Abstracts

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Biochemistry and nutrition

INCREASED CHOLESTEROL ESTERIFICATION IN RAT LIVER MICROSOMES BY PURIFIED NON-SPECIFIC PHOSPHOLIPID TRANSFER PROTEIN. B.J.H.M. Poorthuis and K.W.A. Wirtz (Laboratory of Biochem. State Univ. of Utrecht, Transitorium 3, NL-3508 TB Utrecht (The Netherlands)) *Biochim. Biophys. Acta 710* (1):99-105 (1982). The effect of non-specific phospholipid transfer protein purified from rat liver on the activity of acyl-CoA; cholesterol acyltransferase in rat liver microsomes was studied. The activity of cholesterol acyltransferase was measured from the rate of incorporation of [1-^{14}C]oleoyl-CoA into cholesteryl oleate. Activity was stimulated by preincubation of the microsomes with the non-specific phospholipid transfer protein alone, but most effectively when vesicles consisting of phosphatidylcholine/cholesterol also were present in the preincubation mixture. Preincubation with vesicles consisting of only phosphatidylcholine or phosphatidylcholine/phosphatidylethanolamine had no effect. The stimulating effect is dependent on transfer protein and vesicle concentration and on the length of preincubation. Treatment of the transfer protein with N-ethylamaleimide abolished its effect on cholesterol ester formation. Preincubation of the microsomes with transfer protein and phosphatidylcholine/cholesterol vesicles containing radioactively labeled cholesterol shows that exogenous cholesterol is converted readily to cholesterol ester. This study suggest a role for the transfer protein in modulating cholesterol metabolism by its ability to transport cholesterol between membranes.

INTERACTION BETWEEN THE UNSATURATED FATTY ACIDS ON THE METABOLISM IN PIGS. A. Seher, *Rev. Franc. Corps Gras 29*(2):63-68, french. RFCG 82-05 (1982). The importance of various relations between the oleic, linoleic and linolenic acids on lipid metabolism has been studied in growing pigs. The results showed that the fatty acid variations affect markedly the animal growth and the composition of depot fats, serum and organ lipids and also heart, liver and spleen phospholipids. The linoleic acid metabolism is influenced especially by the linolenic acid, but hardly by the oleic acid. The obtained results have been compared with results in rats and men.

REGULATION OF VOLATILE FATTY ACID UPTAKE BY MITOCHONDRIAL ACYL COA SYNTHETASES OF BOVINE LIVER. C.A. Ricks and R.M. Cook (Dept. of Dairy Sci., Michigan State Univ., East Lansing, MI 48824) *J. Dairy Sci. 64*:2324-2335 (1981). Mitochrondria of bovine liver contain acyl CoA synthetases necessary for the uptake of propionate, butyrate, and valerate whereas acetate is bound only weakly. Purification of these enzymes separated a distinct propionyl CoA synthetase highly specific for propionate and acrylate and a butyrate-activating fraction with broad substrate specificity for short and medium chain fatty acids. Evidence from kinetic studies and sucrose density centrifugation suggested that this latter fraction was composed of two enzymes, a butyryl CoA synthetase and a valeryl CoA synthetase. The apparent molecular weights of the propionyl, butyryl, and valeryl CoA synthetases were 72,000, 67,000, and 65,000. The Michaelis-Menten constants of propionyl CoA synthetase for propionate, adenosine 5'-triphosphate, and coenzyme A were 1.3×10^{-3} M, 1.3×10^{-3} M, and 6.3×10^{-4} M. Enzyme activity is regulated by the concentration of propionate in portal blood. Relative to propionyl, butyryl, or valeryl CoA synthetases little acetyl CoA synthetase could be demonstrated. In ruminants hepatic metabolism is such that use of acetate as an energy source is minimum. This ensures that an alternative energy source to glucose, as acetate units, will reach the extrahepatic tissues. Separation of a distinct propionyl CoA synthetase regulated by the concentration of propionate in portal blood is significant because a primary role of ruminant liver is to synthesize glucose from ruminally derived propionate.

