THE BLOOD LIPIDS OF DIABETIC CHILDREN [1]

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The development of degenerative changes in the cardiovascular system in diabetes has focused attention in recent years on the lipid metabolism of diabetes in childhood, a period in which diabetes occurs in a less complicated form than in the adult. Despite the fact that satisfactory evidence is still lacking for proof, there is a belief that the arteriosclerosis observed today even in the young diabetic is related to the cholesterol level of the blood. The growing importance of the diabetic child, particularly since today he provides a source from which the adult diabetic is recruited, makes highly desirable the accumulation of data on various aspects of his lipid metabolism. In the present investigation, therefore, a study has been made of all blood lipid constituents, namely, total fatty acids, phospholipids, and free and esterified cholesterol, in diabetic children under controlled conditions. Although lipids in the blood of diabetic children have previously been reported (1, 2, 3), these studies are few in number. Some of them have employed unsatisfactory methods or have dealt with a single lipid constituent, i.e., total cholesterol, which a number of workers regard as an index of the level of other lipid constituents in the blood.

EXPERIMENTAL

Forty-nine children were employed in this study. Twenty-three of them were non-diabetic and were used to establish the normal lipid level. The latter were school children who came to the Outpatient Department for routine tests, and in whom no abnormalities—unless otherwise recorded—were found by clinical examinations. No attempt was made to regulate the diet or nutritional state of these normal subjects other than withholding all food for approximately 12 to 14 hours prior to removal of the blood sample.

In 3 cases blood was obtained from the diabetic children at a time when acidosis was present. The remainder of the observations, 26 in all, were made on children under adequate insulin and dietary control. At the time blood was taken for lipid analyses these patients had either been hospitalized for some time or been admitted for a single day for routine laboratory and physical examination as well as for regulation of diet and insulin dosage, a procedure that was carried out at intervals of 2 or 3 months.

Whole blood was used for lipid analyses, and the oxidative methods employed have been previously reported (4). The determinations of blood lipids were carried out in triplicate; the values recorded are the averages of closely agreeing figures.

Okey and Stewart (5) pointed out several years ago that irregularities in the effects produced by anticoagulants and centrifugation make plasma less desirable than whole blood for comparative lipid studies. The errors introduced in the lipid determinations of plasma obtained by the use of oxalate have been studied more recently by Schmidt (6) and by Sperry and Schoenheimer (7), who have shown that oxalated blood plasma contains smaller amounts of phospholipids and cholesterol than heparinized plasma. Despite the unequal distribution of cholesterol between plasma and corpuscles, there seems little justification at the present time for the claim that plasma or serum provides a more significant medium for lipid determination than whole blood. Too little is known of the rôle of the corpuscles in lipid metabolism, particularly in pathological conditions. Hence, in the present investigation, whole blood was used throughout for the comparison of the lipid content of the blood of normal and diabetic children.

