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Phospholipid Partition (Lecithin, Cephalin and Sphingomyelin) of Blood in Pernicious Anemia and Lipemia.

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The development of micromethods for the determination of the individual phospholipids, lecithin, cephalin and sphingomyelin[1] has made possible investigations of the phospholipid distribution in blood. Characteristic patterns for the phospholipid partition among the 3 separate fractions appear to exist for normal plasma, erythrocytes and tissues,[1] however, preliminary analyses presented in this paper demonstrate that certain anomalies occur in pernicious anemia and lipemia.

A marked reduction of the total phospholipid in plasma is a salient feature in pernicious anemia.[2] That some abnormality in the type of phospholipids likewise occurs has been indicated by lowered recoveries of the phospholipid with petroleum ether, following evaporation of the alcohol-ether extracts in air.[3] In view of data which showed that diminished recoveries accompanied lower fatty acid carbon: phosphorus ratios of the precipitated phospholipids (theoretical ratios for lecithin, cephalin and sphingomyelin being 13.9, 13.9 and 7.4, respectively) a higher proportion of sphingomyelin in pernicious anemia was indicated. Recent data from this laboratory have demonstrated that both lecithin and sphingomyelin may be refractory to petroleum-ether extraction under certain conditions, whereas cephalin is extracted completely.[1]

The data given in the table were obtained on petroleum-ether extracts prepared under carefully controlled conditions of evaporation of the preliminary alcohol-ether extracts which effect a far more complete recovery of the phospholipids[4] and confirm the marked reduction of total plasma phospholipid in pernicious anemia.[2] This

1 Erickson, B. N., Avrin, I., Teague, D. M., and Williams, H. H., *J. Biol. Chem.*, 1940, **135**, 671.

2 Williams, H. H., Erickson, B. N., Bernstein, S., Hummel, F. C., and Macy, I. G., *J. Biol. Chem.*, 1937, **118**, 599.

3 Avrin, Ira, Studies on Blood Phospholipids, thesis submitted in partial fulfillment of the requirements for Master of Science in the Department of Chemistry, Wayne University, Detroit, 1937.

4 Williams, H. H., Erickson, B. N., Avrin, I., Bernstein, S. S., and Macy, I. G., *J. Biol. Chem.*, 1938, **123**, 111.

decrease is reflected in all three phospholipid components. With treatment and partial relief of the anemia the total phospholipid content of the plasma is raised, accompanied by corresponding increases in lecithin and sphingomyelin, but with a decrease in cephalin content. When complete remission is attained the total phospholipid is above normal; both cephalin and sphingomyelin are likewise elevated to levels far above normal, whereas the absolute amount and proportion of lecithin is conspicuously diminished.

The total and individual phospholipids of the erythrocytes are slightly reduced in the severe anemia; however, with treatment,

TABLE I.
Phospholipid Partition in Plasma and Erythrocytes of Blood Samples.

	Total phospholipid	Choline phospholipid		Lecithin		Cephalin		Sphingomyelin	
Plasma	mg/100 cc	mg/100 cc	%*	mg/100 cc	%*	mg/100 cc	%*	mg/100 cc	%*
Normal†	189	134	70	99	52	55	30	35	18
Pernicious anemia									
Severe	47	37	80	33	70	10	21	5	10
	70	36	51	14	21	34	49	21	30
	99	60	61	48	48	39	39	12	12
Partial remission	120	99	82	72	59	22	18	27	23
	124	92	74	61	49	32	26	31	25
Complete "	208	102	49	28	13	106	51	74	36
	214	111	52	32	15	103	48	79	37
Lipemia									
Diabetic	741	741	100	668	90	0	0	73	10
" remission	401	401	100	354	88	0	0	47	12
Essential	1232	961	78	888	72	271	22	73	6
Schüller-Christian	163	126	77	56	34	38	23	70	43
	mg/100 g	mg/100 g	%	mg/100 g	%	mg/100 g	%	mg/100 g	%
Cells									
Normal†	317	127	39	77	23	190	61	50	16
Pernicious anemia									
Severe	274	99	36	60	22	175	64	38	14
Partial remission	271	100	37	45	16	170	63	56	21
	180	47	26	8	4	134	74	39	22
Complete "	356	86	34	20	6	271	76	65	18
	353	106	30	25	7	247	70	81	23
Lipemia									
Diabetic	307	126	41	99	32	181	59	27	9
" remission	227	93	41	59	26	134	59	34	15
Essential	337	138	41	—	—	199	59	—	—
Schüller-Christian	321	125	39	38	12	196	61	87	27

*Percent of total phospholipid.
†Average of 4 individuals.[1]

marked alterations in the phospholipid partition, similar to those in the plasma, are produced, *i. e.*, an elevation in total phospholipid, cephalin and sphingomyelin to values higher than normal with the amount of lecithin decidedly decreased. A similar increase of ether-insoluble phospholipid (sphingomyelin) in plasma and cells during treatment of pernicious anemia has been reported by Kirk, although no consistent changes in other phospholipids were observed.[5]

In contrast to the changes in pernicious anemia are those accompanying the elevated total phospholipid in diabetic and essential lipemia.[6] Not only the absolute amount of lecithin but also its proportion in the total was increased. Cephalin was higher, but not proportionately so, in the essential lipemia, whereas no cephalin whatever was found in the plasma of the diabetic lipemia. Sphingomyelin was increased slightly in the plasma of both. The phospholipid partition of the erythrocytes, however, was essentially normal.

Study of an individual with Schüller-Christian disease indicates that in this condition there is a tendency toward an increased amount of sphingomyelin, with a compensatory decrease of lecithin in both plasma and cells.

These preliminary data indicate the need for further investigation concerning the physiological rôles of the individual phospholipids, lecithin, cephalin, and sphingomyelin, in health and disease.

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Relation Between Cerebroside and Neutral Fat Contents of Blood Plasma, Erythrocytes and Stroma.

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That cerebrosides may exist in small amounts in blood has been shown by the development and application of a titrimetric microprocedure for this group of lipids.[1, 2, 3] This method, slightly modified, has been employed on lipid extracts of blood, stroma and brain. The data indicate that in erythrocytes, stroma, and brain, much of the

5 Kirk, E., *Am. J. Med. Sci.*, 1938, **196**, 648.

6 Bernstein, S. S., Williams, H. H., Hummel, F. C., Shepherd, M. L., and Erickson, B. N., *J. Pediat.*, 1939, **14**, 570.

1 Kimmelstiel, P., *Biochem. Z.*, 1929, **212**, 359.

2 Kirk, E., *J. Biol. Chem.*, 1938, **123**, 613.

3 Kirk, E., *J. Biol. Chem.*, 1938, **123**, 637.