Abstracts

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Biochemistry and nutrition

CHOLESTEROL AND TRIGLYCERIDE DISTRIBUTIONS IN AN ADULT EMPLOYEE POPULATION: THE PACIFIC NORTHWEST BELL TELEPHONE COMPANY HEALTH SURVEY. J.J. Hoover, C.E. Walden, R.O. Bergelin, P.W. Wahl, J.J. Albers, W.R. Hazzard and R.H. Knopp (The Northwest Lipid Research Clinic, the Depts. of Epidemiology and Biostatistics, Schl. of Public Health and Community Medicine; and the Dept. of Medicine, Schl. of Med., Univ. of Washington, Seattle, WA) *Lipids* 15, 895–903 (1980). Plasma cholesterol and triglyceride are presented for 4503 adult employees of the Pacific Northwest Bell Telephone Company. Cross-sectional age and sex specific means and percentiles are shown. Females are classified by use or nonuse of exogenous sex hormones. Comparisons are examined among these groups, between blacks and whites, and among education and occupation categories. In these cross-sectional data, cholesterol and triglyceride generally increase with age and exhibit distinct differences by sex and by hormone use.

CHANGES IN LIPIDS AND LIPOPROTEINS IN PATIENTS WITH HYPERLIPIDEMIA TYPE IIb, IV AND V TREATED WITH DIFFERENT LIPID LOWERING DRUGS. V. Hutt, J.G. Wechsler, H.-U. Klör and H. Ditschuneit (Dept. of Med., Div. of Metabolism, Nutrition and Gastroenterology, University of Ulm, West Germany) *Artery* 8, 113–9 (1980). In this study we examined the influence of different lipid lowering drugs (xantinolnicotinate (Xn), bezafibrate (Bf) and a combination of inositolnicotinate and clofibrate (In-Cl) on the lipid and lipoprotein concentration in 61 hyperlipidemics of the types IIb, IV and V. Treatment with the 3 drugs showed a significant LDL-cholesterol decrease in type IIb and a LDL-cholesterol increase in the types IV and V. Concerning protective HDL lipoproteins an increase of HDL-cholesterol could be observed in all three types only by treatment with Xn and Bf. Concomitantly in type V a type conversion to type IV could be observed under drug treatment regarding the chemical composition of the lipoprotein fractions VLDL, LDL and HDL.

FATTY ACID ELONGATION BY A PARTICULATE FRACTION FROM GERMINATING PEA. B.R. Jordan and J.L. Harwood (Dept. of Biochem., Univ. College, P.O. Box 78, Cardiff CF1 1XL, Wales, U.K.) *Biochem. J.* 191, 791–7 (1980). The synthesis of fatty acids from [^{14}C]malonyl-CoA was studied with a high-speed particulate fraction from germinating pea *(Pisum sativum)*. Addition of a series of di-saturated phosphatidylcholines, with different acyl constituents, resulted in stimulation of overall fatty acid synthesis as well as an increase in the radiolabelling of the fatty acid two carbon atoms longer than the acyl chain added. This chain lengthening of fatty acids donated from phosphatidylcholine was due to the action of both fatty acid synthetase and palmitate elongase. The results are discussed in relation to previous data obtained *in vivo* on plant fatty acid synthesis and current suggestions for the role of phosphatidylcholine in this process.

ISOLATION AND PARTIAL CHARACTERIZATION OF THE LIPID PHASES OF HUMAN ATHEROSCLEROTIC PLAQUES. S.S. Katz and D.M. Small (Dept. of Med., Royal Victoria Hosp., Montreal, Quebec H3A 1A1, Canada) *J. Biol. Chem.* 255, 9753–9 (1980). Human atherosclerotic plaques have lipid compositions that fall in the three-phase region of the phase diagram of the major lipids of plaques, cholesterol, cholesterol ester, and phospholipid. The top layer of homogenized plaque ($d < 1.00$ g/ml) consisted of lipid droplets composed of 79.2% cholesterol ester, 7.8% triglyceride, 8.5% cholesterol and 4.5% phospholipid. The top layer of extracted total plaque lipids had a similar composition. The top layer of the extracted lipid system comprised 52% of total lipids closely approximating the 50% calculated from the phase diagram. Homogenate layers were filtered and recentrifugated on a density gradient to further purify the crystals. The composition of the purified crystals was 88.0% cholesterol, 10.0% cholesterol ester, 1.1% triglyceride and 0.9% phospholipid. The $d = 1.054$ layer of the extracted lipid system had a similar composition. Thus, two of the lipid phases of plaques, the cholesterol ester phase and the cholesterol crystalline phase, were isolated in relatively pure form. A fraction of plaque lipids is bound to protein or other more dense plaque constituents, and will have to be considered in future phase equilibrium studies of plaque lipids.

EFFECT OF JOGGING ON SERUM LOW DENSITY LIPOPROTEIN CHOLESTEROL. S. Kaufman, B. Kaufman, D. Reynolds, I. Trayner and G.R. Thompson (Dept. of Human Sciences, Univ. of Technology, Loughborough, England) *Artery* 7, 99–108 (1980). The effects of jogging on serum lipids were assessed in 16 normolipidemic males who ran an average of 5.8 miles (9.3 kilometers) per week for 6 weeks. There was no change in serum triglyceride concentration or clearance nor in HDL-cholesterol, but both total and LDL-cholesterol concentrations decreased significantly, by 5.7 and 8.3% respectively. Individual decreases in LDL-cholesterol were correlated with the distance run and it seems probable that a stimulatory effect of exercise on LDL catabolism was responsible. These findings suggest a possible explanation for the known protective effect of exercise against coronary heart disease, even when taken in amounts insufficient to raise HDL-cholesterol.

THE BILE ACID BINDING AND HYPOCHOLESTEROLEMIC ACTION OF TWO WATER-SOLUBLE POLYMERS. G.W. Kuron, N. Grier and J.W. Huff (Merck Inst. for Therapeutic Research, Rahway, NJ 07065) *Atherosclerosis* 37, 353–60 (1980). The in vitro bile acid binding properties of 2 water-soluble, linear, cationic resins, poly-[(dimethylimino)trimethylene chloride] or 3,3-ione Cl, and poly-diallyldimethylammonium chloride) or CAT-FLOC were determined. Both polymers were substantially more active than cholestyramine. All were compared for hypocholesterolemic effect in normo-cholesterolemic dogs. CAT-FLOC and 3,3-ionene Cl, administered at 1.8 and 1.2 g/day, respectively, exhibited cholesterol-lowering action equivalent to cholesterylamine given at 12 g/day. The results of this study suggest that effective reduction of plasma cholesterol may be achieved with significantly lower doses of bile acid sequestrants.

ALFALFA SAPONINS AND ALFALFA SEEDS. DIETARY EFFECTS IN CHOLESTEROL-FED RABBITS. M.R. Malinow, P. McLaughlin, C. Stafford, A.L. Livingston and G.O. Kohler (Oregon Regional Primate Res. Center, Beaverton, OR) *Atherosclerosis* 37, 433–8 (1980). Since alfalfa meal prevents hypercholesterolemia and atherosclerosis in rabbits and alfalfa saponins prevents the expected rise in cholesterolemia induced by dietary cholesterol in monkeys, the experiments being reported here were performed to determine whether alfalfa saponins affect atherogenesis in rabbits. In addition, the effects of alfalfa seeds were studied. Cholesterol-fed rabbits were randomly assigned to 3 groups: (a) control animals ($N = 18$); (b) animals maintained on a diet containing 1.0 to 1.2% alfalfa saponins ($N = 18$); and (c) animals maintained on a diet containing 40% alfalfa seeds ($N = 17$). Results after a 4-month observation period demonstrated that alfalfa saponins and alfalfa seeds reduce hypercholesterolemia, aortic sudanophilia, and the concentration of cholesterol in aortic intima-plus-media and in the liver, but do not induce changes in the hematocrit.

DYNAMICS OF LIPID-PROTEIN INTERACTIONS. INTERACTIONS OF APOLIPOPROTEIN A-II FROM HUMAN PLASMA DENSITY LIPOPROTEINS WITH DIMYRISTOYLPHOSPHATIDYLCHOLINE. J.B. Massey, A.M. Gotto, Jr., and H.J. Pownall (Dept. of Med., Baylor College of Med., and the Methodist Hosp., Houston, TX 77030) *J. Biol. Chem.* 255, 10167–73 (1980). ApoA-II and dimyristoylphosphatidylcholine (DMPC) spontaneously associate to give three different complexes whose structures are determined by the initial reactant concentration and by the reaction temperature with respect to T_c (23.9°C), the gel to liquid crys-

talline transition temperature of DMPC. These results suggest that the initial lipid/protein ratio and the physical state of a lipid or lipid-protein complex determines the composition and structure of the resulting complex and support the view that lipid-protein interactions are stronger than protein-protein or lipid-lipid interactions.

INCORPORATION AND DISAPPEARANCE OF TRANS FATTY ACIDS IN RAT TISSUES. C.E. Moore, R.B. Alfin-Slater, and L. Aftergood (Univ. of California Schl. of Public Health, Los Angeles, CA 90024) *Am. J. Clin. Nutr.* 33, 2318–23 (1980). An investigation was undertaken to study the rate of incorporation and disappearance of *trans* isomers of octadecenoic and octadecadienoic acids from different tissues of rats fed 15% fat diets containing *trans* fatty acids for 3 months. At the end of 3 months some of the animals were killed and the remaining animals were changed over to a diet containing only trace amounts of *trans* fatty acids. Thereafter, representative animals were killed at 2, 4, 8, and 12 weeks. The fatty acid composition of tissue lipids was measured by gas liquid chromatography. *Trans* octadecenoate was primarily incorporated into phospholipids and triglycerides of plasma, liver, kidney, heart, adipose tissue, and red blood cells. *Trans* isomers of octadecadienoate accumulated in triglycerides of plasma, liver, kidney, heart, and adipose tissue while only small amounts accumulated in tissue phospholipids and cholesteryl esters. After removal of *trans* fatty acids from the diet, the time of disappearance of *trans* isomers of octadecenoate and octadecadienoate from tissues varied.