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TABLE I

Whole blood lipids (postabsorptive) of controlled diabetic children

Case number	Date blood taken	Age	Weight	Insulin	Diet			Cholesterol				Phospholipids	Total fatty acids	Residual fatty acids*	Total lipid
					Fat	Carbohydrate	Protein	Total	Free	Ester					
	1934	*years*	*kgm.*	*units*	*grams*	*grams*	*grams*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*per cent of total*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*
A1	August 18	14	42.5	5–0–15	150	75	90	181	101	80	44	256	370	140	551
A2	August 18	4	18.6	4–0–4	115	50	60	157	106	51	32	231	250	58	407
A3	August 22	8	22.0	10–0–10	120	50	60	165	111	54	33	264	315	99	480
A4	September 6	10	34.5	20–0–0	100	200	70	194	113	81	42	244	331	108	525
A5	September 15	15	54.5	10–5–10	200	80	90	170	119	51	30	231	301	109	471
A6	September 22	16	43.0	17–0–13	80	90	65	187	114	73	39	229	304	97	491
A7	September 22	13	51.2	15–10–15–10	92	150	60	205	133	72	35	246	356	138	561
A8	October 13	13	34.6	10–8–8–5	160	70	70	181	115	66	36	237	305	98	486
A9	October 27	4.5	18.9	6–0–7	95	35	65	189	125	64	34	213	264	74	453
A10	October 27	6	19.8	6–4–5–3	65	100	50	182	118	64	35	237	312	106	494
A11	October 27	8	24.5	10–0–10	100	60	60	178	112	66	37		348		526
A12	November 17	9	26.8	7–3–9–3	145	65	70	221	136	85	38		385		606
A13	November 17	14	47.6	18–14–16–11	144	160	65	171	96	75	44	248	356	135	527
A14	December 8	14	44.0	15–10–15–12	100	100	50	203	129	74	36	247	317	97	520
	1935														
A15	January 9	10	31.0	14–10–12–4	110	150	60	152	113	39	26	227	314	133	466
A16	March 2	13	34.1	20–10–30	140	90	70	177	111	66	37		391		568
A17	March 2	15	59.4	15–10–15	195	100	90	184	122	62	34	287	356	119	540
A18	March 23	12	34.1	8–0–8	205	90	70	162	106	56	35	270	354	132	516
A19	April 20	19	57.3	25–0–25–15	165	100	75	198	101	97	49	280	395	136	593
A20	March 30	5	20.0	0–0–0	100	50	50	162	106	56	35	263	353	136	515
A21	May 11	10	28.7	10–0–8	160	70	55	174	107	67	38	240	330	120	504
A22	July 27	13	35.0	16–10–16–10	150	80	64	173	107	66	38	281	337	101	510
A23	August 28	12	31.0	5–0–5	145	70	60	211	116	95	45	301	409	138	620
A24	August 28	7	26.7	8–0–6	127	55	60	146	97	49	34	249	292	89	438
A25	September 7	5	17.7	10–0–8	110	50	55	192	105	87	45	237	318	95	510
A26	January 12	9	35.2	8–5–8	130	70	50	168	111	57	34	242	313	109	481
	Maximum							221	136	97	49	301	409	140	620
	Minimum							146	96	39	26	213	250	58	407
	Mean							181	113	68	37	250	334	112	514

* Derived chiefly from neutral fat.

RESULTS

The various lipid constituents determined in the whole blood of normal children are shown in Table II, whereas the values for the diabetic children are recorded in Tables I and III. The results obtained for the latter may be grouped according to the degree of control effected by insulin and diet.

1. *Controlled diabetic children.* The concentration of all lipid constituents that was found in the blood of the controlled diabetics corresponded closely to the normal range. Thus the maximum and minimum values for total lipids were respectively 620 and 407 mgm. per cent as compared with values of 595 and 417 mgm. observed in normal subjects. The total fatty acid content of the blood of diabetic children varied from 409 to 250 mgm. per cent, whereas the highest and lowest values for this constituent in the normal children were respectively 387 and 260 mgm. per cent. The phospholipid values fluctuated between 301 and 213 mgm. in the diabetic and between 288 and 184 in the normal children. The close agreement between the cholesterol values of normal and diabetic subjects is particularly striking. Total cholesterol, which was present to the extent of 226 to 141 mgm. per 100 cc. of the blood of the normal children, ranged from 221 to 146 mgm. per cent in the diabetics; the free or uncombined portion of this consisted of 131 to 91 in the nondiabetics and 136 to 96 in the diabetics. The mean values obtained for both groups of children are also in close agreement.

