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Suspected Faulty Essential Fatty Acid Metabolism in Sjögren-Larsson Syndrome

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Summary

The aim of the present study was to examine the fatty acid patterns of plasma phospholipids, cholesteryl esters, triglycerides and free fatty acids in patients with Sjögren-Larsson syndrome in order to detect whether absorption or metabolism of essential fatty acids may be abnormal. The fatty acid patterns were analyzed by gas liquid chromatography. The proportions of 23 fatty acids were calculated. The parameters used for assessment of the essential fatty acid metabolic status were calculated and compared with those from a group of institutionalized mentally retarded patients and from a group of healthy controls. There was no significant difference in either the fatty acid components or parameters used to evaluate the essential fatty acid metabolic study when the mentally retarded and control groups were compared. The relative concentration of linoleic acid (18:2ω6) in plasma phospholipids in patients with Sjögren-Larsson syndrome did not differ significantly from that of the healthy or mentally retarded controls, indicating that the Sjögren-Larsson syndrome does not involve a dietary essential fatty acid deficiency or a defect in absorption of linoleate. In the phospholipids of Sjögren-Larsson syndrome patients, the metabolites derived from linoleic acid were found to be significantly lower than in healthy controls, suggesting a metabolic defect. The total products of Δ6 desaturation were reduced to 3% of that in controls, whereas the products of Δ5 and Δ9 desaturation were not noticeably affected in patients with Sjögren-Larsson syndrome. All individuals with Sjögren-Larsson syndrome exhibited decreased products of Δ6 desaturation which also affected subsequent metabolites in the metabolic sequence.

Speculation

Fatty acid patterns of plasma phospholipids could be used to distinguish between Sjögren-Larsson syndrome and a syndrome of congenital ichthyosis with mental retardation in which spasticity does not develop.

The Sjögren–Larsson syndrome is an autosomal recessively inherited syndrome characterized by congenital ichthyosis, spastic di- or tetraplegia and mental retardation (12, 16, 18, 20). An additional symptom, glistening dots in the retina of the eye, has recently been reported by Jagell *et al.* (11). The basic etiology of the Sjögren–Larsson syndrome is so far unknown. In a recent study, no metabolites suggesting errors in amino acid or organic acid metabolism were found when urinary samples from 35 patients with the Sjögren–Larsson syndrome were examined by gas chromatography/mass spectrometry (9).

Several authors have speculated that the Sjögren–Larsson syndrome, or at least the congenital ichthyosis in that syndrome may be caused by an error in lipid absorption and/or metabolism. Impaired intestinal absorption of lipids was reported in patients with ichthyosis (but without other cardinal symptoms of the Sjögren–Larsson syndrome) (13). Pototsky and Grabovskaya (15) also reported a decreased plasma concentration of phospholipids and a concomitant increase in the neutral lipids in ichthyotic patients. A beneficial effect of medium-chain triglyceride diets on the ichthyosis of three patients with the Sjögren–Larsson syndrome was claimed by Hooft *et al.* (10) and Guilleminault *et al.* (3). Experimental essential fatty acid deficiency in rats causes scaly skin lesions (4, 5), and similar dermal manifestations of deficiency have been observed in humans given a low fat diet (6, 19) or given low essential fatty acid alimentation intravenously (1, 14, 17). The ichthyosis of patients with the Sjögren–Larsson syndrome has some features in common with that of patients with essential fatty acid deficiency.

Ziboh and Hsia (21) reported that arachidonic acid was converted to prostaglandins in the skin of rats and humans, but the physiological relationship between prostaglandins and arachidonic acid in the development of scaly skin is not yet fully defined. However, since one of the cardinal symptoms of the Sjögren–Larsson syndrome is a disorder of the skin, it is tempting to speculate that this could be caused by some defect in the metabolism of polyunsaturated fatty acids or prostaglandins. Thus, the aim of the present study was to examine the fatty acid patterns of plasma phospholipids, cholesteryl esters, triglycerides and free fatty acids in patients with the Sjögren–Larsson syndrome in order to investigate whether essential fatty acid absorption or metabolism may be abnormal in this syndrome. Part of these data have been presented in preliminary form (7).

