SUMMARY

This thesis is composed of a short overview on various aspects of exogenous and endogenous fatty acids, the description of the method used for the fatty acid determinations in the reported studies, and four studies on effects of nutritional and hormonal factors on indirect parameters of fatty acid metabolism.

Chapter I describes various aspects of exogenous and endogenous fatty acids, including fatty acid metabolism and biological effects of exogenous long-chain fatty acids on cellular membranes, prostanoid formation and plasma lipids and lipoproteins.

In chapter II, a method for profiling of total long-chain fatty acids and cholesterol in a variety of biological materials is described. The method uses capillary gas chromatography with flame ionization detection. The within-run precision and day-to-day precision for fifteen fatty acids and cholesterol in erythrocyte samples were investigated. Quantitative data on the analysis of amniotic fluid samples collected from women in 30th to 38th week of gestation are given together with a correlation study on their lecithin/sphingomyelin and 16:0/18:0 ratios. In addition, the method was applied to lumbar cerebrospinal fluid, plasma, isolated leukemic blood cells and neuroblastoma tissue.

The study, described in chapter III, was designed to evaluate the changes of both serum and erythrocyte lipids during short-term continuous carbohydrate hyperalimentation, that is supposed to induce a 18:2c,ω6-deficient condition by inhibition of depot fat lipolysis. Twelve normal men received twice their estimated basal energy requirement by a carbohydrate solution via a nasogastric catheter during 48 hours, followed by a seven-hour fast. Subsequently, in nine of them 0.5 mg epinephrine was given subcutaneously under ongoing fasting. During hyperalimentation, serum triglycerides, phospholipids, total and unesterified cholesterol, phospholipids/unesterified cholesterol ratio, and plasma free fatty acids decreased, whereas the percentage of unesterified cholesterol increased. During fasting and subsequent epinephrine administration triglycerides and free fatty acids rose without reaching basal levels. Plasma and erythrocyte fatty acid composition already changed from two hours after the start of the feeding. Most markedly, a steady decrease in the erythrocyte 18:2c,ω6 level, amounting to more than 17% of the basal value at the end of the observation period was found. Neither in plasma, nor in erythrocytes a concomitant appearance of 20:3c,ω9 was seen. In erythrocytes, the relative amounts of the saturated fatty acids increased, whereas those of monounsaturated and polyunsaturated fatty acids decreased. Erythrocyte content of total fatty acids decreased and that of cholesterol increased. The ratios 16:1c,ω7/16:0 and 18:3c,ω6/18:2c,ω6 in plasma, and 20:3,ω6/18:2c,ω6 in plasma and erythrocytes increased, whereas those of 18:1c,ω7/16:1c,ω7 and 20:3c,ω6/18:3c,ω6 in plasma decreased. After 48 hours feeding serum glutamic pyruvic transaminase and glutamic oxaloacetic transaminase levels were moderately increased and rose further during fasting. Thus, continuous enteral hyperalimentation by carbohydrates alone rapidly

induces profound changes in serum-, plasma-, and erythrocyte lipid compositions and serum parameters of hepatic function. The data suggest a stimulation of de novo fatty acid synthesis, an augmentation of Δ9 and Δ6 desaturase activity along with an impairment of the chain-elongation of unsaturated fatty acids, and a shift of cholesterol from plasma to the erythrocyte membrane.

Chapter IV describes the results of fatty acid analyses of plasma and erythrocyte samples from Type 1 (insulin-dependent) diabetic patients during poor and after improved metabolic control. In comparison to twelve apparently healthy controls, thirteen poorly controlled patients had a low level of 18:3c,ω6, 20:3c,ω6, 22:6c,ω3 and total polyunsaturated fatty acids, and a high level of 18:0 and total saturated fatty acids. Improvement of diabetic control, achieved in seven of these patients by treatment with continuous subcutaneous insulin infusion coincided with an increase of 20:4c,ω6 and a normalization of total polyunsaturated fatty acids, with a concomitant decrease of total saturated fatty acids and total monounsaturated fatty acids, especially 18:1c,ω9. The results of this study can be important for the dietary advice to poorly controlled diabetic patients.