SPECIFICITY AND BINDING AFFINITY OF PHOSPHOLIPIDS TO THE HIGH-AFFINITY CARDIOLIPIN SITES OF BEEF HEART CYTOCHROME *C* OXIDASE. N.C. Robinson (Dept. of Biochem., Univ. of Texas Health Science Center at San Antonio, San Antonio, TX 78284) *Biochemistry 21*:184-188 (1982). Beef heart lipid-depleted cytochrome *c* oxidase, containing only 50% of the two to three essential high-affinity cardiolipin molecules per heme aa_3 complex, was used to study the phospholipid requirements of this enzyme. The lipid-depleted complex had two-thirds of the electron transport activity as enzyme containing a full complement of essential cardiolipin when it was assayed in Tween 80. Incubation of the lipid-depleted enzyme with DPG in the presence of 1% Triton X-100 followed by a 140-fold dilution of the reconstituted complex into Tween 80 restored 100% of the initial activity. Similar incubations of the lipid-depleted enzyme with phosphatidylethanolamine, phosphatidylglycerol, phosphatidylserine, or phosphatidic acid did not stimulate the enzymatic activity in Tween 80 more than 5-10%. In the presence of 1% Triton X-100, bovine DPG reassociated with the vacant high-affinity siles with an apparent dissociation constant of 5 μM based upon the regeneration of electron transport activity in Tween 80. Bacterial DPG measured in a similar manner had a dissociation constant of 2 μM. Reisolation of the complex by discontinuous glycerol gradient centrifugation after incubation with exogenous DPG in 1% Triton X-100 indicated that DPG reassociated only with the high-affinity cardiolipin sites. We conclude that the unique structure of DPG is the structural feature necessary for the binding of exogenous phospholipids to the essential high-affinity sites of cytochrome *c* oxidase and the maintenance of full electron transport activity in Tween 80.

RETINOL ESTERIFICATION BY RAT LIVER MICROSOMES. A.C. Ross (Dept. of Physiology, The Medical College of Pennsylvania, Philadelphia, PA 19129) *J. Biol. Chem. 257*(5):2453-2459 (1982). To explore the nature of retinyl ester synthesis by liver microsomes, membranes prepared from rat or cat liver were incubated under various conditions with [^{3}H] retinol dispersed in dimethyl sulfoxide. When [^{3}H] retinol, buffer, and microsomes were incubated together (basal conditions), some [^{3}H] retinol esterification was consistently observed. However, the rate of esterification could be increased 6- to 11-fold by addition of either palmitoyl-CoA (100 μM) or a fatty acyl CoA-generating system. To determine whether the fatty acid used to esterify [^{3}H] retinol under basal conditions might be derived from an endogenous pool of fatty acyl-CoA associated wih the microsomal preparation, microsomes were pretreated at pH 7.4 with 0.5 M hydroxylamine, a reagent that reacts with coenzyme A thioesters to form hydroxamates. This pretreatment reduced the basal reaction by 69%. However, hydroxylamine-treated microsomes still retained acyltransferase activity, as shown by a 24- to 40-fold increase in retinyl ester synthesis after addition of palmitoyl-CoA. When microsomes were incubated with both [^{3}H] retinol and [^{14}C] palmitoyl-CoA of known specific radioactivities, the ratio of ^{14}C to ^{3}H is newly synthesized retinyl palmitate was essentially equal to that of its putative substrates, indicating that [^{14}C] palmitate did not undergo significant isotope dilution prior to acylation of [^{3}H] retinol. These experiments provide direct evidence for retinol esterification catalyzed by a microsomal acyl-CoA:retinol acyltransferase and indirect evidence for a pool of fatty acyl-CoA in isolated liver microsomes that is available to react with [^{3}H] retinol to form esterified retinol.

RECOGNITION AND RECEPTOR-MEDIATED ENDOCYTOSIS OF THE LYSOSOMAL ACID LIPASE SECRETED BY CULTURED HUMAN FIBROBLASTS. G.N. Sando and V.L. Henke (Department of Internal Medicine and the Arteriosclerosis Specialized Center of Research, University of Iowa, Iowa City, IA 52242) *J. Lipid Res. 23*:114-123 (1982). We have studied the recognition and uptake of acid lipase by human fibroblasts in order to determine requirements for localization and function of the enzyme in lysosomes. Our approach was based on evidence that a number of acid hydrolases involved in mucopolysaccharide metabolism are secreted from cultured fibroblasts and endocytosed by a phosphomannosyl-dependent, receptor-mediated process. Acid fatty acid ester hydrolase activity secreted from human fibroblasts was separable into two major forms by hydrophobic chromatography. The dominant form

from normal cells was deficient in fibroblasts from patients with Wolman's disease, an inherited disorder of lysosomal cholesteryl ester and triglyceride metabolism. The time- and temperature-dependent, saturable uptake of this enzyme by fibroblasts was competitively inhibited by mannose 6-phosphate and was destroyed by pretreatment of the enzyme with phosphatase. Internalized lipase had a half-life of 1 day. Application of the enzyme to Wolman's disease fibroblasts reduced cholesteryl ester storage; this effect was blocked by ammonium chloride, a general inhibitor of lysosomal hydrolysis. Our results indicate that extracellular acid lipase is transported to fibroblast lysosomes by the same receptor-mediated process that functions in the packaging of several lysosomal glycosidases.