2. *Diabetic children in acidosis.* Although this study was concerned primarily with children under control, blood lipids were also obtained from 3 cases suffering from diabetic acidosis (Table III). In 2 of these (A19 and A21) the postabsorptive blood samples obtained during acidosis contained a much higher concentration of total lipids than samples taken during periods in which these patients were under control. The various lipid constituents, however, did not share equally in this rise of the total lipid. While no increase in cholesterol was found in A21 during acidosis, in A19 it rose from a controlled level of

TABLE II

Whole blood lipids (postabsorptive) of non-diabetic children

Case number	Date blood taken	Age	Weight	Cholesterol				Phospholipids	Total fatty acids	Residual fatty acids	Total lipid
				Total	Free	Ester					
	1935	*years*	*kgm.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*per cent of total*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*
C3	Feb. 9	13		146	96	50	34	240	277	80	423
C4	Feb. 9	6	21.6	198	131	67	34	254	325	106	523
C5	Feb. 9	5	17.7	162	107	55	34	253	297	88	459
C6	Feb. 16	14	45.1	173	105	68	39	217	318	123	491
C7	April 13	13	47.2	164	105	59	36	268	304	81	468
C8	April 20	15	49.5	141	91	50	35	222	279	93	420
C9	July 7	4	17.2	154	105	49	32	259	320	110	474
C10	July 7	8	25.2	152	100	52	34	273	325	104	477
C11	Aug. 3	13	38.4	141	94	47	33	249	276	75	417
C12	Sept. 7	15	47.2	158	95	63	40	230	323	123	481
C13	Sept. 7	7	20.9	183	107	76	42	278	298	57	481
C14	Sept. 21	5	15.8	176	96	80	46	219	334	129	510
C15	Sept. 21	9	27.5	181	104	77	43	240	260	43	441
C16	Oct. 26	10	30.0	174	104	70	40	248	280	63	454
C17	Nov. 18	12	31.8	161	108	53	33	220	279	93	440
C18	Nov. 25	12	34.6	150	98	52	35	184	313	152	463
C19	Nov. 25	13	35.6	172	94	78	43	186	288	107	460
C20	Nov. 25	11	35.2	150	100	50	33	186	290	129	440
C21	Dec. 16	12	36.0	208	126	82	39	270	387	147	595
C22	Dec. 16	9	29.3	164	96	68	41	288	338	95	502
C24	Dec. 23	4	14.7	169	92	77	46	218	261	58	430
C25	Dec. 23	7	23.6	198	109	89	45	214	336	127	534
C26	Dec. 23	6	19.7	226	122	104	46	212	283	66	509
	Maximum			226	131	104	46	288	387	152	595
	Minimum			141	91	47	32	184	260	43	417
	Mean			170	104	66	38	236	304	98	474

198 to 238 mgm. per cent during acidosis. But it should be noted that the latter value does not represent a significant rise above the highest normal, namely 226, or for that matter above the highest value found in the controlled diabetics, namely 221 mgm. per cent. Changes in the cholesterol ester or phospholipid content of the blood during acidosis were neither marked nor consistent in these 2 cases.

A6 was brought into control by means of a daily injection of 42 units of insulin and a diet containing 90 grams of fat, 84 grams of carbo-

TABLE III

Blood lipids of diabetic children in acidosis. (Blood samples taken in the postabsorptive state unless otherwise stated)

Case number	Date	Condition	Cholesterol				Phospholipid	Total fatty acids	Residual fatty acids	Total lipid	Insulin	Diet		
			Total	Free	Ester							Fat	Carbohydrates	Protein
			mgm. per 100 cc.	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*per cent of total*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*units*	*grams*	*grams*	*grams*
A6	July 13, 1935	Controlled	163	101	62	38	258	319	101	482	42	90	84	74
	July 20, 1935	Acidosis	182	112	70	38	281	359	120	541	18	90	84	74
	July 25, 1935	Acidosis*	196	113	83	42	389	969	648	1165	26	90	84	74
	July 26, 1935	Acidosis	174	116	58	33	289	356	120	530	95	90	84	74
	July 27, 1935	No acidosis	193	116	77	40	291	375	124	568	40	90	84	74
	August 3, 1935	No acidosis	184	113	71	39	281				56	90	84	74
	August 28, 1936	Controlled	170	109	61	36	278	356	125	526	82	90	84	74
	September 7, 1936	Controlled	160	98	62	39	264	313	92	473	42	40	120	74
	October 5, 1936	Controlled	159	97	62	39	261	322	102	481	24	67	60	74
A19	March 30, 1935	Acidosis	238	129	109	46	268	730	470	968		75	100	75
	April 20, 1935	Controlled	198	101	97	49	280	395	136	593	65	75	100	75
A21	April 29, 1935	Acidosis	165	104	61	37	296	576	333	742		160	70	55
	May 11, 1935	Controlled	174	107	67	38	240	330	120	504	20	160	70	55