The results of a study on the effects of dietary 18:3c,ω6 supplementation on the fatty acid composition of plasma-, erythrocyte,- and platelet lipids from moderately controlled Type 1 (insulin-dependent) diabetic patients are shown in chapter V. In addition to their usual diet, nine diabetic men and ten male controls took 20 g d,α-tocopheryl acetate enriched evening primrose oil (14.45 g 18:2c,ω6, 1.73 g 18:3c,ω6, 400 mg d,α-tocopheryl acetate) daily for one week. At start, diabetic patients had more 14:0, 15:0 and 18:2c,ω6, and less 16:0, 16:1c,ω7, 18:1c,ω7, 18:3c,ω6, 20:3c,ω9, 20:4c,ω6 and 22:6c,ω3 in plasma, erythrocytes and/or platelets. Furthermore, they had lower 16:1c,ω7/16:0, 18:1c,ω7/16:0 and 20:4c,ω6/20:3c,ω6 ratios and a higher 20:3c,ω6/18:3,ω6 ratio. In diabetic patients, α-tocopherol levels in erythrocytes were lower, whereas those in plasma were normal. In both groups, oil intake changed fatty acid profiles. Most markedly, 20:3c,ω6 increased, whereas the ratios 20:3c,ω6/18:3c,ω6 and 20:4c,ω6/20:3c,ω6 decreased. 20:4c,ω6 increased in controls, but not in diabetic patients. Erythrocytes and platelets responded differently in their fatty acid profiles. α-Tocopherol rose in plasma and, although less for diabetic patients, in erythrocytes. In diabetic patients as well in controls, erythrocyte count, haemoglobin level, mean corpuscular haemoglobin content and concentration increased and glycosylated haemoglobin percentage decreased without an apparent decline in blood glucose levels. Plasma ß-thromboglobulin and platelet factor 4 decreased, especially in diabetic patients. In conclusion, diabetic patients had abnormal fatty acid patterns, suggesting an impaired Δ9, Δ6 and Δ5 desaturation and an enhanced chain-elongation, and had lower erythrocyte α-tocopherol levels; and short-term high dose intake of evening primrose oil increased 20:3c,ω6 in both groups, but 20:4c,ω6 only in controls, gave fatty acid responses which were different for erythrocytes and platelets, enhanced erythropoiesis, and lowered indices of in vivo platelet activation.

In chapter VI, the evaluation of the effects of an induced hypothyroidism on indirect parameters of fatty acid metabolism is given. Thirteen patients who were athyreotic as a consequence of ablation treatment for well-differentiated thyroid cancer were studied during triiodothyronine supplementation, and subsequently at the end of a two weeks withdrawal of this medication. Serum and plasma lipid concentrations, erythrocyte cholesterol content and plasma and erythrocyte total fatty acid patterns were measured. In addition, total fatty acid profiles of polymorphonuclear leukocytes of eight patients and scanning electron microscopic studies of erythrocytes of nine patients were made. An increase of the serum concentrations of total and unesterified cholesterol and phospholipids was observed in all patients. Except for two, all patients showed an increase in the serum triglyceride concentration. The relative amounts of 18:2c,ω6 rose and those of 20:3c,ω6 fell in all studied compartments. In addition, the relative amounts of all other ω6 fatty acids, 22:6c,ω3, 20:3c,ω9, 16:0, 18:0 and total saturated fatty acids decreased in plasma, whereas the levels of all monounsaturated increased in the erythrocytes. The level of 20:3c,ω9 rose in the erythrocytes and the 20:3c,ω9/20:4c,ω6 ratio rose in the polymorphonuclear leukocytes. The erythrocyte total fatty acids and cholesterol content and their ratio did not change, nor was any alteration seen in the erythrocyte morphology by scanning electron microscopy. The study reveals that the induction of hypothyroidism in man changes fatty acid patterns of plasma, erythrocytes and polymorphonuclear leukocytes. The nature of these alterations suggests especially a disturbance in the Δ6 desaturase activity. The data point to the possibility of a derangement of prostanoid synthesis in hypothyroidism.