CHEMICAL AND ISOTOPIC MEASUREMENT OF CHOLESTEROL ABSORPTION IN THE RAT. M.H. Green (Div. of Nutr. Sciences, Cornell Univ., Ithaca, NY 14853) *Atherosclerosis* 37, 343–52 (1980). Data are presented on cholesterol absorption in 6 non-fasted lymph duct-cannulated rats during continuous infusion of oil or oil plus cholesterol (mass + isotope). Endogenous thoracic duct lymph cholesterol averaged 2 μmoles/h during infusion of triolein. Lymph cholesterol flux increased to 3.3 μmoles/h during infusion of oil plus a low dose of cholesterol (1.7 μmoles/h), to 4.8 μmoles/h at a medium dose (4.4 μmoles/h) and to 8.9 μmoles/h during infusion of a high dose of cholesterol (20 μmoles/h). The transport of endogenous cholesterol was significantly decreased by the high infusion rate of cholesterol. At each level of cholesterol infusion, about 90% of the increase in lymph cholesterol was due to cholesteryl ester. Radioactive cholesterol significantly underestimated the percent of cholesteryl ester in the increased cholesterol flux due to cholesterol infusion, especially at the low dose. The percent of infused radioactive cholesterol absorbed was a fairly accurate monitor of the increase in lymph cholesterol due to the exogenous loads. However, small numerical discrepancies at the medium and high doses suggest that the use of isotopic cholesterol to measure cholesterol absorption in careful balance studies may have limitations.

SPECIFIC CHANGES OF BILE ACID METABOLISM IN SPONTANEOUSLY DIABETIC WISTAR RATS. A.S. Hassan, M.T. Ravi Subbiah, and P. Thiebert (Depts. of Pathology and Medicine (Lipid Res. Center), Univ. of Cincinnati Med. Center, Cincinnati, OH 45267) *Proc. Soc. Exp. Biol. Med.* 164, 449–52 (1980). Bile acid metabolism has been investigated in a newly described animal model depicting juvenile human diabetes (spontaneously diabetic Wistar (BB) rat) and compared to normoglycemic control from the Wistar strain. Diabetic animals used were on insulin treatment except for the last 24 hr. The plasma glucose levels (mg%) of diabetic rat (D) was significantly higher than control rats (C) (150 ± 35 in C vs 340 ± 32 in D). The total bile acid pool (mg/100 g) in D was significantly ($P < 0.05$) higher when compared to C (9.0 ± 0.8 in C vs 14.9 ± 1.7 in D). The pool of cholic acid was significantly ($P < 0.05$) increased while that of chenodeoxycholic acid was significantly ($P < 0.05$) decreased (cholic acid: 5.9 ± 0.45 in C vs 10.06 ± 1.2 in D; chenodeoxycholin 0.90 ± 0.1 in C vs 0.57 ± 0.06 in D). This increased the cholin/chenodeoxycholin acid ratios from 6.6 ± 0.4 in controls to 19.3 ± 2.4 in diabetic rats. These studies have shown diverse alteration in the concentration of the two primary bile acids in the diabetic state.

TRIGGERING OF THE MACROPHAGE AND NEUTROPHIL RESPIRATORY BURST BY ANTIBODY BOUND TO A SPIN-LABEL PHOSPHOLIPID HAPTEN IN MODEL LIPID BILAYER MEMBRANES. D.G. Hafeman, J.T. Lewis and H.M. McConnell (John Stauffer Lab. for Physical Chem., Stanford Univ., Stanford, CA 94305) *Biochemistry* 19, 5387–94 (1980). The specific antibody-dependent stimulation of the respiratory burst (cyanide-insensitive oxygen consumption, 1-C-glucose oxidation) of RAW264 macrophage cell line by haptenated lipid vesicles depends strongly on the physical properties of the lipid membrane, as well as the surface density of antibodies on the vesicles. Lipid membranes that are "solid" at 37° C (dipalmitoylphosphatidylcholine, DPPC) are much more effective, per vesicle bound, than are "fluid" membranes (dimyristoylphosphatidylcholine, DMPC). Vesicle membranes that have both fluid and solid regions (DPPC containing < 20 mol% cholesterol) show both enhanced binding rates (due to the fluid regions) and enhanced resporatory rates (due to the solid regions). In contrast to these results, the specific antibody-dependent respiratory burst of neutrophils due to haptenated vesicles parallels the antibody-dependent vesicle binding and shows no significant difference between fluid and solid target membranes.

EFFECT OF DIET COMPOSITION AND FASTING ON LIPOGENESIS IN LEAN AND POLYGENIC OBESE MICE. B. Hennig, T.M. Sutherland, M.M. Mathias and B.A. Smith (Dept. of Animal Sci. and Food Sci. and Nutr., Colorado St. Univ., Fort Collins, CO 80523) *Lipids* 15, 908–12 (1980). A line of mice was developed which exhibited spontaneous obesity when fed commercial laboratory ration low in fat content. Obese mice were compared to a nonobese related line to determine whether energy source in the diet would affect onset of obesity. Experimental diets—beef tallow, corn oil or low-fat—were instituted ad libitum at the time of weaning. Fatty acid synthesis was inhibited by high-fat diets compared to low-fat diet in both lines. Of the 2 high-fat diets, the corn oil diet inhibited fatty acid synthesis about twice as much as beef tallow diet. There was no line effect on tritium incorporation into cholesterol. Cholesterol synthesis from glucose-U-^{14}C was greater in obese than lean mice. Diets had no effect on tritium and glucose-U-^{14}C incorporation into cholesterol. Fasting reduced fatty acid synthesis in all mice, but total body fatty acid synthesis was not affected by lines or dietary treatment under fasted conditions. A failure of inhibition of lipogenesis or an enhanced efficiency in fat deposition by feeding beef tallow compared to corn oil diet may explain the fact that lean mice fed the beef tallow diet tended to be more obese than lean mice fed corn oil or low-fat diets.

LIPOGENESIS IN MAN. PROPERTIES AND ORGAN DISTRIBUTION OF ATP CITRATE (PRO-3S)-LYASE. G.E. Hoffmann, H. Andres, L. Weiss, C. Kreisel and R. Sander (Klinisch-chemisches Institut and 1. Medizinische Abteilung, Krankenhaus Harlaching, Sanatoriumplatz 2, D-8000 München 90 (F.R.G.)) *Biochem. Biophys. Acta* 620, 151–8 (1980). 1. The lipogenic enzyme ATP citrate lyase is partially purified from human liver by ammonium sulfate fractionation and anion-exchange chromatography. 2. K_m values for the substrates are $1.1*10^{-5}$, $1.3*10^{-3}$, and $1.2*10^{-4}$ M for CoASH, ATP and citrate, respectively. The hypolipidemic drug L (-)-hydroxycitrate is a competitive inhibitor with respect to citrate ($K_i = 3*10^{-4}$). 3. Specific activities measured in liver, adipose tissue and intestinal mucosa (autopsie and biopsie material) are in the range of 1 mU/mg protein suggesting that the citrate pathway does not significantly contribute to human lipogenesis. No. stimulation is found after a 3-day carbohydrate-rich diet. 4. Specific activities of other key-enzymes of the acetyl-CoA production from carbohydrates (pyruvate dehydrogenase, cytosolic acetyl-CoA synthetase) are of the same low magnitude.

STUDIES ON ACYL-CoA SYNTHETASE IN RAT ARTERIAL WALL. N. Morisaki, N. Matsuoka, K. Shiral, Y. Sato and A. Kumagai (2nd Dept. of Internal Med., Schl. of Med., Chiba Univ., Chiba, Japan) *Atherosclerosis* 37, 439–47 (1980). The properties and characteristics of acyl-CoA synthetase from the arterial wall of rats were investigated. The enzyme is located mainly in the microsomes. Its activity was found to be maximal at pH 7.0–8.0, and to be completely dependent on ATP, CoASH and Mg^{2+}. The *Km* values for these substances were the same as those of the enzyme in liver. The activity was affected by serum, divalent cations, albumin, lipoproteins and phospholipids. In rats, the activity was decreased in various pathological conditions, such as tocopherol deficiency, hypertension and diabetes mellitus and was increased in hypercholesterolemia. The physiological significance of this enzyme in free fatty acid metabolism is discussed on the basis of these results.

HDL-CHOLESTEROL CONCENTRATION AND SEVERITY OF CORONARY ATHEROSCLEROSIS DETERMINED BY CINEANGIOGRAPHY. H.K. Naito, R.L. Greenstreet, J.A. David, W.L. Sheldon, E.K. Shirey, R.C. Lewis, W.L. Proudfit and R.G. Gerrity (Cleveland Clinic Foundation, 9500 Euclid Ave., Cleveland, Ohio

44106) *Artery* 8, 101–12 (1980). We studied 226 adult male subjects who underwent coronary arteriography. Their serum lipid and lipoprotein levels were correlated with the severity of coronary artery disease. Studies showed a slight but statistically significant correlation between CAD and HDL-P/TC, HDL-C/TC, followed by LDL-C/HDL-P and HDL-P. HDL-C and TC were significant at the $P < 0.05$ level; P value of TG was nonsignificant. Subjects were conveniently grouped based on degree of coronary artery narrowing: normal, mild (1–50%); moderate-severe (51–99%) and very severe (100% occlusion). Of the 11 lipid variables, the best predictor of the stage of the CAD was HDL-P/TC as measured by one-way analysis of variance. This trend was unaltered even after adjustment for covariates. HDL-P, LDL-C/HDL-P and HDL-C/TC were also significant, but the other lipid parameters were not. The study indicates that HDL-C, by itself, is not as effective a predictor of CAD as HDL-P/TC. Also, the small but statistically significant inverse relationship between HDL-P/TC and CAD suggests that a low HDL-P/TC ratio can be considered a risk factor for CAD but not as a dependable clinical diagnostic aid for predicting the severity of CAD on an individual basis.

