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Studies on the blood lipids and lipoproteins in thalassaemia and sickle cell anaemia

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SYNOPSIS In Cooley's anaemia the serum lipid fraction, determined by chemical analysis, was found to be decreased. The lipoprotein distribution by paper electrophoresis showed a characteristic pattern with abnormally low α_1 fraction and high concentrations of the β fractions. There is no relationship between age and serum lipoprotein distribution. A correlation was found between the electrophoretic pattern, liver function tests, and the E/C index. Similar changes but of lesser degree were found in sickle cell anaemia. Liver damage is thought to be the probable cause of the reduced α_1 fraction.

Previous studies from this clinic and from other centres (Allamanis, 1955; Panizon, 1957) have demonstrated disturbances in the electrophoretic pattern of the blood proteins in thalassaemia major and sickle cell anaemia consisting of a slight to moderate fall of the albumin fraction, a raised γ globulin fraction, and abnormal liver function tests. The relative value of these findings led us to study the lipid metabolism (Ackermann, Toro, and Kountz, 1954; Rafstedt, 1955; Salt and Wolff, 1957) of chronic haemolytic anaemias.

The sera of 32 patients with severe Cooley's anaemia, of nine patients with sickle cell anaemia, and of six patients with miscellaneous types of anaemia were studied. Twenty-seven normal cases of similar ages served as controls. Serum, 1·3 ml., was used for the determinations: Total lipids were determined by the Kunkel method (Kunkel, Ahrens, and Eisenmenger, 1948) using 0·2 ml. serum. Total cholesterol and its esters were calculated by Bloor's method and lipid phosphorus by the method of Fiske and Sabbarow. The lipid phosphorus was multiplied by the factor 25 to give the total phosphatides. (These two determinations together required 1 ml. serum.) A slight modification of the micromethod described by Swahn (1953) was employed to determine the relative concentrations of lipid in electrophoretically separated lipoprotein fractions, using 0·1 ml. serum. All sera were obtained from the patient in the fasting state before any blood transfusion had been given and examined in the next 48 hours.

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RESULTS

GROUP I: CONTROLS The findings are reported in Table I and Fig. 1. The results are within normal limits.

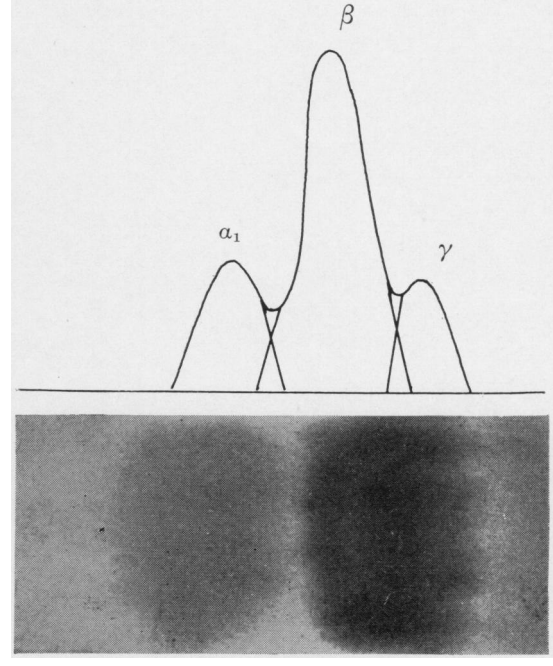

FIG. 1. *Electrophoretic pattern and levels of lipid fractions in normal controls.*

TABLE I

MEAN VALUE OF LIPID FRACTIONS AND LIPIDOGRAM IN 27 NORMAL CASES

Lipidogram			Total Lipid	Cholesterol	Esterified Cholesterol	$\frac{E}{C}$	Lipid Phosphorus or Phosphatides	$\frac{\beta}{\alpha_1}$
α_1	β	γ						
Ten Adults								
30·7	59·55	8·97	554	180	118	0·63	6·22 or 155 mg. %	1·93
Six children aged 6 to 11 years old								
30·94	59·27	9·69	461	163	114	0·73	5·43 or 136 mg. %	1·91
Seven children aged 2 to 6 years								
30·11	59·09	10·62	436	160	104	0·72	7·13 or 178 mg. %	1·96
Four babies aged 0 to 2 years								
31·38	57·27	11·19	476	122	96	0·78	6 or 150 mg. %	1·82