EFFECT OF PHOSPHOLIPID OXIDATION PRODUCTS ON TRANSBILAYER MOVEMENT OF PHOSPHOLIPIDS IN SINGLE LAMELLAR VESICLES. J.M. Shaw and T.E. Thompson (Dept. of Biochem. Virginia Commonwealth Univ., Med. College of Virginia, Richmond, VA 23298) *Biochemistry 21*:920-927 (1982). Single lamellar phosphatidyl[*methyl*-^{2}H] choline vesicles were incubated wih an excess of unlabeled phosphatidylcholine vesicles or phosphatyidylcholine-cholesterol vesicles containing 8 mol % glucuronosyldiglyceride. *Incubation of the two vesicle populations* was performed in the presence or absence of a purified phosphaidylcholine exchange protein. The negatively charged glycolipid donor vesicles could be completely removed by column chromatography on DEAE-Sephacel. Following incubation with exchange protein and subsequent fractionation, the -$N(CD_3)_3$ phosphatidylcholine acceptor vesicles exhibited a 61-73% enrichment of the unlabeled phosphatidylcholine in the outer monolayer. Upon incubation in an air atmosphere, no appreciable transbilayer movement of the outer monolayer -$N(CH_3)_3$ phosphatidylcholine was observed for at least 5 days. Between 5 and 7, however, extensive transbilayer movement occurred, leading to an outer monolayer/inner monolayer phosphatidylcholine ratio of 2.1 on day 7. In phosphatidylcholine-6 mol % cholesterol vesicles treated similarly, the outside/inside ratio of the unlabeled phospholipid was 6.7, suggesting a much smaller percentage of transbilayer movement. The loss of transbilayer asymmetry which occurred during a 36-h period after day 5 could be estimated at the upper limit, $t_{1/2} \sim 7.3$ h for phosphatidylcholine vesicles and $t_{1/2} \sim 53$ h for phosphatidylcholine-cholesterol vesicles. The actual rates for transbilayer movement, however, were likely more rapid. Transbilayer movement occurred at a time period when oxidized phospholipid breakdown products had reached critical levels.

INFLUENCE OF A VITAMIN D DEFICIENCY ON EGG SHELL, MEMBRANE, AND EGG SHELL WEIGHT. H. Shen, J.D. Summers, and S. Leeson (Department of Animal and Poultry Science, University of Guelph, Guelph, Ontario) *Poultry Sci. 61*:745-749 (1982). Hens, 59 weeks of age, were offered a corn, soya-type diet with no supplemental vitamin D_3 for a 28-day period. Egg production remained relatively constant to the end of the second week and then began to fall precipitously. Egg shell weight remained constant for 10 days, and then a marked linear decrease took place. Shell membrane weight and egg weight were not influenced by a reduction in shell weight. Older hens, or hens previously subject to a vitamin D_3 deficient diet, seemed better able to cope with a subsequent vitamin D deficiency.

THE EFFECTS OF DIETARY TRILINOELAIDIN ON FATTY ACID AND ACYL DESATURASES IN RAT LIVER. J.L. Shimp, G. Bruckner and J.E. Kinsella (Institute of Food Science, Cornell University, Ithaca, NY 14853) *J. Nutr. 112*:722-735 (1982). The effects of incremental amounts of dietary t,t-18:2 on liver microsomal Δ5 and Δ6 acyl desaturase activities were studied. The hepatic concentration of t,t-18:2 increased linearly from 0 to 1.6 mg/g liver as dietary, t,t-18:2 was increased from 0-50% of dietary fat. This apparently inhibited the conversion of linoleic to arachidonic acid in liver tissue because linoleic acid increased from 1.2 go 3.1 mg/g liver, while arachidonic acid concurrently decreased from 3.9 to 1.9 mg/g liver tissue. This reflected the inhibition of Δ6 desaturase by 5,5-18:2. The Δ6 desaturase activity in liver microsomes of rats fed 10,20, and 50% of t,t-18:2 in their dietary lipids was 97, 75, and 51% of the activity of rats fed no t,t-18:2. In vitro tests showed that t,t-18:2 specifically inhibited liver Δ6 desaturase. The Δ5 desaturase activities did not increase significantly as dietary 5,t-18:2 levels increased. This study showed that dietary t,t-18:2 by depressing Δ6 desaturase activity may affect essential fatty acid metabolism.