DIETARY REGULATION OF DIPALMITOYL PHOSPHATIDYLCHOLINE IN THE LUNG. EFFECTS OF ESSENTIAL FATTY ACID DEFICIENCY. M. Nakamura, T. Wawamoto and T. Akino (The Third Dept. of Internal Med., Dept. of Biochem., Sapporo Med. Col., Sapporo 060 Japan) *Biochim. Biophyis. Acta* 620, 24-36 (1980). An essential fatty acid deficiency resulted in a significant decrease of saturated phosphatidylcholine in rat lung tissue, with the reduction being mainly due to that of dipalmitoyl species. This decrease was almost completely reversed by administration of a diet containing linoleate for seven days. The features of saturated phosphatidylcholine synthesis in the deficient rat lung slices were studied with labeled precursors in the presence of different concentrations of linoleate and oleate in the medium. While the utilization of 1-[1-^{14}C]palmitoyl glycerophosphocholine by lung tissue was enhanced in the deficient state, in the presence of linoleate it showed almost the same level as that of the controls. The essential fatty acid deficiency resulted in an increase in the activity of liver choline kinase by 46%. However, other enzyme activities involved in phosphatidylcholine synthesis in the lung and liver were unaffected by the deficient state.

IN VIVO AND IN VITRO INHIBITION OF RAT LIVER VITAMIN D_3-25-HYDROXYLASE ACTIVITY BY 19-HYDROXY-10(S),19-DIHYDROVITAMIN D_3. H.E.Paaren, R.M. Moriarty, H.K. Schnoes and H.F. DeLuca (Dept. of Biochem., College of Agricultural and Life Sciences, Univ. of Wisconsin—Madison, WI 53706) *Biochemistry* 19, 5335–9 (1980). Rats treated with varying amounts of 19-hydroxy-10(S),19-dihydrovitamin D_3 prior to administration of physiologic doses of vitamin D_3 exhibit normal intestinal calcium transport but are unable to mobilize bone calcium. In contrast, 19-hydroxy-10(R),19-dihydrovitamin D_3 had no inhibitory activity. Circulating serum levels of 25-hydroxy-[^{3}H]vitamin D_3 and 1α,25-dihydroxy[^{3}H]vitamin D_3 are markedly suppressed but not totally eliminated in animals predosed with 19-hydroxy-10(S),19-dihydrovitamin D_3 before [^{3}H]vitamin D_3. Hepatic 25-hydroxyl[^{3}H]vitamin D_3 levels were approximately equal in both 19-hydroxy-10(S),19-dihydrovitamin D_3 treated and untreated rats. However, the rate of conversion of [^{3}H]vitamin D_3 to 25-hydroxyvitamin D_3 in vivo is greatly reduced in the treated rats. The inhibitory vitamin analogue was also shown to block hepatic microsomal 25-hydroxylation in vitro. These results indicate that 19-hydroxy-10(S),19-dihydrovitamin D_3 is a specific inhibitor for a hepatic microsomal vitamin D_3-25-hydroxylase system.

METABOLISM OF GLYCOSAMINOGLYCANS AND LIPIDS IN SMOOTH MUSCLE CELLS FROM ATHEROSCLEROTIC RABBIT AORTAS IN CULTURE. K. Pietilä, S. Ylä-Herttuala, O. Jaakkola and T. Nikkari (Dept. of Biomed. Sciences, Univ. of Tampere, Tampere, Finland) *Atherosclerosis* 37, 449-56 (1980). Glycosaminoglycan (GAG) and lipid synthesis in smooth muscle cells cultured from normal and atherosclerotic rabbit aortas were studied. The incorporation of [^{3}H]oleate into phospholipids was enhanced in cells from atherosclerotic aortas indicating more rapid synthesis of this lipid fraction in these cells. Concentrations of free and esterified cell cholesterol were similar. The results indicate that the enhanced synthesis of sulphated GAGs typical of proliferative atherosclerosis in vivo is maintained in the third passage cultures of cells from atherosclerotic rabbit aortas. In addition there was an enhancement in the synthesis of phospholipids in these cells.

THE ROLE OF MEMBRANE PHOSPHOLIPID IN EXPRESSION OF ERYTHROCYTE Rh_o(D) ANTIGEN ACTIVITY. F.V. Plapp, M.M. Kowalski, J.P. Evans, L.L. Tilzer, and M. Chiga (Dept. of Path. and Onc., Univ. of Kansas Med. Center, Kansas City, KA 66103) *Proc. Soc. Exp. Biol. Bed.* 164, 561–8 (1980). Previous investigators have reported that the expression of Rh_o(D) antigen activity by human erythrocytes and their membranes depended on the presence of phospholipid. In order to further elucidate the role of phospholipids in expression of Rh_o(D) antigen activity, erythrocyte membranes and partially purified Rh_o(D) antigens were incubated with bee venom phospholipase A_2. Treatment of erythrocyte membranes with phospholipase A_2 resulted in loss of Rh_o(D) antigen activity as detected by hemagglutination inhibition assays. However, subsequent solubilization of these treated membranes with deoxycholate allowed recovery of Rh_o(D) antigen activity. Phospholipase treatment of solubilized Rh_o(D) antigens, which had been partially purified by affinity chromatography on anti-Rh_o(D) IgG agarose columns, did not destroy Rh_o(D) antigen activity. These results suggested that phospholipids did not affect the antigenic determinants of the Rh_o(D) antigen since solubilized, partially purified Rh_o(D) antigens retained their antigenicity following exposure to phospholipase. Phospholipids were presumably required for proper orientation of Rh_o(D) antigens within erythrocyte membranes since Rh_o(D) membranes lost their antigenicity following phospholipase treatment.

PLASMA HIGH-DENSITY LIPOPROTEIN METABOLISM IN SUBJECTS WITH PRIMARY HYPERTRIGLYCERIDAEMIA: ALTERED METABOLISM OF APOPROTEINS AI AND AII. S.N. Rao, P.J. Magill, N.E. Miller and B. Lewis (Dept. of Chemical Path. and Metabolic Disorders, St. Thomas' Hosp., London SE1 7EH, England) *Clin. Sci.* 59, 359–67 (1980). The metabolism of the major proteins of plasma high-density lipoprotein (HDL), apoproteins AI and AII, have been studied in 10 normotriglyceridaemic subjects and in 11 hypertriglyceridaemic subjects (plasma triglyceride 4.5–25 mmol/l) by kinetic analysis of the plasma specific radioactivity versus time curves of the apoproteins after intravenous injection of autologous ^{125}I-labelled high-density lipoprotein. The plasma apoprotein AI and AII concentrations were significantly lower in the hypertriglyceridaemic subjects than in the normotriglyceridaemic subjects. Kinetic analysis showed that this was associated with a lower rate of synthesis of apoprotein AI ($P < 0.01$) and a higher fractional catabolic rate of apoprotein AII ($P < 0.01$) in the hypertriglyceridaemic group. Thus hypertriglyceridaemia appears to be frequently associated with divergent abnormalities of the metabolism of the major high-density lipoprotein apoproteins.

INTRAINDIVIDUAL VARIABILITY OF PLASMA CHOLESTEROL AND TRIGLYCERIDES AND THE EFFECT OF PROPANOLOL TREATMENT. K. Rühling, I. Schauer and K. Thielmann (Dept. of Pathobiochemistry, Medical Academy of Erfurt, 506 Erfurt, DDR) *Artery* 8, 140-5 (1980). In 114 male subjects cholesterol and triglyceride concentrations in plasma after overnight fasting were followed up during 12 weeks. About one third of the individuals showed pronounced day to day variations of their cholesterol or/and triglyceride levels. Considerable intraindividual variability was moreover found for HDL cholesterol. Plasma lipid instability was more frequent in hyperlipemics and in subjects with low HDL cholesterol than in normolipemics. It was tried to level out the fluctuations by a beta blocking agent. Propranolol was used and proved to reduce the fluctuations of total cholesterol. However, at the same time the concentrations of triglycerides were increased and those of HDL cholesterol decreased. Practical consequences of both the fluctuating plasma lipid concentrations and the propranolol effects are stressed.

EFFECTS OF ALCOHOL INGESTION ON LIPIDS AND LIPOPROTEINS IN NORMAL MEN: ISOCALORIC METABOLIC STUDIES. C.J.Gleuck, E. Hogg, C. Allen and P.S. Gartside (General Clinical Research and Lipid Research Clinic, Univ. of Cincinnati, College of Med., Cincinnati, OH) *Am. J. Clin. Nutr.* 33, 2287–93 (1980). To investigate metabolic relationships between alcohol ingestion and fasting plasma high density lipoprotein cholesterol (C-HDL) and triglycerides, seven young normal males were assessed with isocaloric substitution of alcohol for carbohydrate in the diet. For a 5-week study period, an isocaloric low cholesterol diet containing 20% of the calories as protein, 40% as fat, and 40% as carbohydrate, with <300 mg cholesterol per day, P/S, 1.5/1, was ingested. In weeks 2 and 3, 35 and 53 g/day of 100 proof Vodka were ingested, with isocaloric substitution of alcohol for dietary carbohydrate during

these study days. By two-way analysis of variance and Scheffe's paired t tests, there were no significant differences in either C-HDL or triglyceride levels for any of the five metabolic diet, alcohol substitution diet periods; additionally, there were no significant effects of lecithin on plasma lipids or lipoproteins. Alcohol's effect on C-HDL and triglyceride probably involves an interaction with total calories, and perhaps with dietary composition (cholesterol, saturated fat, carbohydrate content), as well as the amount of ethanol ingested, and duration of intake.

EFFECT OF HYDROXY ACIDS ON HYPERCHOLESTEROLAEMIA IN RATS. R.D. Sharma (National Inst. of Nutr., Indian Council of Medical Res., Jamai Osmania (P.O.), Hyderabad 500007, A.P. India) *Atherosclerosis* **37**, 463–8 (1980). Hydroxy acids (aliphatic and aromatic) which are present in legumes were added as supplements to a diet causing hypercholesterolaemia in rats. Ferulic, *p*-coumaric, phytic and uronic acids showed hypolipidemic activity while vanillic, caffeic and cinnamic acids did not. The trace mineral content of serum was not affected by these acids.

