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Study of Certain Tissue Lipids in Generalized Lipodystrophy ("Lipohistiodiaresis").*

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An unusual opportunity to study the lipid composition of various tissues in an extremely rare condition, that of generalized lipodystrophy, was offered when death occurred in a 9-year-old boy in whom an almost complete absence of adipose tissue from the body had been present for the past 6 years (Case 1). In addition to this remarkable apparent lack of body fat, the symptom complex was composed of cirrhosis of the liver, chronic fibrosis of the spleen, pancreas and certain lymph nodes, and diabetes mellitus. Necropsy was begun within one hour following demise, at which time samples of various tissues were obtained. After being weighed, the specimens (usually about 1 g of tissue) were placed in 95% alcohol and allowed to stand for 24 hours. The tissues were then ground with sea sand in a mortar, rinsed several times with alcohol and ether, returned to the original flasks, and sufficient ether added to make approximately a 3:1 alcohol-ether mixture. The flasks were immersed in a boiling water bath for about 5 minutes and allowed to cool; the contents were filtered through fat-free filter paper into volumetric flasks, brought to volume, and stored in a refrigerator until analyses were made. Aliquots were measured and the following procedures employed: The method of Wilson and Hansen[1] was used for the determination of the unsaponifiable and saponifiable fractions, while the technic followed by Hansen[2] was used for the determination of the fatty acids in the acetone-insoluble (phospholipid) fraction and the acetone-soluble (cholesterol ester-neutral fat) fraction. The total cholesterol and cholesterol esters were determined by the procedure described by Bloor,[3, 4] the photoelectric colorimeter being used in obtaining the final readings. For the control studies, similar tissues from a 14-year-old boy dying in

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1 Wilson, Wm. R., and Hansen, Arild E., *J. Biol. Chem.*, 1936, **112**, 457.

2 Hansen, Arild E., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 376.

3 Bloor, W. R., *J. Biol. Chem.*, 1916, **24**, 227.

4 Bloor, W. R., and Knudson, A., *J. Biol. Chem.*, 1916, **27**, 107.

TABLE I.
Lipid Composition of Various Tissues in Child with Generalized Lipodystrophy (Case 1—D.Z.) and in Child with Subacute Nephritis (Case 2—G.C.).

	Perirenal		Subcutaneous	Liver		Skin	
Lipid fraction	Case 1	Case 2	Case 2	Case 1	Case 2	Case 1	Case 2
Unsap. fraction*	459	902	694	1,197	615	306	316
Total fatty acids							
Sap.*	452	44,610	51,144	1,490	3,156	340	10,025
M.W.	292	—	279	294	290	276	274
I.N.	102	62	66	107	102	68	64
Acet. Sol. F. A.							
Sap.*	214	36,075	50,076	607	1,498	209	10,034
M.W.	268	274	278	293	281	—	274
I.N.	86	60	65	83	74	68	64
Acet. Insol. F.A.							
Sap.*	244	199	309	797	1,599	127	160
M.W.	294	—	—	301	296	—	—
I.N.	127	—	—	123	121	—	—
Cholesterol							
Total*	296	242	—	893	356	162	102
Ester*	83	194	—	329	77	29	32
Neutral Fat F. A.* (Calc.)	130	44,320	50,000	360	1,500	190	10,010

*Expressed in mg per 100 g wet tissue.

uremia from subacute nephritis (Case 2), the best available material at the time, were used.

The results are summarized in Table I.

It is readily apparent from inspection of the data in Table I that the total fatty acids of the various tissues are distinctly less in the child with the generalized lipodystrophy (Case 1) than in the control subject (Case 2). In the perirenal tissues, the unsaponifiable fraction and the cholesterol esters are also less in Case 1, while the values for the acetone-insoluble (phospholipid) fatty acids are essentially the same in both cases. As regards the subcutaneous material, it was impossible to find any adipose tissue in Case 1 which was suitable for analysis. In the liver, the value for the total fatty acids in Case 1 is but one-half that of Case 2, while the unsaponifiable fraction as well as the total cholesterol and cholesterol ester values are higher in this child with lipodystrophy. The acetone-insoluble (phospholipid) fatty acids in this tissue are definitely less in Case 1. As regards the skin, it is interesting to note that the values for the unsaponifiable fraction, total cholesterol, cholesterol esters, and the acetone-insoluble (phospholipid) fatty acids are essentially the same in both cases. On the other hand the

total fatty acid values of the skin in Case 1 are greatly diminished when compared with those of the control subject (Case 2). In spite of the great difference in the amount of fat present in this tissue, we find that the qualitative characteristics of the fatty acids as regards average molecular weight and average iodine number are practically the same in both instances.

That there is a definite lack of fatty acids in these tissues becomes even more striking when we consider the calculated values for the neutral fatty acids. These calculations disclose that the approximate values for the neutral fat fatty acids in the hepatic tissue of our control subject (Case 2) are 5 times that of those for the child with the generalized lipodystrophy, while those in the skin are 50 times that of those in Case 1. Even more striking is the finding that the tissues in the perirenal region of Case 2 contained almost 400 times as much neutral fat as those in Case 1. From these data, it appears that there is a marked lack of fatty material in the body of the child with generalized lipodystrophy, which confirms the clinical and pathological (gross and microscopic) diagnosis. Further, we may conclude that this deficiency apparently is specifically due to a lack of neutral fat fatty acids from the various tissues studied. The name "lipohistiodiaresis" (lack of fat in the tissues) has been suggested to describe this phase of the condition.

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Increased Serum Phosphatase Activity Without Hyperbilirubinemia after Ligation of Hepatic Ducts in Dogs.

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In man with complete obstruction of the common bile duct, hyperbilirubinemia is associated with markedly increased phosphatase activity of the serum. When obstruction of the common duct is incomplete (as frequently in choledocholithiasis, cholangeitis) or in intrahepatic biliary tract obstruction (hepatic metastases, etc.), little or no jaundice may result but the serum phosphatase is usually

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