MATERIALS AND METHODS

Blood samples were collected from 11 patients with the Sjögren–Larsson syndrome, 5–72 years of age (mean age 23 years) from both sexes. All the patients had the typical clinical signs of the syndrome: congenital ichthyosis, mental retardation, and spastic di- or tetraplegia. All of them also had glistening dots in the ocular fundus (11). Two other patients, who were siblings, were initially suspected of having the Sjögren–Larsson syndrome because of congenital ichthyosis (which, however, was clinically different from that seen in the Sjögren–Larsson syndrome) and mental retardation, although they had no spasticity or glistening dots in the fundus of the eye. Blood samples were also collected from 15 institutionalized mentally retarded patients, 7–70 years of age (mean age 23 years) and from 14 healthy controls, 5–77 years of age (mean age 24 years) from both sexes. Three of the patients with the Sjögren–Larsson syndrome were permanently at institutions and eight lived with their families. The control groups were chosen to match the patients with the Sjögren–Larsson syndrome as far as possible with regard to institutionalization, age, sex and dietary influence on plasma lipids.

Blood samples were taken by venipuncture after overnight fasting and placed in heparinized tubes. These were immediately centrifuged and the plasma samples were collected. A few drops of chloroform: methanol (1:3) were added as a preservative before the samples were frozen. The samples were shipped by air to the Hormel Institute in dry ice and stored at −25°C until analyzed. Analyses of plasma free fatty acids, phospholipids, cholesteryl esters and triglycerides were performed by gas liquid chromatog-

raphy as previously described (8). The proportions of 23 fatty acids were determined and several parameters used for assessment of essential fatty acid status were calculated and compared by a PDP-12 laboratory computer. Each fatty acid or parameter was compared for the Sjögren–Larsson patient group *versus* healthy controls, Sjögren–Larsson patient group *versus* mentally retarded controls, healthy controls *versus* mentally retarded controls. Significance was expressed as probabilities and calculated by Student's *t* test. The shorthand notation used to identify the fatty acids and show metabolic relationships gives the number of carbon atoms, a colon, the number of methylene-interrupted *cis* double bonds, omega, and the number of carbon atoms beyond the last double bond and including the terminal methyl group. Thus, arachidonic acid is written 20:4ω6. The calculated parameters to evaluate essential fatty acid status have been reviewed (6).

RESULTS

CONTROLS

Comparison was made between the fatty acids profiles in four lipid classes, which were measured in the mentally retarded and healthy control groups. In the phospholipids class, neither the fatty acids nor the parameters calculated from them differed significantly between these two groups. In cholesteryl esters, only palmitic acid ($P < 0.01$) and total saturated acids ($P < 0.05$) were significantly higher in the mentally retarded group than in the healthy controls. In triglycerides, 16:1ω7 was higher ($P < 0.05$), 18:0 was lower ($P < 0.05$), ω9 metabolites higher ($P < 0.05$), the elongation ratio 22:4ω6/20:4ω6 was lower ($P < 0.05$) and products of Δ5 desaturation were higher ($P < 0.05$) in the group of mentally retarded compared with healthy controls. In the free fatty acids, neither the individual fatty acids nor the parameters calculated from them differed significantly between the group of mentally retarded and healthy controls. Thus, these two groups were not significantly different in the important fatty acid components or parameters used to evaluate the essential fatty acid metabolic status.

PHOSPHOLIPIDS

The fatty acid patterns in phospholipids of serum or plasma have been found to respond to essential fatty acid deficiency to a greater extent than those of other blood lipids (4, 8), and therefore

Table 1. *Fatty acid patterns of plasma phospholipids from patients with Sjögren-Larsson syndrome (SLS) compared with mentally retarded (MR) and healthy controls (HC)*[1]