EFFECT OF LOW CHOLESTEROL, LINOLEIC ACID ENRICHED DIET ON THROMBOTIC TENDENCY AND PLASMA LIPOPROTEINS IN PATIENTS WITH ANGINA PECTORIS. J.V. Turck, U.M.T. Houtsmuller, R.N. Lussenburg (G.J.H. den Ottolander Municipal Hospital Bergweg, Bergselaan 62, Rotterdam; Unilever Research, P.O. Box 114, 3130 AC Vlaardingen, The Netherlands) *Artery* **8**, 134–9 (1980). Eighteen patients with an established angina pectoris aged 46–74 years were investigated. These patients received a low cholesterol, linoleic acid enriched diet during a period of three months. Of these patients seventeen terminated the three months period. The adherence to the diet was assessed by determining the fatty acid pattern in cholesterol and triglycerides. Both were found to increase significantly and to the same extent. When comparing the values between the entry to the study and after three months of dietetic intervention we found a significant improvement in the fibrinogen level, haematocrit, the aggregation of platelets, the PAT I test according to Breddin and in the test according to Wu and Hoak. However, the fibrinolytic activity before occlusion of an arm was diminished. The changes in ADP -, collagen -, adrenalin and thrombin induced platelet aggregation were not uniform. We found a significant lowering of VLDL, LDL, phospholipids and total cholesterol. HDL did not change significantly. It seems that the diet had a favourable effect on several thrombotic and lipoprotein parameters in these patients.

PARTITION OF KETONE BODIES INTO CHOLESTEROL AND FATTY ACIDS IN VIVO IN DIFFERENT BRAIN REGIONS OF DEVELOPING RATS. Y.-Y. Yeh (Lab. of Nutr. and Metab., St. Jude Children's Res. Hosp., Memphis, TN 31801) *Lipids* **15**, 904–7 (1980). The proportions of labeled ketone bodies and glucose incorporated into cholesterol and fatty acids in different regions of the brain in developing rats were compared. In cerebrums of 15- and 18-day-old rats, the ratios of dpm cholesterol/dpm fatty acids incorporated from [3-^{14}C]acetoacetate and [3-^{14}C)β-hydroxybutyrate ranged from 0.4 to 0.7, or 50 to 100% higher than values obtained with [U-^{14}C]glucose. Much higher ratios were obtained with younger animals: from 1 to 12 days of life, the values ranged from 1.0 to 1.3 with [3-^{14}C]β-hydroxybutyrate as substrate, and, from 1 to 5 days, with [3-^{14}C]acetoacetate, they were 1.0 or greater. Clearly, a greater proportion of acetoacetate and β-hydroxybutyrate was incorporated into cholesterol during the first week of life than the remaining suckling period. Like cerebrum, other brain regions yielded higher ratios of dpm cholesterol/dpm fatty acids from [3-^{14}C] β-hydroxybutyrate during the first 12 days of life than on day 17. Since active synthesis of cholesterol from ketone bodies during the early postnatal period coincides with a period of rapid brain growth, the results indicate that ketone bodies are more important early in the suckling period as sources of cholesterol for brain growth.

EFFECT OF CHRONIC INGESTION OF DDT ON PHYSIOLOGICAL AND BIOCHEMICAL ASPECTS OF ESSENTIAL FATTY ACID DEFICIENCY. D.A. Sampson, R.E. Pitas and R.G. Jensen (Dept. of Nutr. Sciences, Univ. of Connecticut, Storrs, CT 06268) *Lipids* **15**, 815–22 (1980). Male weanling rats were fed semipurified diets with and without essential fatty acid (EFA) and DDT (150 ppm) for 14 weeks to determine the effects of the pesticide on physiological and biochemical aspects of EFA deficiency (EFAD). DDT did not affect EFAD-induced reduction in growth rate or final body weight, nor did the pesticide affect EFAD-induced changes in feed efficiency or skin dermatitis. The pesticide did increase liver/body mass ratios, but did not interact with EFAD, which also increased this ratio. The pesticide produced complex changes in total fatty acid composition of liver and tail skin: liver levels of 18:0, 18:2 and 20:3ω9 were increased, whereas levels of 12:0, 14:0 and 16:0 were decreased. In both tissues, DDT interacted with EFA to increase 18:2 levels. DDT did not change the total fatty acid 20:3ω9/20:4ω6 ratio in either tissue. In this study, although DDT did not exacerbate the physiological aspects of EFAD, DDT-induced changes in fatty acid composition of liver and tail skin indicated that 150 ppm DDT in the diets did alter lipid metabolism of the rats in an unexplained manner.

FREQUENTLY USED LIPID-LOWERING DRUGS HAVING NO GUARANTEED EFFECT. W. Scheffler and W. Schwartzkopff (The Lipid-metabolic Outpatient Department at the Klinikum Charlottenburg of the Free University of Berlin, Soorstr. 83, 1000 Berlin 19, West Germany) *Artery* **8**, 120–7 (1980). The therapeutic value of frequently used lipid-lowering agents such as the essential phospholipids (EPL), pyridoxal-phosphate (PP) and cynarin as well as the use of chenodeoxycholic acid and disaccharidase inhibitors in the treatment of various forms of hyperlipoproteinaemia is discussed critically. In our two clinical studies with orally administered EPL and PP in hyperlipoproteinaemic outpatients we were unable to establish clinically relevant effects on blood lipid and lipoprotein levels. In our opinion reported positive results with EPL, PP and cynarin are partially due to the methods of administration, selection of inpatients and dietary influences.

DOES DE NOVO SYNTHESIS OF LYSOPHOSPHATIDYLCHOLINE OCCUR IN RAT LUNG MICROSOMES? A.J. Aarsman and H. Van Den Bosch (Lab. of Biochem., Padualaan 8, 3584 CH Utrecht, The Netherlands) *Biochim. Biophys. Acta* **620**, 410–7 (1980). Incubation of rat lung microsomes with CDP[*Me*-^{14}C]choline resulted in formation of radioactive lysophosphatidylcholine and phosphatidylcholine. Evidence is provided which suggests that lysophosphatidylcholine formation cannot be ascribed completely to phospholipase A degradation of phosphatidylcholine. Lysophosphatidylcholine production can be stimulated by addition of monoacylglycerol or diacylglycerol. It is suggested that diacylglycerol is partly hydrolyzed to monoacylglycerol and subsequently converted to lysophosphatidylcholine. A direct transfer of phosphocholine from CDPcholine to monoacylglycerol is demonstrated by equimolar incorporation of 1(3)-[9,10-^{3}H$_2$]palmitoylglycerol and phospho[*Me*-^{14}C]choline into lysophosphatidylcholine.

METABOLISM OF PHOSPHATIDYLCHOLINE IN THE FROG RETINA. R.E. Anderson, M.B. Maude, P.A. Kelleher, T.M. Maida and S.F. Basinger (Cullen Eye Institute, Baylor College of Medicine, Texas Medical Center, Houston, TX 77030) *Biochim. Biophys. Acta* **620**, 212–26 (1980). The biosynthesis and the turnover of phosphatidylcholine were studied in the frog retina following either (a) injection into the animal of $^{32}PO_4$, $^{33}PO_4$, [1,3-^{3}H]glycerol, [2-^{3}H]glycerol, or [methyl-^{3}H]choline, or (b) incubation of isolated retinas in solutions containing [methyl-^{3}H]choline. 1. Examination of the pools of lipid precursors in the retina demonstrated that the choline and phosphate pools are long-lived compared to the glycerol pool. 2. The peak in specific activity of phosphatidylcholine synthesized from labeled glycerol occurred earlier, and was higher in the microsomal fraction than in the rod outer segments. 3. Autoradiography of retinas incubated in vitro with tritiated choline revealed a diffuse labeling pattern in the rod outer segments. Biochemical studies following injections of labeled glycerol showed an exponential decline in specific radioactivity of phosphatidylcholine in the rod outer segments. 4. The half-life of phosphatidylcholine in the rod outer segments synthesized from labeled glycerol was found to be 18–19 days. Based on these values, calculations were made which indicated that phosphatidylcholine in the outer segments is turning over faster than integral disc membrane proteins.

PURIFICATION OF HUMAN PLASMA LIPOPROTEIN LIPASE. I. Becht, O. Schrecker, G. Klose and H. Greten (Klinisches Institut für Herzinfarktforschung an der Medizinischen Universitätsklinik, Bergheimer Strasse 58, D-6900 Heidelberg, F.R.G.) *Biochim. Biophys. Acta* **620**, 583–91 (1980). Human plasma lipoprotein lipase was purified in a highly active form. Addition of the non-ionic detergent Triton X-100 led to stabilization of enzyme activity during the purification procedure. Antithrombin III, the major contaminant after affinity chromatography with heparin-Sepharose 4B, could be removed by gelfiltration on Bio-Gel A-5m. The application of Tris-glycine buffer in the

absence of denaturing agents allowed identification of the protein band corresponding to lipoprotein lipase activity on polyacrylamide gels.

INFLUENCE OF HUMAN LOW DENSITY AND HIGH DENSITY LIPOPROTEIN CHOLESTEROL ON THE IN VITRO PROSTAGLANDIN I_2 SYNTHETASE ACTIVITY. J. Beitz and W. Förster (Institut für Pharmakologie und Toxikologie, Martin-Luther-Universität, Halle-Wittenberg, Leninallee 4, DDR-402 Halle/Saale, G.D.R.) *Biochim. Biophys. Acta* 620, 352–5 (1980). We investigated in vitro the influence of low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL) cholesterol separated from human serum on prostaglandin I_2 synthetase activity studied by the conversion of prostaglandin H_2 to prostaglandin I_2 by the microsomal fraction of pig aorta. 6-Oxo-prostaglandin $F_{1\alpha}$ was analyzed by gas-liquid chromatography using prostaglandin $F_{1\alpha}$ as internal standard. We found a linear negative correlation ($P < 0.001$) between the amount of LDL cholesterol in the incubation solution and prostaglandin I_2 synthetase activity, whereas there was a positive correlation ($P < 0.01$) between HDL cholesterol and prostaglandin I_2 synthesis. A very low concentration of LDL cholesterol and a high concentration of HDL cholesterol stimulated prostaglandin I_2 synthesis, whereas a high LDL cholesterol concentration inhibited prostaglandin I_2 biosynthesis by 64%. The concentration range of LDL and HDL cholesterol was representative of physiologically low, normal or elevated levels of lipoproteins.