TABLE II

MEAN VALUE OF LIPID FRACTIONS AND LIPIDOGRAM IN 32 CASES OF COOLEY'S ANAEMIA

Lipidogram			Total Lipid	Cholesterol	Esterified Cholesterol	$\frac{E}{C}$	Lipid Phosphorus or Phosphatides	$\frac{\beta}{\alpha_1}$	Remarks
α_1	β	γ							
Normal lipidogram									
35·07	52·98	11·9	326	125	89	0·71	5·4 or 135 mg. %	1·42	Child 0 to 2 years old
39·99	53·54	9·95	358	110	53	0·48	6·58 or 165 mg. %	1·34	Child > 6 years old
Moderate decrease of α_1 fraction									
27·89	59·46	12·59	395	117	73	0·63	4·84 or 121 mg. %	2·11	0 to 2 years old, 2 cases
27·12	62·48	10·37	385	136	69	0·51	3·94 or 98·5 mg. %	2·30	> 6 years old, 4 cases
Definite decrease of α_1 fraction									
23·29	66·03	10·55	361	152	72	0·47	6·17 or 154 mg. %	2·83	0 to 2 years old, 2 cases
23·49	63·37	13·12	449	187	99	0·54	5·32 or 133 mg. %	2·71	2 to 6 years old, 6 cases
21·26	70·13	8·59	240	100	38	0·38	3·95 or 99 mg. %	3·29	> 6 years old, 1 case
Very low α_1 fraction									
18	70·34	11·54	374	120	61	0·51	5·01 or 125 mg. %	3·90	0 to 2 years old, 7 cases
17·27	70·71	12	335	118	61	0·52	4·15 or 104 mg. %	4·09	2 to 6 years old, 5 cases
14·78	73·79	11·41	329	140	76	0·53	3·66 or 91 mg. %	4·99	> 6 years old, 3 cases

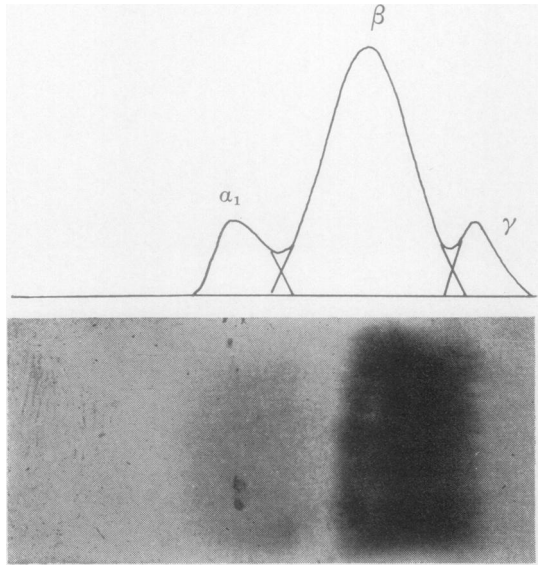

FIG. 2. *Electrophoretic pattern and levels of lipoprotein in patients with Cooley's anaemia.*

GROUP II: COOLEY'S ANAEMIA (Table II, Fig. 2) The serum of all lipid fractions determined by chemical analysis was found to be decreased. The mean value of the total serum lipids was 357 mg. %. The reduction of esterified cholesterol was greater than of cholesterol so that the mean valueof the index E/C = $0{\cdot}52\left(\frac{\text{esterified cholesterol}}{\text{cholesterol}}\right)$. The mean value of the phosphatides was 122 mg. %. The paper electrophoretic pattern of lipoproteins showed that α_1 lipoproteins were decreased whereas the β fraction was increased (Table II and Fig. 2). Only two cases have a normal electrophoretic pattern of lipoproteins, In six cases the percentage value of the α_1 fraction was moderately decreased, in nine cases definitely decreased, and in 15 cases greatly decreased. In the majority of cases (19 out of 28), the reduction of the α_1 fraction of lipoproteins was associated with a decreased E/C index and positive flocculation tests. On the remaining nine cases, the E/C index and flocculation tests were normal in six cases, in two cases the E/C index was increased while the flocculation tests