* Blood sample obtained at 3:00 p.m.

hydrate and 74 grams of protein. From July 14 to 27 the insulin was gradually reduced so that by July 18 he was receiving 18 units, and this was continued until July 25. Blood lipids were examined on 3 different occasions during the period in which the patient showed acetonuria. Slight rises in total cholesterol occurred, but these were in no way marked when compared with the values obtained several days later when the patient was free of acetonuria. Indeed, the highest value observed during acidosis was 30 mgm. per cent below the highest figure found among the normal children. In 2 of the 3 blood samples taken during acidosis (July 20 and 26) small increases were noted in phospholipids and neutral fat. But again, if these values are compared with those obtained a few days later when the acidosis had disappeared, or with the highest values obtained in the normal subjects, it is questionable whether much significance can be attached to such increases. A striking rise in these 2 lipid constituents did occur, however, in the blood examined at the height of acidosis (July 25), but since this sample was obtained at 3 p.m. instead of in the postabsorptive state, it is difficult to differentiate between the effects of the 2 previous meals and those of the acidosis. It should be noted, however, that, as judged by previous observations made in this laboratory, such increases in neutral fat are not encountered in a normal alimentary lipemia (8).

DISCUSSION AND SUMMARY

The frequency with which the diabetes of the adult and elderly subject is associated with other pathological conditions makes difficult the interpretation of studies made in these age periods. This difficulty, however, is not so frequently met in the diabetes of childhood. In the group of diabetic children reported in this investigation, abnormalities other than diabetes were not present at the time lipid studies were made. The diabetic child thus provides the most satisfactory patient from whom metabolic disturbances due to diabetes per se may be deduced. The results of the present study show quite definitely that, when controlled by insulin and diet, diabetic children have blood lipid levels well within the normal range. This was found to be the case with all lipid constituents, i.e., free and esterified cholesterol, phospholipids and fatty acids. Normal lipid values were found whether the diabetes was of 3 months' or 3 years' duration, and whether the subject required 68 or 10 units of insulin. These observations on children are thus in accord with the results recently reported by Man and Peters (9) for adult and elderly patients. They found no relation between serum cholesterol and the severity of the diabetes as judged by insulin requirement or carbohydrate tolerance.

From a comparison of the values obtained from 3 patients during acidosis and control, it is apparent that a pronounced increase in the cholesterol content of the blood need not accompany mild acidosis in diabetic children. In no case during acidosis was a value found significantly above the highest normal. Despite the fact that a high cholesterol level has been suggested as a precursor of complications, nevertheless a number of observations now indicate that the cholesterol content of the blood is not a reliable index of the degree of control in diabetes. Thus in 65 of their 94 cases of acidosis, White and Joslin (10) found cholesterol values within or slightly above the normal range. Moreover, Man and Peters (11) have shown that cholesterol falls below the acidosis level during the period immediately following the disappearance of acidosis and dehydration, and that at this time the cholesterol content of the blood may be even lower than at the end of convalescence.

While neutral fat, the changes in which are reflected in the total fatty acid determination, fluctuated widely at times, commensurate changes did not always occur in the cholesterol fraction. The most striking example of this was found in A6 and A21 (Table III). Over a period of 5 days, residual fatty acids rose from 120 to 648 mgm. per cent (A6) at the same time that total cholesterol rose from 182 to 196 mgm. Although 2 days later residual fatty acids dropped to 124, cholesterol still remained practically unchanged. A similar lack of relation between cholesterol and total fatty acids has been observed by others (11, 12). It follows, therefore, that cholesterol cannot be employed as a guide for the level of other lipid constituents in the blood.

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