IDENTIFICATION OF 4-HYDROXYNONENAL AS A CYTOTOXIC PRODUCT ORIGINATING FROM THE PEROXIDATION OF LIVER MICROSOMAL LIPIDS. A. Benedetti, M. Comporti and H. Esterbauer (Istituto di Patologia Generale dell'Universita di Siena, Via Laterino 8, 53100 Siena, Italy) *Biochim. Biophys. Acta* 620, 281–96 (1980). During the NADPH-Fe induced peroxidation of liver microsomal lipids, products are formed which show various cytopathological effects including inhibition of microsomal glucose-6-phosphatase. The major cytotoxic substance has been isolated and identified as 4-hydroxy-2,3-*trans*-nonenal. The structure was ascertained by means of ultraviolet, infrared and mass spectrometry and high-pressure liquid chromatographic analysis. The biochemical and biological effects of synthetic 4-hydroxyalkenals have been studied in great detail in the past. The results of these investigations together with the finding that 4-hydroxyalkenals, in particular 4-hydroxynoneal, are formed during NADPH-Fe stimulated peroxidation of liver microsomal lipids, may help to elucidate the mechanism by which lipid peroxidation causes deleterious effects on cells and cell constituents.

THE ISOLATION AND CHARACTERIZATION OF THE 25-HYDROXYVITAMIN D-BINDING PROTEIN FROM CHICK SERUM. R. Bouillon, H. Van Baelen, B.K. Tan, and P. De Moor (Laboratorium voor Experimentele Geneeskunde, Katholieske Universiteit Leuven, B-3000 Leuven, Belgium) *J. Biol. Chem.* 255, 10925–30 (1980). The binding protein for 25-hydroxyvitamin D_3 (25-OH-D_3) was isolated from chick serum. The amino acid composition is very similar to that of the human and rat binding protein. The concentration of chick 25-hydroxyvitamin D_3-binding protein was higher in egg-laying hens (10 μM) than in immature hens (4 μM) or immature or adult roosters (4 μM). Chick plasma contains virtually only a 4 S form of the 25-hydroxyvitamin D_3-binding protein but partially hemolyzed chick serum also contains a 6 S form. Addition of pure actin to chick plasma or serum converts all 4 S form to the 6 S form. The serum 25-hydroxyvitamin D_3-binding protein is thus heterogenous since it exists in two 4 S forms (with different pI) and a 6 S form (complexed with actin). No evidence was found for the existence of a separate vitamin D_3-binding protein.

FACTORS AFFECTING LIPID PEROXIDATION IN GUINEA-PIG ADRENAL MICROSOMES. W.C. Brogan, III, P.R. Miles and H.D. Colby (Dept. of Physiol., West Virginia Univ. Schl. of Med., Morgantown, WV 26506) *Biochim. Biophys. Acta* 663, 230–8 (1981). Studies were carried out to examine the effects of and interactions between NADPH, Fe^{2+}, Fe^{3+} and ascorbate on lipid peroxidation in guinea-pig adrenal microsomes. Fe^{2+}, at levels between 10^{-6} and 10^{-3} M, produced concentration-dependent increases in lipid peroxidation in adrenal microsomes. By contrast, Fe^{2+} and Fe^{3+} had quantitatively similar effects on lipid peroxidation. NADPH alone had no effect on malonaldehyde production by adrenal microsomes. However, in the presence of low Fe^{2+} concentrations (10^{-6} M), NADPH stimulated malonaldehyde production. In the presence of high Fe^{2+} levels (10^{-3} M), NADPH produced a concentration-dependent inhibition of lipid peroxidation. Ascorbate alone increased malonaldehyde production by adrenal microsomes. At all concentrations (10^{-6} to 10^{-3} M) of Fe^{3+} studied, ascorbate synergistically increased the production of malonaldehyde. The results indicate that interactions between various endogenous substances may be important in the control of adrenal microsomal lipid peroxidation and that there are differences in the regulation of adrenal and hepatic lipid peroxidation.

MOLECULAR CLONING OF THE GENE SEQUENCES OF A MAJOR APOPROTEIN IN AVIAN VERY LOW DENSITY LIPOPROTEINS. L. Chan, A. Dugaiczyk and A.R. Means (Depts. of Cell Bio. and Med., Baylor College of Medicine, Houston, TX 77030) *Biochemistry* 19, 5631–7 (1980). Hormone treatment resulted in a 12,000-fold increase in the concentration of apo VLDL-II specific sequences within 12 h after DES. In contrast, such sequences were not detected (up to a R_0t of 3×10^3) in RNA samples isolated from the breast muscles of these animals.

BIOSYNTHESIS OF CHOLESTEROL AND CHOLESTEROL PRECURSORS IN PLATELETS OF FEMALE RATS TREATED WITH ORAL CONTRACEPTIVES. M. Ciavatti, G. Michel and S. Renaud (I.N.S.E.R.M., Unite 63, 22 Avenue du Doyen Lepine, 69500 Bron-Lyon, France) *Biochim. Biophys. Acta* 620, 297–307 (1980). Rat platelets were incubated with sodium [U-^{14}C]acetate and labeled lipids were analyzed. The major part of the radioactivity was found in phospholipids and in acylglycerols. When the incubation was performed with platelets of female rats treated with contraceptives, the total incorporation of labeled acetate in lipids was 2-fold higher and 33.6% of the radioactivity was found in lanosterol plus 24-dihydrolanosterol. Moreover, there is labeling of cholesterol. All these compounds were analyzed and identified by gas-liquid chromatography/mass spectrometry. In the incubation with sodium [2-^{14}C]mevalonate the labeling of lanosterol plus 24-dihydrolanosterol and of cholesterol was increased by 30% in platelets of treated rats. The effect of contraceptives on one step of cholesterol biosynthesis is discussed and a possible explanation of the correlation between oral contraceptives and thromboembolic accidents is suggested.

PLASMA HIGH DENSITY LIPOPROTEIN IN SEVERE OBESITY AFTER STABLE WEIGHT LOSS. F. Contaldo, P. Strazzullo, A. Postiglione, G. Riccardi, L. Patti, G. Di Biase and M. Mancini (Centre for Atheriosclerosis and Metabolic Diseases, Semeiotica Medica, 2nd Medical School, University of Naples. Naples (Italy)) *Atherosclerosis* 37, 163–7 (1980). Changes in plasma lipoprotein pattern, with particular attention to high density lipoprotein cholesterol (HDL-C) concentration, were evaluated in 7 (5 female, 2 male) obese patients before and 15 ± 1 months after they had lost weight (mean 20.7 ± 3.1 kg), when the patients' food intake had been ad libitum for at least 6 months, and they had been maintaining their weight loss. Plasma low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein triglyceride (VLDL-TG) concentrations were lower than baseline values: on the other hand, plasma HDL-C concentration, which was below normal values before weight reduction, was found to be significantly increased ($P < 0.05$). These data indicate that, among the favorable changes in plasma lipoprotein pattern, an increase in HDL-C may be achieved after remarkable and stable weight loss in severe obesity.

VERY LOW DENSITY LIPOPROTEIN BINDING TO ADIPOCYTES. K.S. Desai, G. Steiner, I. Takeuchi and C.H. Hollenberg (Depts. of Med. and Physiol., Univ. of Toronto, Toronto, Ontario M5S 1A8, Canada) *Biochim. Biophys. Acta* 620, 341–51 (1980). Human very low density lipoprotein (VLDL) has been found to interact with both isolated adipocytes and adipocyte membranes in a manner which is saturable, reversible and dependent on time and temperature. Except for a difference in maximum binding capacity, a similar pattern is seen with both rat epididymal adipocytes and human omental adipocytes. The capacity of rat cells is 0.04 μg VLDL per 2×10^5 cells. For human cells the capacity is 0.321 μg VLDL per 2×10^5 cells. Scatchard plots of the competition data are linear. This, and dissociation studies conducted in the presence or absence of unlabelled VLDL suggest that there is no cooperative interaction between the binding sites. Unlabelled VLDL and HDL each compete equally with ^{125}I-labelled VLDL for binding sites. LDL is 25 times weaker as a competitor. Intralipid and unrelated peptides have no effect. These data suggest that the ligand is not apolipoprotein B and not apolipoprotein A. The

competitive effect of HDL is not dependent on its apolipoprotein E content. A preparation of C apolipoproteins (75% C-11) is as potent as unlabelled VLDL in competing with ^{125}I-labelled VLDL for binding sites. These data indicate that VLDL can bind to adipocytes. The receptor can interact with other lipoproteins. It differs from the LDL receptor as it does not interact with apolipoprotein B or apolipoprotein E, but binds to a C apolipoprotein.

1,25-DIHYDROXYVITAMIN D_3 STIMULATED INCREASE OF 7,8-DIDEHYDROCHOLESTEROL LEVELS IN RAT SKIN. R.P. Esvelt, H.F. DeLuca, J.K. Wichmann, S. Yoshizawa, J. Zurcher, M. Sar and W.E. Stumpf (Dept. of Biochem., College of Agr. and Life Sciences, Univ. of Wisconsin–Madison, Madison, WI 53706) *Biochemistry* 19, 6158–61 (1980). A convenient, accurate assay was developed for determining skin cholesta-5,7-dien-3β-ol (7,8-didehydrocholesterol) concentrations. Ultraviolet spectrophotometry provided quantitation of the sterol from rat skins following saponification and chromatography on Lipidex and high-performance liquid chromatography. Correction for recoveries was accomplished by using 7,8-didehydro [3α-^{3}H]cholesterol as an internal standard. Chronic dosing of vitamin D-deficient rats with 1,25-dihydroxyvitamin D_3 caused a 4-fold increase in skin 7-dehydrocholesterol content. This rise was not the result of changes in food consumption, body weight, or plasma calcium. Cholesterol concentrations were not significantly elevated although some of the other nonsaponifiable lipid components found in the high-performance liquid chromatogram appeared to be increased by the treatment. These results suggest that the vitamin D hormone 1,25-$(OH)_2D_3$ may exert a positive feedback regulation on the production of vitamin D_3 in skin.

THE TIME COURSE OF ALTERATIONS IN PLASMA LIPID AND LIPOPROTEIN CONCENTRATIONS DURING EIGHT WEEKS OF ENDURANCE TRAINING. P.A. Farrell and J. Barboriak (Dept. of Biochemistry, Wood Veterans Hospital, Wood, WI) *Atherosclerosis* 37, 231–8 (1980). Sixteen subjects (σ = 7, φ = 9) participated in 8 weeks of endurance training (70% VO_{max}, 30 min/day, 3–4 days/wk). Plasma lipid and lipoprotein concentrations in venous blood were assessed prior to and at 2-week intervals during the 8 weeks of training. VO_{2max} was determined prior to training and at 4-week intervals. Results indicate that after an insignificant decline at 2 weeks (53.8 → 51.1 mg/dl), plasma high density lipoproteins (HDL) increased significantly ($P < 0.05$) at 8 weeks of training (51.1 → 57.4 mg/dl). This increase was linear after 2 weeks ($r = 0.98$) with a slope of +1 mg/dl/wk. VO_{2max} (42.2 → 43.8 → 45.9 ml/kg · min) increased significantly ($P < 0.05$) during training. Plasma triglycerides decreased significantly from 4 to 8 weeks of training, a period when HDL's were increasing. Over the last 4 weeks of training, the relationship between HDL's and triglycerides was significant, $r = -0.65$ ($P < 0.05$). These results suggest that alterations in HDL's lag behind changes in total cardiovascular fitness and increase simultaneously with a decline in plasma triglycerides after 4 weeks of endurance training.