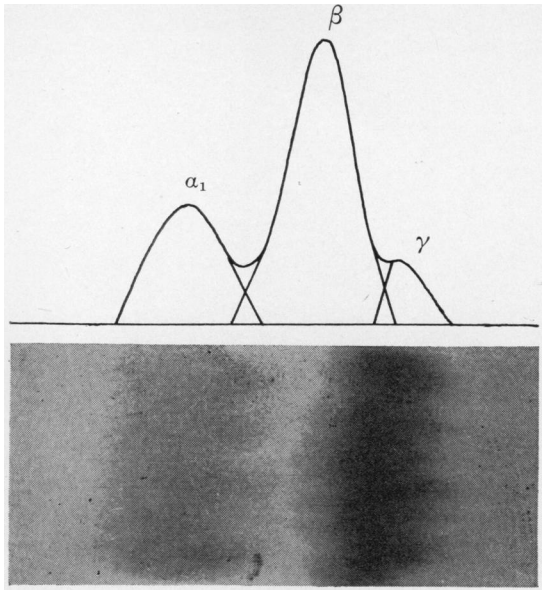

FIG. 3. *Electrophoretic pattern and levels of lipoprotein in patients with sickle cell anaemia.*

were normal, and in one with a positive flocculation test the E/C index was within normal limits.

GROUP III: SICKLE CELL ANAEMIA Although all fractions of blood lipids were seen to be reduced, the reduction was of smaller degree than in Cooley's anaemia.

The lipidogram showed minimal changes. The α_1 fraction was slightly decreased. In five patients the moderate reduction of the α_1 fraction was associated with a decreased E/C index and abnormal liver function tests. In three other patients with normal flocculation tests the E/C index was normal (two cases) or decreased (one case), but in another case positive flocculation tests were associated with a normal E/C index. These findings are illustrated in Table III and Fig. 3.

GROUP IV: MISCELLANEOUS In three cases of iron-deficiency anaemia, two of congenital spherocytosis, and one of haemolytic anaemia (Marchiagava Micheli) the α_1 fraction of lipoproteins was found to be within normal limits (Table IV).

DISCUSSION

In Cooley's anaemia all lipid fractions determined by chemical analysis were found to be decreased. The lipoprotein distribution by paper electrophoresis showed a characteristic pattern with diminished α_1 values and increased β values. Similar changes but of lesser degree were observed in sickle cell anaemia.

Our findings suggest that there is no relationship between age and serum lipoprotein distribution.

From the available literature the view could be upheld that the characteristic electrophoretic pattern with an abnormal α_1 fraction and the reduction of all lipid fractions is due to the liver damage which is found in advanced cases. This hypothesis is supported when the above findings are correlated with the abnormal liver tests and the reduced E/C index.

TABLE III

MEAN VALUE OF LIPID FRACTIONS AND LIPIDOGRAM IN SICKLE CELL ANAEMIA

Lipidogram			*Total Lipid*	*Cholesterol*	*Esterified Cholesterol*	$\frac{E}{C}$	*Lipid Phosphorus or Phosphatides*	$\frac{\beta}{\alpha_1}$	*Remarks*
α_1	β	γ							
25·25	61·03	12·91	375	135	62	0·40	5·66 or 141 mg. %	2·41	2 to 6 years old, 2 cases
27·77	60·58	11·60	386	144	71	0·52	5·15 or 129 mg. %	2·19	> 6 years old, 7 cases

TABLE IV

MEAN VALUE OF LIPID FRACTIONS AND LIPIDOGRAM IN MISCELLANEOUS CASES

Lipidogram			*Total Lipid*	*Cholesterol*	*Esterified Cholesterol*	$\frac{E}{C}$	*Lipid Phosphorus or Phosphatides*	$\frac{\beta}{\alpha_1}$
α_1	β	γ						
Three cases of iron-deficiency anaemia								
29·74	60·40	10·18	409	144	71	0·49	6·22 or 167 mg. %	2·30
Two cases of spherocytic anaemia								
36·04	54·99	8·96	367	111	53	0·55	3·31 or 94 mg. %	1·52
One case of haemolytic anaemia (Marchiafava Micheli)								
40·50	49·30	10·18	433	184	96	0·52	5·24 or 131 mg. %	1·21

However, some of the results are not readily explained.

There is no relationship between age and serum lipoprotein distribution and reduced lipid fractions, though severity of the disease increases with advancing age. Moreover, in some cases there is no correlation between the reduced α_1 fraction, flocculation tests, and E/C index.

In view of the above findings further studies are needed to determine if the liver damage is due to the anaemia alone or has its onset in early life and its severity is simply exaggerated by the progress of the chronic haemolytic process.

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