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Occurrence of Fatty Livers in Rats Fed a Diet Containing Dried, Whole Liver.

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Our observation of the presence of an abnormal amount of fat in the livers of rats fed a diet high in protein was first made in a series of rats in which we were attempting to determine the stages of development of chronic nephritis. In rats placed on Liver Diet I and killed from 2 to 3 months later, we found that we could tell from the presence of fatty infiltration of the liver which rats were on the diet and which were not; whereas, we were unable to detect any difference between the kidneys of the rats on the Control or the Liver I diet. This observation led to a search for the cause of the phenomenal difference in the livers of the rats fed the 2 diets.

The livers of rats fed Liver Diet I contain very large amounts of cholesterol and fat but less than the normal amount of lecithin. The

TABLE I.
Fat Content of Rat Livers.

Rat No.	Days on Diet	Cholesterol	Lecithin	Fatty Acids less Lecithin	Diet	I	IV	VII
		%	%	%				
202	59	2.67	2.37	9.48	Beef liver, dried	75		
203	59	2.77	2.27	10.32	Liver residue, aq. ext.		75	
204	59	3.66	2.25	10.51	" " alc. "			63
205	64	3.20	2.21	11.48	Lard	16	15	28
206	64	2.94	2.11	10.97	Yeast, dried	5	5	5
207	64	2.14	2.31	10.32	Cod liver oil	3	3	3
					Salt mixture*	1	1	1
212	61	0.49	3.24	3.34	Calc. carb.		1	
213	61	0.47	2.73	3.26				
214	61	0.36	2.82	2.70				
215	62	0.33	2.42	1.97				
216	62	0.45	2.63	3.39				
217	62	0.51	2.98	3.08				
224	58	0.44	3.01	3.36				
225	58	0.31	3.12	3.17				
226	58	0.39	3.20	3.49				
227	62	0.46	3.11	3.98				
228	62	0.68	3.13	5.44				
229	62	0.29	3.04	3.96				

* Salt mixture, Osborne and Mendel.

values for cholesterol have ranged from 2.14 to 5.51% and those for total fatty acids minus lecithin from 9.48 to 11.48%. The values for lecithin have varied from 2.11 to 2.37%.

When the liver residue remaining after the aqueous extraction of the pernicious anemia fraction replaces the dried, whole liver in the above diet, there is no excessive deposition of fat in the liver, (Liver Diet IV). Likewise, when dried, whole liver extracted with hot 95% alcohol is fed, fatty livers are not found, (Liver Diet VII).

All of these diets are high in fat and protein and contain very small amounts of carbohydrate. Liver Diets I and IV contain about the same large quantities of cholesterol and lecithin, while Liver Diet VII is practically free of these substances. The results with Liver Diet IV show that the development of the fatty livers is not caused by the large amounts of protein and fat in these diets.

Neither the addition of 1% of uric acid nor of 5% of yeast nucleic acid to Liver Diet IV gives rise to the typical fatty condition which results from the feeding of dried, whole liver.

All of the rats on Liver Diet I showed marked, diffuse fatty infiltration of the small and large droplet type by the end of 2 months. Aside from the abnormal amount of fat nothing of note was observed. The most marked accumulation of fat occurred in the liver cells in the peripheral part of the liver lobule. Rats fed Liver Diet IV showed no fat in the liver 2 months after they had been placed on the diet. The only thing worth noting in these livers was the apparent increase in the number of nuclei. Many of the liver cells showed 2 or 3 nuclei. The rats which ate Liver Diet VII showed a great irregularity in the amount of fat present. Rat 228 showed almost as much fatty infiltration as did some of the animals on Liver Diet I. Rat 225 showed no fat in the liver. The remainder of the rats in this series showed scattered single or small groups of cells filled with fat. The livers in this series showed nothing of special note aside from the variation in fat content.

From the pathological examination of these livers we determined only the presence of free fat as demonstrable by staining frozen sections with Scharlach R. The chemical determination of the fat, in terms of fatty acids, is the more accurate index of the total fat content of the liver.

It appears that there is a substance in dried, whole liver the ingestion of which causes the development of fatty livers. This substance is soluble in water and in 95% alcohol. Experiments are under way to determine whether this substance is present in fresh liver or whether it is formed during the drying process.