MONOGLYCERIDE HYDROLASE ACTIVITIES OF RAT PLASMA AND PLATELETS: THEIR PROPERTIES AND ROLES IN THE ACTIVITY OF LIPOPROTEIN LIPASE. C.J. Fielding (Cardiovascular Res. Inst. and Dept. of Physiol., Univ. of California, San Francisco, San Francisco, CA 94143) *J. Biol. Chem.* 256, 876–81 (1981). Rat plasma contains monoglyceride hydrolase activities against both 1(3)- and 2-monoglycerides. These activities are present as lipoprotein complexes recovered by either density flotation or by agarose gel chromatography with plasma high density lipoprotein. However neither activity is complexed with the major apoproteins (apo-A-I, apo-E) of this lipoprotein class. 2-Monoglyceride hydrolase (but not 1(3)-monoglyceride hydrolase) activity associates with the triglyceride-rich lipoprotein class. The two activities are also noncompetitive with respect to substrate, and differ in pH- and cofactor-dependence and sensitivity to inhibition by diethyl p-nitrophenyl phosphate. Rat platelets also contain both 1(3)- and 2-monoglyceride hydrolase activities. These differ in reactivity with antiesterase and after solubilization and electrophoretic migration with each other and with the corresponding plasma activities. Studies with the isolated perfused rat heart suggest that a major role in the catabolism of 2-monoglyceride generated from lipoprotein lipase activity at the coronary bed is played by the plasma 2-monoglyceride hydrolase activity.

METABOLISM OF ALL-*trans*-RETINYL ACETATE TO RETINOIC ACID IN HAMSTER TRACHEAL ORGAN CULTURE. C.A. Frolik, L.L. Dart and M.B. Sporn (Lab. of Chemoprevention, National Cancer Inst., National Institutes of Health, Bethesda, MD 20205) *Biochim. Biophys. Acta* 663, 329–35 (1981). All-*trans*-[^{3}H] retinyl acetate has been shown to be metabolized to all-*trans*-[^{3}H]retinoic acid in a target tissue of vitamin A action, the hamster trachea in organ culture. That the compound produced is indeed all-*trans*-retinoic acid is demonstrated by chromatography of the biosynthetically produced retinoic acid with synthetic all-*trans*-retinoic acid in two different high-pressure liquid chromatographic systems, either as the free acids in a reverse-phase system or as the methyl esters in a normal-phase system. The all-*trans*-[^{3}H]retinoic acid was also found in the tracheal epithelium and cartilage as well as in the medium. In addition the tracheal tissue also contained retinyl palmitate and other esters. Finally, further in vitro metabolism of [^{3}H]retinyl acetate paralleled the metabolism of [^{14}C]retinoic acid suggesting that these two compounds are being metabolized through similar pathways.

COMBINED EFFECT OF CHOLESTEROL FEEDING AND SYMPATHECTOMY ON THE LIPID CONTENT IN RABBIT AORTAS. K. Fronek and J.D. Turner (Dept. of AMES-Bioengineering and Dept. of Med., University of California, San Diego, La Jolla, CA 92093) *Atherosclerosis* 37, 521–8 (1980). There is indirect evidence that sympathetic innervation may have an effect on the metabolic rate of the vessel wall. To shed some light on this question, this investigation was designed to study whether or not diminished adrenergic nerve activity in the arterial wall leads to greater susceptibility to atherosclerosis. A total of 48 rabbits was studied of which, 26 were chemically sympathectomized. Both groups of rabbits were subdivided further into a group fed regular rabbit chow and a group fed regular rabbit chow containing 1% cholesterol. Both groups, control and 6-hydroxydopamine (6-OHDA) treated, had similar plasma lipids as well as the lipid content in their aortae. After 80 days of 1% cholesterol dietary supplement the plasma lipids rose gradually with no significant difference between controls and 6-OHDA-treated animals. The aortas of sympathectomized rabbits contained significantly more cholesterol and total lipids than those from fully innervated controls. It is concluded that the reduction of a continuous barrage of sympathetic nervous impulses to the arterial wall modified its metabolism. In combination with additional exogenous influences, e.g., high cholesterol intake, the sympathectomized arteries become more susceptible to lipid accumulation.

THE ROLE OF HIGH DENSITY LIPOPROTEINS IN RAT ADRENAL CHOLESTEROL METABOLISM AND STEROIDOGENESIS. J.T. Gwynne and B. Hess (Div. of Endocrinology, Dept. of Med., Univ. of North Carolina Schl. of Med., Chapel Hill, NC 27514) *J. Biol. Chem.* 255, 10875–83 (1980). Addition of rat or human high density lipoproteins (HDL) or human low density lipoproteins (LDL) to rat adrenocortical cells in vitro was found to enhance steroid production and increase cell cholesterol content. These effects of HDL were not observed in cultured mouse Y-1 adrenal cells, suggesting that rat adrenal cells possess a specific mechanism for uptake of HDL cholesterol not found in Y-1 cells. The effects of HDL were most marked on cells previously stimulated with adrenocorticotropin (ACTH) and depleted of their endogenous cholesterol stores. Such cells were prepared either by treatment in vivo with 4-aminopyrazolopyrimidine or in vitro with ACTH (10^{-7} M) in lipoprotein-poor media. The results indicate that rat adrenocortical cells possess a specific, saturable, ACTH-dependent mechanism for uptake of HDL cholesterol. Moreover, cellular uptake of HDL cholesterol exceeded by at least 4-fold the amount of cholesterol associated with HDL apoprotein degraded by the cells, suggesting that utilization of HDL cholesterol does not require endocytosis and lysosomal degradation of the entire HDL particle.

FAT METABOLISM IN HEAVY EXERCISE. N.L. Jones, G.J.F. Heigenhauser, A. Kuksis, C.G. Matsos, J.R. Sutton and C.J. Toews (Dept. of Med., McMaster Univ., Hamilton, Ontario, Canada) *Clin. Sci.* 59, 469–78 (1980). To investigate differences between the metabolic effects of light and heavy exercise, five healthy males (mean maximal oxygen intake 3.92 litres/min) exercised for 40 min at 36% maximum power (light work) and 70% maximum power (heavy work) on separate days, after an overnight fast. In light exercise fat metabolism may be controlled to favor adipose tissue lipolysis and extraction of free fatty acids by muscle from the circulation, whereas in heavy exercise adipose tissue lipolysis is inhibited and hydrolysis of muscle triglycerides may play a more important part. The finding of a high respiratory ex-

change ratio may not exclude the use of fat as a major fuel source in exercise associated with lactate production.

FATTY ACID COMPOSITION OF CHOLESTERYL ESTERS IN SERUM IN BOYS FROM 16 DEVELOPING AND DEVELOPED COUNTRIES. J.T. Knuiman, C.E. West, R.J.J. Hermus and J.G.A.J. Hautvast (Dept. of Human Nutr., Agricultural Univ. 6703 BC Wageningen, The Netherlands) *Atherosclerosis* 37, 617–24 (1980). The fatty acid composition of the cholesteryl esters in serum was measured in 7- and 8-year-old boys in groups from 16 countries. The ratio of esterified cholesterol : total cholesterol was also measured. All sample collections and analyses were carried out under standardized conditions. The proportion of palmitic acid in the cholesteryl esters was high in the groups from Asia and Africa (0.17–0.26) compared with that in the groups from the U.S.A. and Europe (0.14–0.18). The proportion of linoleic acid in the cholesteryl esters was low in the groups from Asia and Africa (0.39–0.48) and high in the groups from the U.S.A. and Europe (0.45–0.58). The proportion of oleic acid, arachidonic acid, palmitoleic acid and stearic acid showed little variation between the groups. The proportion of linoleic acid in the cholesteryl esters was positively correlated with the concentration of total cholesterol ($r = 0.75$, $n = 26$, $P < 0.005$).

RAPID ACYLATION AND DEACYLATION OF ARACHIDONIC ACID INTO PHOSPHTIDIC ACID OF HORSE NEUTROPHILS. E.G. Lapetina, M.M. Billah and P. Cuatrecasas (Dept. of Molecular Biol., The Wellcome Res. Labs., Res. Triangle Park, NC 27709) *J. Biol. Chem.* 255, 10966–70 (1980). Horse neutrophils incorporate exogenous [^{14}C]arachidonate into phosphatidic acid very rapidly. This acylation of phosphatidate with arachidonate is followed quickly and spontaneously by its deacylation. This transient formation of arachidonyl-phosphatidate, which reflects a rapidly turning over pool of arachidonate-associated lipid, is not observed with stearic acid or other phospholipids or triglycerides. When cells are prelabeled for 2 h with very high quantities of (^{32}P) orthophosphate, a very substantial fraction (i.e. 20 to 30%) of the phospholipid radioactivity is associated with phosphatidic acid. However, on addition of exogenous arachidonate, there is no increase in [^{32}P]phosphatidate in these prelabeled cells. The entire phosphatide molecule does not appear to be turned over during the process described above. Inhibitors of cyclooxygenase and lipoxygenase activities such as BW755C, nordihydroguaiaretic acid, and low concentrations of indomethacin do not affect the labeling of phospholipids. However, eicosatetraynoic acid, an analog of arachidonate, and high concentration (0.1 mM) of indomethacin can block [^{14}C]arachidonate incorporation into lipids. The rapid turnover of the 2-acyl position in phosphatidate might be related to a specific process of fatty acid mobilization within neutrophils.