Fatty acids	SLS	HC	*P*	SLS/HC	MR	*P*	SLS/MR
	(11)[2] Mean[1] ± S.E.	(14)[2] Mean[1] ± S.E.		Ratio	(15)[2] Mean[1] ± S.E.		Ratio
12:0	0.01 ± 0.01	0.09 ± 0.01	<0.001	0.10	0.19 ± 0.06	<0.05	0.05
14:0	0.12 ± 0.02	0.44 ± 0.04	<0.001	0.27	0.61 ± 0.16	<0.05	0.19
14:1	0.16 ± 0.04	0.39 ± 0.14		0.42	0.41 ± 0.09	<0.05	0.40
16:0	28.54 ± 1.11	25.01 ± 0.98	<0.05	1.14	27.37 ± 1.52		1.04
16:1ω7	1.20 ± 0.17	1.58 ± 0.21		0.76	1.56 ± 0.19		0.77
16:2	0.01 ± 0.01	0.15 ± 0.05	<0.05	0.06	0.10 ± 0.02	<0.01	0.09
18:0	13.13 ± 0.54	12.32 ± 0.94		1.07	12.04 ± 0.83		1.09
18:1ω9	12.03 ± 0.38	10.81 ± 0.49		1.11	11.13 ± 0.50		1.08
18:2ω6	20.81 ± 0.95	19.32 ± 0.93		1.08	18.69 ± 1.01		1.11
18:3ω6	0.00 ± 0.00	0.13 ± 0.06		0.00	0.18 ± 0.11		0.00
18:3ω3	0.17 ± 0.03	0.43 ± 0.11	<0.05	0.40	0.78 ± 0.20	<0.05	0.22
20:2ω9	0.00 ± 0.00	0.21 ± 0.10	<0.05	0.00	0.29 ± 0.22		0.00
20:2ω6	0.36 ± 0.02	1.00 ± 0.25	<0.05	0.36	0.73 ± 0.24		0.50
20:3ω9	1.50 ± 0.13	0.90 ± 0.27		1.67	0.72 ± 0.13	<0.001	2.08
20:3ω6	2.71 ± 0.20	4.35 ± 0.40	<0.01	0.62	3.39 ± 0.38		0.80
20:4ω6	9.15 ± 0.26	9.36 ± 0.55		0.98	9.16 ± 0.37		1.00
20:4ω3	0.02 ± 0.01	0.45 ± 0.13	<0.01	0.04	0.43 ± 0.14	<0.05	0.04
20:5ω3	1.69 ± 0.18	2.38 ± 0.43		0.71	2.05 ± 0.31		0.82
22:4ω6	1.44 ± 0.14	0.75 ± 0.20	<0.01	1.92	0.96 ± 0.16	<0.05	1.50
22:4ω3	0.61 ± 0.09	0.85 ± 0.36		0.72	0.66 ± 0.14		0.92
22:5ω6	0.15 ± 0.03	0.90 ± 0.39		0.16	0.58 ± 0.09	<0.001	0.25
22:5ω3	1.26 ± 0.18	2.53 ± 0.54	<0.05	0.50	1.82 ± 0.27		0.69
22:6ω3	5.17 ± 0.52	5.78 ± 0.63		0.89	6.26 ± 0.90		0.83
Double bond index	1.49 ± 0.04	1.69 ± 0.09		0.88	1.60 ± 0.08		0.93
Total PUFA	45.05 ± 0.93	49.50 ± 2.11		0.91	46.81 ± 1.95		0.96
Total ω6 acids	34.61 ± 0.97	35.82 ± 0.86		0.97	33.69 ± 1.18		1.03
ω6 metabolites	13.80 ± 0.39	16.49 ± 0.89	<0.05	0.84	15.00 ± 0.66		0.92
Total ω3 acids	8.93 ± 0.74	12.43 ± 1.70		0.72	12.01 ± 1.53		0.74
ω3 metabolites	8.75 ± 0.73	12.00 ± 1.76		0.73	11.23 ± 1.38		0.78
Total ω9 acids	13.53 ± 0.36	11.92 ± 0.59	<0.05	1.14	12.13 ± 0.66		1.11
ω9 metabolites	1.50 ± 0.13	1.11 ± 0.36		1.35	1.01 ± 0.33		1.49
Monoene acids	13.39 ± 0.40	12.78 ± 0.72		1.05	13.10 ± 0.58		1.02
Saturated acids	41.79 ± 1.09	37.85 ± 1.56	<0.05	1.10	40.22 ± 2.10		1.04
20:3ω9/20:4ω6	0.17 ± 0.02	0.10 ± 0.03		1.59	0.08 ± 0.01	<0.001	2.07
20:4ω6/18:2ω6	0.45 ± 0.03	0.50 ± 0.03		0.91	0.51 ± 0.04		0.88
22:4ω6/20:4ω6	0.16 ± 0.02	0.09 ± 0.02	<0.05	1.78	0.11 ± 0.02	<0.05	1.50
4-desaturation products	5.32 ± 0.52	6.68 ± 0.96		0.80	6.84 ± 0.93		0.78
5-desaturation products	12.34 ± 0.32	12.64 ± 0.79		0.98	11.93 ± 0.59		1.03
6-desaturation products	0.01 ± 0.01	0.28 ± 0.10	<0.05	0.03	0.28 ± 0.11	<0.05	0.03
9-desaturation products	13.39 ± 0.40	12.78 ± 0.72		1.05	13.10 ± 0.58		1.02
Elongation products	6.40 ± 0.32	10.14 ± 1.29	<0.05	0.63	8.28 ± 0.88		0.77

