

# Improvement of Lipid Status in Diabetic Boys: The 1971 and 1979 Joslin Camp Lipid Levels

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Since 1972, young type I diabetic patients seen by Joslin Clinic physicians have been advised to use a low cholesterol diet with a high proportion of polyunsaturated fat. Mean fasting cholesterol and triglyceride levels at admission to the Joslin Boys Camp for the years 1971 (N = 129) and 1979 (N = 79) were compared. In 1979, the mean cholesterol level was lower by 44 mg/dl ( $P < 0.001$ ) and the mean triglyceride by 21 mg/dl ( $P < 0.001$ ) compared with 1971. The incidence of hyperlipoproteinemia decreased from 21.6% to 7.6% with a complete disappearance of types IV and V during the same period. A decrease in the development of arteriosclerotic cardiovascular diseases in type I diabetic patients might be anticipated from this diet modification. DIABETES CARE 6: 64-66, JANUARY-FEBRUARY 1983.

It is generally recognized that life expectancy in diabetic persons is significantly reduced by arteriosclerotic vascular disease.<sup>1</sup> The pathogenesis of atherosclerosis is multifactorial, but a major cause seems to be elevated lipid levels, especially cholesterol.<sup>2</sup>

In a previous report, the short-term effect of a diet restricted in cholesterol and saturated fats on the plasma lipids of type I diabetic children was described.<sup>3</sup> A significantly reduced incidence of hyperlipoproteinemia was noted 2 wk after the introduction of this diet.

In 1979, the lipid levels in a similar group of male type I diabetic patients were measured and the results compared with those obtained in 1971. This comparison indicated lower lipid levels in the recent group with a dramatic decrease of Fredrickson's type IV and V hyperlipoproteinemia.

## PATIENTS AND METHODS

**The 1971 study.**<sup>3</sup> Fasting lipid levels from the 129 boys who attended the Joslin Summer Camp in 1971 were retrieved. These were measured in blood samples obtained one day after admission to the camp by a modified Lieberman-Burchard reaction<sup>4</sup> for the total cholesterol, and the method of Kessler and Lederer<sup>5</sup> for triglyceride, according to the Lipid Research Clinics' methodology.<sup>6</sup> Both of these procedures have since been further modified in our laboratory, and currently cholesterol and triglyceride are determined by an enzymatic technique,<sup>7</sup> which eliminates the need for an isopropanol extraction step while still employing the Technicon AutoAnalyzer II system.<sup>6</sup> To compare the lipid levels from these two methods, those obtained by the older extraction (Ext) method

were converted to the enzymatic (Enz) method equivalent, using the following linear regression equations:

$$\text{Chol(Enz)} = 1.41 \text{ Chol(Ext)} - 62 \text{ mg/dl.}$$

$$\text{Tg(Enz)} = 0.91 \text{ Tg(Ext)} - 7.7 \text{ mg/dl.}$$

These equations were calculated from 138 samples measured for cholesterol and 118 samples measured for triglyceride by both methods. The levels (enzymatic method) of cholesterol ranged from 100 to 430 mg/dl and those for triglyceride ranged from 30 to 450 mg/dl. The coefficient of variation (C.V.) for simultaneously run "low" (mean  $\pm$  1 SD =  $187 \pm 3.6$  mg/dl) and "high" ( $275 \pm 4.5$  mg/dl) cholesterol concentrations of quality-control samples in our laboratory was 1.9% and 1.7%, respectively. For triglycerides, the C.V. for low ( $80 \pm 4.0$  mg/dl) and high ( $246 \pm 6.3$  mg/dl) concentrations was 5.0% and 2.6%, respectively.

**The 1979 study.** A total of 79 diabetic boys participated in the study. Written informed consent was obtained from patients and their parents. Ten milliliters of venous blood was taken in EDTA tubes between 7 and 8 a.m., after an overnight fast, on the day after admission to the Joslin Camp. The tubes were kept on ice and processed within 4 h. The criteria of Frederickson et al.<sup>8</sup> were employed for age- and sex-adjusted normal lipid levels.

In the 1979 study, HDL-cholesterol levels were also determined. For this purpose, the HDL was separated from other lipoproteins by a chemical separation technic using sodium phosphotungstate and magnesium chloride.<sup>9</sup> The LDL-cholesterol was calculated by the method of Friedwald et al.<sup>10</sup>

TABLE 1

Characteristics of diabetic boys at entry to camps (mean  $\pm$  SD). The left panel shows the data from all campers in 1971. The center panel shows the data from the 1979 study. The right panel shows the data for the 1971 campers after exclusion of patients with type IV and V hyperlipidemia

	1971	P	1979	P	1971
N	129	—	79	—	116
Age (yr)	12.6 $\pm$ 1.8	NS	12.5 $\pm$ 4.7	NS	12.2 $\pm$ 1.7
Duration DM (yr)	5.1 $\pm$ 3.2	NS	5.2 $\pm$ 3.6	NS	5.2 $\pm$ 3.3
Weight (kg)	43.1 $\pm$ 9.4	NS	41.2 $\pm$ 11.4	NS	42.6 $\pm$ 9.1
Fasting cholesterol (mg/dl)	224 $\pm$ 62	<0.001	180 $\pm$ 36	<0.0001	214 $\pm$ 49
Fasting HDL-cholesterol (mg/dl)	—	—	60 $\pm$ 15†	—	—
Fasting LDL-cholesterol (mg/dl)	—	—	112 $\pm$ 33†	—	—
Fasting triglyceride (mg/dl)	71 $\pm$ 39	<0.001	50 $\pm$ 20	<0.001	62 $\pm$ 22
Fasting blood glucose (mg/dl)	142 $\pm$ 75	NS	139 $\pm$ 46	NS	139 $\pm$ 72
% CHO*	14 $\pm$ 12	NS	13 $\pm$ 11	NS	15 $\pm$ 11

\*Percentage of daily carbohydrate intake lost in the urine during the first week of camp.