DIETARY FAT AND CHOLESTEROL EFFECTS ON PLASMA LECITHIN : CHOLESTEROL ACYLTRANSFERASE ACTIVITY IN CEBUS AND SQUIRREL MONKEYS. A.H. Lichtenstein, R.J. Nicolosi and K.C. Hayes (Dept. of Nutrition, Harvard School of Public Health, Boston, MA 02115) *Atherosclerosis* 37, 603–16 (1980). Plasma LCAT activity was assessed in cebus and squirrel monkeys fed diets containing either corn or coconut oil with or without 0.1% cholesterol. In vitro enzyme activity was determined by measuring the incorporation of [1,2-^{3}H] cholesterol into cholesteryl ester. Three assay conditions were used to assess overall enzyme activity and to differentiate between the concentration of enzyme and substrate effects. LCAT activity was affected primarily by species and dietary fat and to a lesser extent by dietary cholesterol in squirrel monkeys. Specifically, plasma from both species of monkeys fed corn oil diets had comparable overall rates of LCAT activity. In all monkeys fed the coconut oil diets percent esterification was lower than in those monkeys fed the corn oil diets, and was lowest in squirrel monkeys. Coconut oil feeding also resulted in lower substrate activity in all monkeys, whereas cholesterol feeding had no significant effect on substrate activity. Squirrel monkeys always had lower substrate activity than cebus for any diet group. Evaluation of enzyme activity indicated that the greater esterification in cebus monkeys fed the coconut oil diet was associated with the ability of cebus, but not squirrel monkeys, to increase their enzyme activity. Cebus monkeys maintained greater LCAT substrate and enzyme activities than squirrel monkeys made hypercholesterolemic with coconut oil.

EFFECT OF EXERCISE CONDITIONING ON PLASMA HIGH DENSITY LIPOPROTEINS AND OTHER LIPOPROTEINS. L.C. Lipson, R.O. Bonow, E.J. Schaefer, H.B. Brewer, and F.T. Lindgren (Building 10, Room 7B-15, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD 20205) *Atherosclerosis* 37, 529–38 (1980). Epidemiologic studies have demonstrated an inverse correlation between HDL-cholesterol and the incidence of coronary artery disease. Although physically active individuals tend to have higher HDL levels than their sedentary peers, they also have lower body weights. It has yet to be shown that physical activity by itself can raise HDL when other variables such as body weight are maintained constant. We examined the effect of a 6-week exercise conditioning program on 10 young normal subjects who were maintained on a constant composition, iso-weight diet. A training effect was documented by an increase in maximum oxygen consumption from 44 to 49 ml/min/kg and by a fall in heart rate at submaximal exercise from 120 to 109 beats/min. Total plasma cholesterol levels decreased significantly from 156 to 140 mg/dl. However, there was no significant change in plasma triglyceride, VLDL, LDL or HDL-cholesterol levels, although all these values decreased. Thus, under the conditions of this study in which diet and weight were controlled, exercise conditioning did not elevate HDL-cholesterol levels. HDL levels have been shown to be inversely related to body weight. These data are consistent with the concept that exercise conditioning may affect HDL via alterations in body weight.

LIPID DYNAMICS AND LIPID-PROTEIN INTERACTIONS IN RAT HEPATOCYTE PLASMA MEMBRANES. C.J. Livingstone and D. Cehachter (Dept. of Phys., Columbia Univ. College of Physicians and Surgeons, New York, NY 10032) *J. Biol. Chem.* 255, 10902–8 (1980). Rat hepatocyte plasma membranes were isolated and examined by differential scanning calorimetry and by steady state florescence polarization of 1,6-diphenyl-1,3,5-hexatriene, 12-anthroyl stearate, and 2-anthroyl stearate. Calorimetry of the intact membranes revealed a reversible lipid thermotropic transition with lower and upper critical temperatures of 18° and 31° C, respectively. The transition was also observed in lipid extracts of the membrane, both dried and rehydrated. The transition observed in the native membranes is broad and of low enthalpy, owing in part to the relatively high cholesterol content and to protein-lipid interactions. Arrhenius studies of membrane 5′-nucleotidase and alkaline phosphatase give two-slope plots with breakpoints, respectively, of approximately 17° and 26° C. These break points and others reported for a number of hepatocyte membrane protein activities cluster uniformly at either the lower or upper critical temperature of the lipid transition observed by differential scanning calorimetry.

REGULATION OF PALMITATE ESTERIFICATION/OXIDATION BY GLUCAGON IN ISOLATED HEPATOCYTES. The role of α-glycerophosphate concentration. H. Lund, B. Borreback and J. Bremer (Inst. of Medical Biochem., Univ. of Oslo, P.O. Box 1112, Blindern, Oslo 3, Norway) *Biochim. Biophys. Acta* 620, 364–71 (1980). Lipolysis was measured as the disappearance of [^{3}H]glycerol previously incorporated into triacylglycerol, diacylglycerol and phosphatidic acid. There was no effect of glucagen on the lipolysis of any of these lipids. A transient increase in cellular α-glycerophosphate was induced by addition of glycerol during incubation. This resulted in an immediate and temporary decrease in oxidation and increase in esterification of palmitate while the uptake of palmitate from the incubation medium was unchanged. The change in α-glycerophosphate was also correlated with a transient drop in acyl-CoA and acylcarnitine. The lactate/pyruvate ratio was increased by the glycerol addition, but was still elevated for some while after the transient change in α-glycerophosphate. Similar effects were obtained by addition of dihydroxyacetone instead of glycerol. It is concluded that fatty acid esterification/oxidation can be changed by variations in the concentration of α-glycerophosphate, and the glucagon acts on lipid metabolism by decreasing the level of this metabolite.

INHIBITION OF DESATURATION OF PALMITIC, LINOLEIC AND EICOSA-8,11,14-TRIENOIC ACIDS IN VITRO BY ISOMERIC *cis*-OCTADECENOIC ACIDS. M. Mahfouz, S. Johnson and R.T. Holman (Hormel Inst., Univ. of Minnesota, 801 16th Ave., N.E., Austin, MN 55912) *Biochim. Biophys. Acta* 663, 58–68 (1981). The effects of the positional isomers of *cis*-18:1 acids on the desaturation of 18:2ω6→18:3ω6 (Δ^6 desaturase), 20:3ω6→20:4ω6 (Δ^5 desaturase) and 16:0→16:1 (Δ^9 desaturase) were investigated using essential fatty acid deficient rat liver microsomes. The isomeric *cis*-18:1 acids were found to be inhibitory for the Δ^6, Δ^5 and Δ^9 desaturases, and the position of the double bond is important in determining the degree of inhibi-

tion. The effects of the several *cis*-18:1 isomers on Δ^6 and Δ^5 desaturases were parallel in magnitude except for the *cis*-Δ^6 isomer which gave 17.5% inhibition for Δ^6 desaturase (*cis*-Δ^8 18:1) was also the most potent inhibitor for Δ^5 desaturase, and the weakest inhibitor for Δ^6 desaturase (*cis*-Δ^9 18:1) was the least effective inhibitor on Δ^5 desaturase. The Δ^9 desaturase was maximally inhibited by *cis*-Δ^{10} and Δ^{11} 18:1 isomers. The *cis*-18:1 acid isomers in partially hydrogenated edible fats may have effects on the lipid metabolism through their inhibitory effects on the desaturases.

PREPARATION AND PROPERTIES OF IMMOBILIZED LIPOPROTEIN LIPASE. N. Matsuoka, K. Shirai and R.L. Jackson (Depts. of Pharmacology and Cell Biophys., Biological Chem. and Med., Univ. of Cincinnati Med. Center, 231 Bethesda Avenue, Cincinnati, OH 45267) *Biochim. Biophys. Acta* 620, 308–16 (1980). Purified bovine milk lipoprotein lipase has been covalently attached to CH-Sepharose with water-soluble carbodiimide. The immobilized enzyme retained enzymic activity and was stimulated 7-fold by the addition of human apolipoprotein C-II. Both [^{3}H]heparin and ^{125}I-labeled apolipoprotein C-II bound to the immobilized enzyme; unlabeled heparin and apolipoprotein C-II competed for binding of their respective labeled compounds. Apolipoprotein C-II did not compete for binding of [^{3}H]heparin and vice versa. Human apolipoprotein C-III did not bind to the immobilized enzyme nor did it compete for apolipoprotein C-II binding. We conclude from these studies that both apolipoprotein C-II and heparin interact with immobilized lipoprotein lipase and that they have different binding sites.

THE POSSIBLE ANTIKETOGENIC AND GLUCONEOGENIC EFFECT OF THE ω-OXIDATION OF FATTY ACIDS IN RATS. P.B. Mortensen (Res. Lab. for Metabolic Disorders, Univ. Dept. of Clin. Chem., Aarhus Kommunehospital, DK-8000 Aarhus C, Denmark) *Biochim. Biophys. Acta* 620, 177–85 (1980). The urinary excretion of C_1–C_{10}-dicarboxylic acids and 3-hydroxybutyric acid was examined in rats on ketogenic stimulation due to fat-feeding. The urinary excretion of succinic acid decreased while the urinary excretion of adipic and suberic acids increased prior to the appearance of ketosis, and this pattern of excretion was almost independent of the degree of the subsequent ketosis. After administering adipic acid to the ketotic rats, urinary excretion of succinic acid increased at the same time as ketosis decreased and blood glucose increased. The possibility of a physiological antiketogenic and gluconeogenic effect of the ω-oxidation of fatty acids to dicarboxylic acids is discussed.

SYNTHESIS AND BIOLOGICAL ACTIVITY OF VITAMIN D_3-SULFATE. L.E. Reeve, H.F. DeLuca and H.K. Schnoes (Dept. of Biochem., College of Agr. and Life Sciences, Univ. of Wisconsin-Madison, Madison, WI 53706) *J. Biol. Chem.* 256, 823–6 (1981). Vitamin D_3-3β-sulfate has been synthesized using pyridine sulfur trioxide as the sulfate donor. It has been shown to be pure by high performance liquid chromatography and spectral methods. Unlike previous reports, the product has been identified unambiguously as the 3β-sulfate ester of vitamin D_3 by its ultraviolet, nuclear magnetic resonance, infrared, and mass spectra. The biological activity of vitamin D_3-sulfate was then determined in vitamin D-deficient rats. Vitamin D_3-sulfate has less than 5% of the activity of vitamin D_3 to mobilize calcium from bone and approximately 1% of the ability of vitamin D_3 to stimulate calcium transport, elevate serum phosphorus, or support bone calcification. These results disprove previous claims that vitamin D_3-sulfate has potent biological activity, and they further do not support the contention that vitamin D-sulfate represents a potent water-soluble form of vitamin D in milk.