[1] Figures refer to relative concentration in %

[2] Number of individuals.

emphasis was placed upon plasma phospholipids in this study. The fatty acid patterns of the 11 patients with Sjögren–Larsson syndrome differed significantly from those of mentally retarded and healthy controls. For all fatty acids measured and parameters calculated, the direction of change observed for the patients with Sjögren–Larsson syndrome was the same whether compared with the group of healthy controls or with the group of institutionalized mentally retarded patients. The differences were generally more pronounced in the comparisons with healthy controls than with the group of mentally retarded patients (Table 1, Fig. 1).

The content of linoleic acid (18:2ω6) in plasma phospholipids of the patients with Sjögren–Larsson syndrome did not differ significantly from that of healthy controls or the mentally retarded.

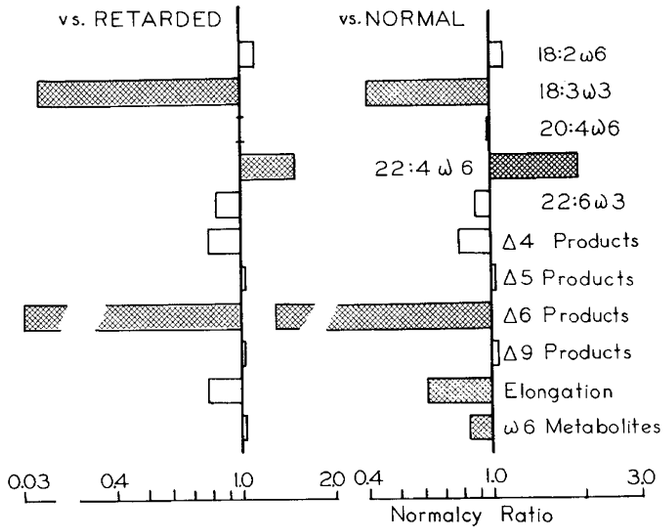

Fig. 1. Comparison of fatty acid patterns of plasma phospholipids in patients with Sjögren–Larsson syndrome with those in mentally retarded controls and in healthy controls. Values are expressed as the ratio between Sjögren–Larsson patients and controls for parameters indicated, and are, presented on a logarithmic scale. Light cross-hatching indicates statistically significant differences ($P < 0.05$) and dark crosshatching indicates $P < 0.01$.

This indicates that this syndrome does not involve a nutritional essential fatty acid deficiency or a defect in absorption of linoleic acid. However, the metabolites derived from this acid (ω6 metabolites) in plasma phospholipids were found to be significantly lower in the Sjögren–Larsson syndrome than in the group of healthy controls (Table 1) suggesting a metabolic defect. This group of acids was also lower in the Sjögren–Larsson patients than in mentally retarded patients, but not significantly so. Concerning the fatty acids of the linoleate family (ω6), 20:2ω6 and 20:3ω6 were significantly lower in Sjögren–Larsson patients than the healthy controls. The 22:5ω6 acid was significantly lower in the Sjögren–Larsson syndrome only when compared with mentally retarded patients and 22:4ω6 was significantly higher in the Sjögren–Larsson syndrome compared with both control groups. The groups of Sjögren–Larsson patients and healthy controls did not differ in their content of arachidonic acid (20:4ω6). The 18:3ω6 acid was not detectable, and 22:4ω6 was increased in the group of Sjögren–Larsson patients to 192% of the level in healthy controls. The total products of Δ6 desaturation, 16:2ω7 and 18:3ω6 were reduced to 3% of control values, whereas the products of Δ5 and Δ9 desaturation were not noticeably affected in the Sjögren–Larsson syndrome. The products of chain elongation, 20:2ω9, 20:2ω6, 20:4ω3, 22:4ω6, 22:4ω3 and 22:5ω3, were, as a group, significantly decreased in the Sjögren–Larsson group to 63% of those in the group of healthy controls, but did not differ significantly from those in the group of mentally retarded. All individual acids of this group were decreased in the Sjögren–Larsson syndrome except 22:4ω6 which was significantly higher.