† = N of 75.

**Diets.** In 1971, it was found that the "diabetic diet" was high in cholesterol (700–1500 mg/day) and had a polyunsaturated/saturated ratio of 0.1. Since then, after noting impressive changes in plasma lipids following a short-term dietary change,<sup>3</sup> it has been our policy to recommend a diet low in cholesterol (300–500 mg/day) and high in polyunsaturated fats (P/S ratio 0.8–1.0). This was accomplished by replacing butter with margarine, whole milk with skim milk, and by limiting the number of eggs per week. This diet is generally well accepted. Fifty-four campers out of 79 (68%) were either Joslin Clinic patients or had been instructed concerning this diet during a previous summer camp period. Among the 25 campers who had not been exposed to the diet, interviews did not reveal an elevated consumption of animal fat or eggs. However no attempt was made to quantify precisely the home food intake.

**Blood glucose.** Whole blood glucose was measured on each sample by an AutoAnalyzer method.<sup>11</sup>

#### RESULTS AND DISCUSSION

The mean demographic and biochemical characteristics for the two groups of diabetic boys are summarized in Table 1 (left panel). The groups did not differ significantly with regard to age, duration of diabetes, weight, or fasting blood glucose. In 1979, the mean total cholesterol was lower by 44 mg/dl ( $P < 0.001$ ) and the mean triglyceride was lower by 21 mg/dl ( $P < 0.001$ ) in comparison with the 1971 mean

levels. Even more striking was the complete disappearance of type IV and V hyperlipoproteinemia and a small decrease in the incidence of type II (Table 2). Table 3 summarizes the results of the 1971 and 1979 lipids compared with the 95th percentile values for normal populations of white males described by Frederickson et al.<sup>8</sup> and Morrison et al.<sup>12</sup>

The 1971 study<sup>3</sup> demonstrated clearly that dietary manipulations, even without improvement of diabetes control, could greatly reduce the incidence of lipid abnormalities in diabetic children. Since abnormal lipid levels, particularly cholesterol, have been reported to be associated with a high rate of atherosclerosis,<sup>2,13,14</sup> we have since advised our diabetic population to achieve the best possible metabolic control and to change their diet. In 1979, the lipid status of diabetic boys was considerably different from that observed in the 1971 group with a marked decrease of type IV and V hyperlipoproteinemias. To evaluate more precisely the effect of the diet on the lipid levels, thus minimizing the impact of poorly controlled diabetes (commonly associated with type IV and V hyperlipidemia), the lipid values of the 1971 group were reanalyzed after exclusion of the campers with these types of hyperlipidemia and compared with the 1979 group. The results are given in Table 1 (right panel). For nearly identical demographic and biochemical data, the 1979 group

TABLE 3

Percentage of diabetic boys at entry to camps with fasting cholesterol and triglyceride above the 95th percentile for normal controls. Data for controls from Frederickson et al.<sup>8</sup> and Morrison et al.<sup>12</sup>

Normal population 95th percentile	Percentage of diabetic boys above the 95th percentile	
	1971	1979
Frederickson (1967)		
Cholesterol 230 mg/dl	17.1	8.9
Triglyceride 140 mg/dl	10.8	0
Morrison (1978)		
Cholesterol 203 mg/dl	45.7	24.1
Triglyceride 116 mg/dl	14.0	1.3

TABLE 2

Hyperlipoproteinemia in diabetic boys at entry to camps. The criteria are those of Frederickson et al. in 1967<sup>8</sup>

	1971		1979	
	N	%	N	%
Type II	15	11.6	6	7.6
Type IV	9	6.9	—	—
Type V	4	3.1	—	—
Total all types	28	21.6	6	7.6

still showed significantly lower lipid levels than the non-hyperlipoproteinemia 1971 group. Furthermore, using the coefficient of determination (coefficient of correlation<sup>2</sup> × 100), it was estimated that the control of diabetes represented by blood glucose and 24-h urine glucose excretion contributed only from 10 to 24% of the variability in the observed lipid levels.

Using the criteria of hyperlipoproteinemia described in 1967 by Frederickson et al.,<sup>8</sup> the 1971 population had an incidence of hyperlipoproteinemia of 21.6% versus 7.6% in 1979 (Table 2). However, over the years, there has been continuous improvement in the lipid levels in the general population<sup>15</sup> and the 1979 campers have been judged with the criteria adjusted to this trend (Table 3). It appears that our type I population had better lipid levels in 1979 compared with 1971, but that elevated cholesterol values are still prevalent when compared with an age-sex-race-matched population. This picture may be somewhat misleading because among the 75 campers in whom the HDL-cholesterol was measured,<sup>16</sup> 20% showed "hyper-alpha-lipoproteinemia" (i.e., HDL-cholesterol greater than 70 mg/dl and LDL-cholesterol lower than 170 mg/dl), a condition which is associated with a decreased risk of atherosclerotic cardiovascular disease.<sup>17,18</sup> Even excluding the individuals with hyper-alpha-lipoproteinemia, the percentage of campers above the 95th percentile on Table 3 remains abnormally high for cholesterol levels: 15.2% by Frederickson's criteria and 63% by Morrison's criteria. HDL-cholesterol was not measured in 1971, therefore comparison with this earlier group was not possible. It appears, however, that further lowering of total and LDL-cholesterol is still desirable. If this trend continues it is likely that a decrease in atherosclerotic cardiovascular disease will ensue in diabetic persons<sup>19</sup> as has been observed in the normal population.<sup>20</sup>

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