients dying of some form of malignancy, the total liver lipids were slightly lower in several instances than the average normal value.

On the basis of the analyses done, the amount and character of the fat in the liver do not seem to be influenced significantly unless the liver itself is subject to disease. Cirrhosis of the liver, or the type of fatty infiltration that is seen most often in alcoholics, has more influence on the amount and distribution of the liver lipids than do other diseases. It is interesting that, in the very few diabetic cases analyzed, there was no appreciable increase in the amount of fat in the liver.

Breusch and Scalabrino (4) analyzed the livers

TABLE V

Cardiovascular disease

Number case	Age	Sex	Nutrition of patient	Weight of liver	Total lipid	Unsaponified	Fatty acid	Cholesterol		Lecithin	Neutral fat	Pathology of the liver and other disease processes
								Free	Total			
				grams	*grams per cent*	*grams per cent*	*grams per cent*	*mgm. per cent*	*mgm. per cent*	*grams per cent*	*grams per cent*	
7	57		Obese	1440	4.03	1.06	2.33	294	323	1.43	1.43	Hypertensive and arteriosclerotic heart disease, cerebral arteriosclerosis diabetes mellitus, normal liver
10	50		Obese	1330	7.43	0.83	6.17	259	335	1.31	5.52	Arteriosclerotic heart disease, CPC of liver
13	82		Good	1300	4.63	0.89	2.84		284	1.39	2.00	Arteriosclerotic heart disease, periportal cirrhosis of the liver
37	52		Good	1270	3.67	0.85	2.71		462	1.69	1.50	Coronary thrombosis, CPC of liver
6	53		Fair	1500	9.99	0.81	8.10	219	321	2.20	6.92	Coronary sclerosis, alcoholism
44	72		Good	1610	12.90	0.76	10.90		315	2.09		Coronary sclerosis, arteriosclerosis, normal liver
46	50		Good	1560	13.10	1.04	11.80		386	1.41		Coronary thrombosis
55	70		Good	1450	5.08	0.85	3.51		312	1.99	2.30	Coronary thrombosis with rupture of left ventricle
66	50		Poor	1410	4.18	0.51	2.94			2.05	1.66	Cardiac failure, alcoholism, normal liver
87	72		Poor	1350	3.97	0.57	3.13					Hypertensive heart disease, fatty liver
92	50		Obese	2490	19.63	0.46	18.71		237			Coronary thrombosis, enlarged and fatty liver
93	78		Fair	1350	3.48	0.78	2.08					Cardiac failure, lobar pneumonia, normal liver
97	27		Good	1550	4.44	0.74	2.96					Luetic aortitis, normal liver
98	65		Good	1600	3.27	0.65	2.05					Cardiac failure, CPC of liver and spleen
5	40		Fair	1720	3.88	0.67	2.44	236	256	2.57	0.75	Essential hypertension, pitocin poisoning, normal liver
45	55		Poor	1650	5.04	0.95	3.27		287	2.07	1.88	Ruptured cerebral aneurysm, subarachnoid hemorrhage, normal liver
Average	58			1535	6.80	0.78	5.37	252	320	1.84	4.11	

of 72 patients. Of these, 11 died of malignancy, 8 of tuberculosis, 10 of liver cirrhosis or atrophy, 4 in uremia, 6 of arteriosclerosis and hypertension, and 6 of pneumonia. The average total lipids in these groups varied from 4.72 to 7.68 grams per cent. The average total cholesterol varied from 312 to 277 mgm. per cent. In 1 of the cases of tuberculosis the total lipid was 20 grams per cent. In 1 of the cases of cirrhosis of the liver the total liver lipid was 12.5 grams per cent. The average total liver lipid for these two groups was not, however, elevated. The figures of Breusch and Scalabrino substantiate our findings. Apparently, the ability of the liver to handle fats is not easily impaired, and probably is only significantly affected when the liver itself is affected, as in cirrhosis.

SUMMARY

Analyses were done on 60 human livers. Of these, 16 were from patients dying of acute infections in whom no cirrhosis of the liver was found at autopsy. Five were from patients dying of acute infections in whom some cirrhosis or fatty infiltration was noted postmortem. Ten were from patients dying of chronic infections, 7 from patients dying with malignant diseases, 12 from patients dying with some disturbance of metabolism, and 16 were from patients dying with some form of heart disease.

The outstanding finding was in the 5 cases of acute infections in whom cirrhosis or fatty infiltration of the liver was present. The average total liver lipid in these cases was increased well above the normal range (15.48 grams per cent), and the total cholesterol was increased. There were no striking changes in the average lipid values in the other groups studied.

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