In the Sjögren–Larsson syndrome, the fatty acids of the linolenic acid family (ω3) were, as a group, not significantly different from those in the controls; only 20:4ω3 formed by chain elongation was significantly lower in comparison with both control groups. Linolenic acid itself, 18:3ω3, was significantly lower than the control values.

CHOLESTERYL ESTERS

The content of 18:2ω6 in plasma cholesteryl esters in the Sjögren–Larsson syndrome was not different but the total ω6 metabolites were significantly lower than those in healthy controls (Table 2). In the Sjögren–Larsson syndrome, 22:6ω3 formed by a desaturation at position 4, was elevated 2– to 3–fold in the cholesteryl esters, where it reached 5.8% of the fatty acids. In the

Table 2. *Fatty acid patterns of plasma lipids of Sjögren-Larsson syndrome (SLS) and healthy controls (HC)*[1]

	Cholesteryl esters			Triglycerides			Free fatty acids		
	SLS (11)[2] Mean[1] ± S.E.	*P*	HC (14)[2] Mean[1] ± S.E.	SLS (11)[2] Mean[1] ± S.E.	*P*	HC (14)[2] Mean[1] ± S.E.	SLS (11)[2] Mean[1] ± S.E.	*P*	HC (14)[2] Mean[1] ± S.E.
18:1ω9	21.57 ± 1.20		20.25 ± 1.25	41.26 ± 1.01	<0.05	38.06 ± 0.74	39.25 ± 1.77	<0.001	26.99 ± 2.11
18:2ω6	47.54 ± 1.41		47.85 ± 2.80	13.85 ± 0.87	<0.05	16.48 ± 0.76	12.45 ± 1.11		16.32 ± 1.68
20:3ω9	0.10 ± 0.02		0.21 ± 0.07	0.10 ± 0.01	<0.05	0.19 ± 0.03	0.05 ± 0.03		0.41 ± 0.18
20:4ω6	4.42 ± 0.28	<0.05	5.41 ± 0.33	0.88 ± 0.09		1.03 ± 0.09	1.04 ± 0.19	<0.05	3.28 ± 0.71
22:6ω3	5.79 ± 1.31	<0.01	1.98 ± 0.51	0.88 ± 0.25		0.91 ± 0.11	0.46 ± 0.13	<0.001	0.04 ± 0.03
Total PUFA	61.78 ± 2.19		62.46 ± 2.47	18.13 ± 1.12	<0.001	23.81 ± 0.70	17.05 ± 1.19	<0.05	25.42 ± 2.43
Total ω6 acids	53.90 ± 1.48		56.08 ± 2.50	15.30 ± 0.90	<0.01	18.85 ± 0.75	14.85 ± 1.18	<0.01	22.08 ± 2.05
ω6 metabolites	6.36 ± 0.56	<0.05	8.22 ± 0.47	1.44 ± 0.09	<0.001	2.37 ± 0.18	2.40 ± 0.53	<0.05	5.76 ± 1.08
Total ω3 acids	7.58 ± 1.34		5.69 ± 0.89	2.58 ± 0.40	<0.001	4.38 ± 0.26	2.14 ± 0.31		2.27 ± 0.46
Monoenoic acids	24.86 ± 1.46		24.55 ± 1.50	46.19 ± 1.08	<0.05	43.78 ± 0.61	41.55 ± 1.94	<0.01	32.63 ± 2.13
Saturated acids	13.92 ± 0.88		13.16 ± 1.02	36.15 ± 0.94	<0.01	32.32 ± 0.85	41.59 ± 1.68		39.36 ± 3.45
20:3ω9/20:4ω6	0.02 ± 0.01		0.04 ± 0.01	0.09 ± 0.01	<0.01	0.19 ± 0.03	0.04 ± 0.02		0.13 ± 0.05
20:4ω6/18:2ω6	0.09 ± 0.01		0.16 ± 0.06	0.06 ± 0.01		0.07 ± 0.01	0.09 ± 0.01		0.25 ± 0.07
22:4ω6/20:4ω6	0.22 ± 0.10	<0.05	0.03 ± 0.01	0.10 ± 0.02		0.11 ± 0.02	0.05 ± 0.03		0.01 ± 0.01
4-desaturation	5.90 ± 1.32	<0.05	2.66 ± 0.48	0.98 ± 0.25		1.14 ± 0.12	0.73 ± 0.17	<0.01	0.12 ± 0.09
5-desaturation	5.32 ± 0.31	<0.05	6.93 ± 0.47	1.21 ± 0.14	<0.05	1.68 ± 0.12	1.35 ± 0.23	<0.05	3.74 ± 0.77
6-desaturation	0.40 ± 0.09	<0.001	1.34 ± 0.15	0.14 ± 0.01	<0.001	0.59 ± 0.09	0.33 ± 0.29		1.22 ± 0.33
9-desaturation	24.86 ± 1.46		24.55 ± 1.50	46.19 ± 1.08	<0.05	43.78 ± 0.61	41.55 ± 1.94	<0.01	32.63 ± 2.13
Elongation	2.40 ± 0.41		2.82 ± 0.46	1.09 ± 0.08	<0.01	2.00 ± 0.20	0.98 ± 0.14		1.86 ± 0.48