BLOOD PLASMA LIPOPROTEIN AND TISSUE CHOLESTEROL OF CALVES FED SOYBEAN OIL, CORN OIL, VEGETABLE SHORTENING OR TALLOW. M.J. Richard, J.W. Stewart, T.R. Heeg, K.D. Wiggers and N.L. Jacobson (Nutritional Physiology Group, Animal Science Dept., Iowa State Univ., Ames, IA 50011) *Atherosclerosis* 37, 513–20 (1980). The objective of this study was to determine cholesterol content of blood plasma, blood plasma lipoproteins and tissues of calves fed fats of differing compositions. Groups of 2-week-old calves were fed one of the following fats in a reconstituted milk formula: soybean oil, corn oil, vegetable shortening or tallow. The diets contained no dry feed or added cholesterol. Blood plasma cholesterol concentrations increased with time for all groups. After 15 weeks, cholesterol concentrations were greater in the blood, liver and fat of the groups fed soybean oil and corn oil than in those of the groups fed vegetable shortening and tallow. Low density lipoprotein was identified as the carrier of the increased amounts of cholesterol noted in the blood.

PHOSPHOLIPID SYNTHESIS IN *Escherichia coli*. CHARACTERISTICS OF FATTY ACID TRANSFER FROM ACYL-ACYL CARRIER PROTEIN TO *sn*-GLYCEROL 3-PHOSPHATE. C.O. Rock, S.E. Goelz and J.E. Cronan, Jr. (Dept. of Molecular Biophys. and Biochem., Yale Univ., New Haven, CT 06510) *J. Biol. Chem.* 256, 736–42 (1981). Two kinetically distinguishable *sn*-glycerol 3-phosphate (glycerol-P) acyltransferase activities were detected in *Escherichia coli* inner membranes using acyl-acyl carrier protein (ACP) substrates. The first system was characterized as having a Michaelis constant (K_m) for glycerol-P of 90 μM and utilized palmitoyl-ACP to form primarily 1-acylglycerol-P. Palmitoyl-CoA and *cis*-vaccenoyl-ACP were also utilized by this system but, with these substrates, significantly more phosphatidic acid was formed as compared to palmitoyl-ACP. Although palmitoyl-ACP and palmitoyl-CoA had kinetically indistinguishable glycerol P sites, distinct acyl donor binding sites were inferred from kinetic experiments using acyl carrier protein as an acyltransferase inhibitor. A second enzyme system, characterized as having a K_m for glycerol-P of 700 μM, was found using palmitoleoyl-ACP as a substrate. This acyltransferase had a slightly higher pH optimum than the low K_m acyltransferase activity, and phosphatidic acid was the major product. Two degradative reactions were identified in this system. One reaction yielded diacylglycerol when palmitoyl-ACP was the substrate. The other degradative reaction produced glycerol. Glycerol was formed in all incubations but was most pronounced when palmitoleoyl ACP was the substrate.

CHOLESTEROL AND PHOSPHOLIPID BIOSYNTHESIS IN GUINEA PIG MEGAKARYOCYTES. B.P. Schick and P.K. Schick (Dept. of Physiol. and Biochem., Medical College of Pennsylvania, Philadelphia, PA 19129) *Biochim. Biophys. Acta* 633, 249–54 (1981). We have investigated lipid synthesis from [U-^{14}C]acetate in isolated guinea pig megakaryocytes with the goal of elucidating the genesis of platelet lipids. Cholesterol was the major product of megakaryocyte lipid synthesis from [U-^{14}C] acetate. Megakaryocytes also synthesized cholesterol from [U-^{14}C]glucose. In contrast, platelet sterol synthesis was negligible. Both megakaryocytes and platelets synthesized phospholipids from [U-^{14}C]acetate. Phosphatidylcholine accounted for 62% of the phospholipid radioactive label in megakaryocytes and 78% in platelets. Phospholipid radioactivity was associated with the fatty acids. We hypothesize that the megakaryocyte may synthesize a major portion of platelet cholesterol and that the phospholipid and fatty acid synthetic pathways available to the platelet are derived from the megakaryocytes.

AN IN VIVO EVALUATION IN MAN OF THE TRANSFER OF ESTERIFIED CHOLESTEROL BETWEEN LIPOPROTEINS AND INTO THE LIVER AND BILE. C.C. Schwartz, Z.R. Vlahcevic, L.G. Halloran and L. Swell (Lipid Research Lab. and Div. of Gastroenterology, Depts. of Med. and Surgery, Veterans Administration Medical Center and Medical College of Virginia, Richmond, VA 23249) *Biochim. Biophys. Acta* 663, 143–62 (1981). The metabolism of the esterified cholesterol fractions of HDL and LDL has been studied in vivo in man with regard to their ability to serve as precursors for bile acid synthesis and biliary cholesterol secretion. Information was also obtained on the exchange of cholesterol esters between the lipoprotein classes. The observed ^{3}H/^{14}C ratios in bile acids, biliary cholesterol, lipoprotein free cholesterol and red blood cell cholesterol were similar and markedly divergent from the lipoprotein esterified cholesterol ^{3}H/^{14}C ratios. The ^{3}H/^{14}C ratios in HDL esterified cholesterol were midway between the ratio in LDL esterified cholesterol and plasma free cholesterol, indicating that HDL esterified cholesterol is derived from more than one source. These sources could be LDL esterified cholesterol and esters formed de novo from plasma free cholesterol. A precursor-product relationship was found between the specific activities of lipoprotein free cholesterol and the bile steroids. The results support the view that lipoprotein free cholesterol is the major source of bile acids in man. Also, that esterified cholesterol fractions of VLDL and LDL originate from HDL, that some LDL ester is transferred back to HDL, and that the cholesterol liberated from hydrolyzed esters undergoes recirculation into the free cholesterol pool.

CHARACTERIZATION OF A SPECIFIC, HIGH AFFINITY BINDING MACROMOLECULE FOR 1α,25-DIHYDROXYVITAMIN D_3 IN CULTURED CHICK KIDNEY CELLS. R.U. Simpson, R.T. Franceschi and H.F. DeLuca (Dept. of Biochem., College of Agr. and Life

Sciences, Univ. of Wisconsin-Madison, Madison, WI 53706) *J. Biol. Chem.* 255, 10160-6 (1980). Cytosol prepared from vitamin D_3-deficient kidney cells in culture contains 3.7 S protein that specifically binds 1,25-dihydroxyvitamin D_3 with high affinity and low capacity. Whole kidney homogenate cytosol preparations are shown to possess two 1,25-dihydroxyvitamin D_3 binding macromolecules. The kidney cells respond to 1,25-dihydroxyvitamin D_3 by diminishing 25-hydroxyvitamin D_3 1α-hydroxylation and increasing 24R-hydroxylation. Cultured cells provide a preparation of cytosol which has allowed extensive characterization of the renal 1,25-dihydroxyvitamin D_3 receptor and should facilitate investigations into the role this receptor plays in renal control of vitamin D_3 metabolism.

INFLUENCE OF DIETARY FAT SATURATION ON LIPID ABSORPTION IN THE RAT. D.M. Sheehe, J.B. Green and M.H. Green (Nutr. Program, The Pennsylvania St. Univ., University Park, PA 16802) *Atherosclerosis* 37, 301-10 (1980). Flux (μmole/h) of triglycerides, phospholipids and cholesterol into the thoracic duct lymph was measured in rats receiving a constant intraduodenal infusion of a cholesterol-free oil rich in either polyunsaturated (P/S = 4.8) or saturated (P/S = 0.2) fatty acids. Rats had ad libitum access to a fat-free semisynthetic diet throughout the experiment. Although absorption of the infused oils approximated 100%, triglyceride flux was significantly lower during infusion of the saturated compared to the polyunsaturated oil. Phospholipid and total cholesterol fluxes were not significantly affected by the type of oil, but the percent of lymph total cholesterol which was esterified was slightly but significantly lower during infusion of the unsaturated oil. Using the molar phospholipid/triglyceride ratio as an index of lymph lipoprotein size, it was found that absorption of the oil rich in polyunsaturated fatty acids resulted in an increase in the mean size of lymph lipoproteins. The potential significance of an influence of dietary fat saturation on lymph lipoprotein size and cholesterol esterification for the ultimate metabolic fate of absorptive lipoprotein constituents is discussed.

LIPID CHANGES IN ATHEROSCLEROTIC AORTAS OF *Macaca fascicularis* AFTER VARIOUS REGRESSION REGIMENS. S.R. Srinivasan, D. Patton, B. Radhakrishnamurthy, T.A. Foster, M.R. Malinow, P. McLaughlin and G.S. Berenson (c/o F.S. Berenson, M.D., Louisiana State University Medical Center, 1542 Tulane Ave., New Orleans, LA 70112) *Atherosclerosis* 37, 591-601 (1980). Plasma and aortic tissue lipid changes in atherosclerotic *Macaca fascicularis* monkeys were studied following various regression regimens for 18 months. Atherosclerosis was in-

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duced in groups of 18 *Macaca fascicularis* monkeys by feeding a semipurified diet containing 43% of the calories as fat and 1.2 mg/kcal cholesterol for 6 months. Five groups of animals were continued on the same diet containing 0.34 mg/kcal cholesterol during the regression period, and were given the following hypocholesterolemic regimens: none (positive controls); D-thyroxine; pyrimidine derivative; cholestyramine; and alfalfa. Another group of animals was maintained on regular monkey chow alone during the regression period (negative control). Cholestyramine very effectively reduced the plasma cholesterol, and aorta free- and esterified cholesterol and phospholipids. D-Thyroxine significantly lowered the plasma cholesterol levels but tissue lipid levels were the highest among the groups studied. Alfalfa tended to reduce the plasma and tissue lipids more than the other drugs. Pyrimidine derivative actually increased the mean levels of plasma and tissue cholesterol. Thus the effectiveness of any hypocholesterolemic regimen is probably dependent on achieving a favorable lipoprotein distribution in plasma without any adverse effect on the arterial wall metabolism.

PUBLICATIONS ABSTRACTED

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