[1] Figures refer to relative concentration in %.

[2] Number of individuals.

phospholipid fraction, it was not altered. Products of Δ5 desaturation were low in the Sjögren–Larsson patients, and products of Δ6 desaturation were significantly decreased to 30% of the healthy control value.

TRIGLYCERIDES

The degree of total unsaturation (double bond index) of fasting triglycerides in the Sjögren–Larsson syndrome was 85% of that in healthy controls ($P < 0.001$) and 82% of that in the group of mentally retarded. The change of total unsaturation was due largely to a highly significant lower amount of total polyunsaturated fatty acids (76%) that was compensated by an increase in endogenous saturated and monoenoic acids (Table 2). In the Sjögren–Larsson syndrome, linoleate of triglycerides was decreased and its metabolic products were 61% of those in the group of healthy controls ($P < 0.001$). When compared with the mentally retarded, there was no significant difference. Products of Δ5 desaturation were 72% of those in the group of healthy controls ($P < 0.05$). Products of Δ6 desaturation were 24% of those in healthy controls ($P < 0.001$) and 15% of the values in the group of mentally retarded ($P < 0.01$). Elongation products were 55% of those in healthy controls ($P < 0.01$) and 42% of the values in the mentally retarded ($P < 0.01$). Thus the composition of plasma triglycerides also suggests impairment of Δ6 desaturation and possibly elongation reactions in patients with the Sjögren–Larsson syndrome.

FREE FATTY ACIDS

In the Sjögren–Larsson syndrome the double bond index of free fatty acids was lower than in healthy controls or in the mentally retarded. This was attributed to a significant decrease of polyunsaturated fatty acids to 67% of the level in healthy controls.

SUSPECTED SJÖGREN-LARSSON SYNDROME

The two patients suspected of having the Sjögren–Larsson syndrome exhibited divergent changes in fatty acid composition of plasma phospholipids. In one of the patients, 18:2ω6 was 91%, 18:3ω3 was 93%, 20:4ω6 was 73%, 22:4ω6 was 74%, and 22:6ω3 was 69% of the comparable values in healthy controls. The products of Δ4 desaturation were 69%, Δ5 desaturation 90%, and Δ9 desaturation 96% of the values in healthy controls. Products of Δ6 desaturation were not detectable, indicating impairment of desaturation and products of elongation were 106% of the healthy control values. In the other sibling, 18:2ω6 was 120%, 18:3ω3, 23%, 20:4ω6, 88%, 22:4ω6, 160% and 22:6ω3, 197% of the values in healthy controls. Products of Δ4 desaturation were 172%, Δ5 desaturation 88%, and Δ9 desaturation 88% of those in healthy controls. Products of Δ6 desaturation were not detected, indicating impairment of desaturation and products of elongation were 62% of those in healthy controls. Compared with Sjögren–Larsson patients, the first patient had 74% as much 20:4ω6 and 390% as much 22:4ω6, indicating an accentuated conversion of 20:4ω6 to 22:4ω6. The second patient had a lower content of 22:4ω6 in plasma phospholipids but an extremely elevated content of 22:6ω3 compared with the Sjögren–Larsson group.

DISCUSSION

Although linoleic acid deficiency is not a part of the Sjögren–Larsson syndrome, an abnormal metabolism of polyunsaturated fatty acids may be involved. The fatty acid pattern in plasma phospholipids of healthy and mentally retarded control patients, supported that conclusion. The defects appear to be in the Δ6 desaturation of polyunsaturated fatty acid metabolism. The metabolism of linoleic acid is shown in Figure 2, to illustrate the reactions affected. The decrease of plasma long chain ω6 acids derived metabolically from linoleic acid should have effects upon the composition and function of cellular membranes. Microsomal, mitochondrial and extracellular membranes would shift in composition and perhaps also in function. In patients with Sjögren–Larsson syndrome, both dermatological and neurological functions are impaired. It is tempting to speculate that an abnormal composition of polyunsaturated fatty acids in structural lipids such as phospholipids could be the underlying cause. In this study, all 11 Sjögren–Larsson syndrome patients showed a decrease in products of Δ6 desaturation, which also affected subsequent metabolites in the metabolic sequence. Our investigation of two siblings suspected of having the Sjögren–Larsson syndrome re-

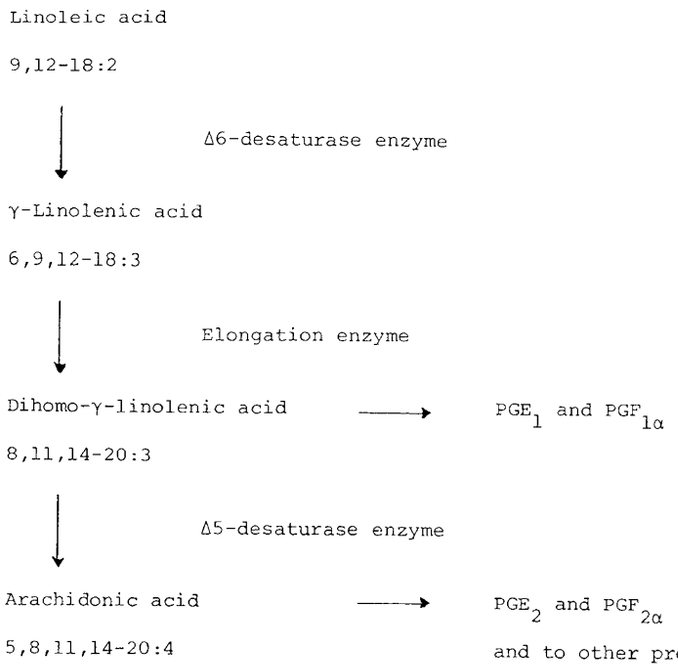

Fig. 2. The metabolic conversion of linoleic acid to long-chain polyunsaturated fatty acids of the ω6 family. In this abbreviation of Geneva nomenclature *cis,cis* 9,12-octadecadienoic acid (linoleic acid) is written 9,12–18:2.

vealed differences in their capacity to elongate polyunsaturated fatty acids. Fatty acid patterns of plasma phospholipids might help to distinguish between the Sjögren–Larsson syndrome and a syndrome of congenital ichthyosis with mental retardation in which spasticity does not develop. Analysis of the polyunsaturated fatty acid pattern as described here may thus have a diagnostic value. Compensation for some of the results of the metabolic defects in essential fatty acid metabolism may be afforded by diets rich in γ-linolenic acid (18:3ω6), arachidonic acid (20:4ω6) and long-chain ω3 acids. Alternatively, the Δ6 desaturase activity can perhaps be enhanced by zinc supplementation (2). These possibilities are now under investigation.

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22. The samples were collected after informed consent from the parents and the study was approved by the Ethical Committee of the University of Umeå.
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