VITAMIN E RESPONSE TO HIGH DIETARY VITAMIN A IN THE CHICK. D. Sklan and S. Donoghue (Department of Clinical Studies, School of Veterinary Medicine, University of Pennsylvania, Kennett Square, PA 19348) *J. Nutr. 112*:759-765 (1982). Chicks were fed diets containing three levels of tocopherol, and control or high levels of retinyl palmitate for at least 24 days. Glutathione peroxidase activity in erythrocytes, plasma and liver was enhanced in tocopherol-depleted chicks, and in chicks fed high dietary vitamin A. Hepatic malonaldehyde production increased in high vitamin A chicks. Superoxide dismutase activity was increased in erythrocytes and livers of chicks on low tocopherol diets and depressed by high dietary vitamin A. The effects of high dietary vitamin A were at least partially attenuated by addition of tocopherol to the diet. Chicks fed high vitamin A, low vitamin E diets demonstrated a sixfold increase in clearance of labeled tocopherol from plasma. Additional dietary tocopherol partially prevented the rapid clearance of tocopherol due to vitamin A. Absorption studies with a nonabsorbed reference substance (^{141}Ce) revealed that a greater fraction of dietary tocopherol was oxidized prior to the digesta reaching the duodenum when high vitamin A levels were present in the diet although no differences in percentage tocopherol absorption were observed. Secretion into the intestine of glucuronides of tocopherol was enhanced almost twofold by feeding high vitamin A. It is concluded that the interactions between tocopherol and vitamin A include: enhanced oxidation of dietary tocopherol prior to the intestine, increased tocopherol turnover, due, in part, to increased conjugation of glucuronides, and selective changes in enzymes involved in protection of cells against oxidative damage.

MEASUREMENT OF RECEPTOR-INDEPENDENT LIPOPROTEIN CATABOLISM USING 1,2 CYCLOHEXANEDIONE-MODIFIED LOW DENSITY LIPOPROTEIN. H.R. Slater, C.J. Packard, and J. Shepherd (University Department of Biochemistry and Medical Cardiology, Royal Infirmary, Glasgow, G4 OSF, United Kingdom) *J. Lipid Res. 23*:92-96 (1982). The utility of 1,2 cyclohexanedione-modified low density lipoprotein (CHD-LDL) as a marker for the measurement of receptor independent LDL catabolism has been assessed by examining its metabolic properties in cultured human fibroblasts and in rabbits. Cell culture studies showed that the inhibition of high affinity membrane receptor binding produced by the modification could be partially reversed by prolonged incubation of the CHD-LDL at 37 C. Pre-exposure of the complex to alkaline pH (pH 10.5) prevented this and yielded a product that was apparently stable. Despite its regained ability to bind to the fibroblast receptor, ^{125}I-labeled CHD-LDL incubated at 37 C for 24 hr either in vivo or in vitro was removed from rabbit plasma in the same manner as freshly prepared ^{131}I-labeled CHD-LDL and as ^{131}I-labeled CHD-LDL that had been treated at pH 10.5. However, its plasma clearance was significantly faster than that of reductively methylated LDL. We believe that this may result from differential catabolism of these modified lipoproteins rather than from susceptibility of the CHD-LDL to receptor-directed catabolism.

EFFECTS OF ETHANOL DIETS ON CHOLESTEROL CONTENT AND PHOSPHOLIPID ACYL COMPOSITION OF RAT HEPATOCYTES. T.L. Smith, A.E. Vickers, K. Brendel, and M.J. Gerhart (Veterens Administration Medical Center, Research Service (151), Tucson, AZ 85723) *Lipids 17*(3):124-128 (1982). Chronic treatment of adult male rats with ethanol liquid diets resulted in alterations in phospholipid and cholesterol contents as well as the acyl composition of phosphatidylethanolamine (PE), phosphatidylinositol (PE)-phosphatidylserine (PS) mixture, and phosphatidylcholine (PC) of isolated hepatocytes. The influence of ethanol on these lipids was largely dependent on the proportion of dietary fat. Phospholipid and total cholesterol contents were elevated 23 and 27%, respectively, by ethanol when offered in a low-fat diet (5% corn oil). Only the percentage of arachidonic acid from PI-PS was significantly reduced in the low-fat ethanol group. Exposure to a high-fat (34% corn oil) diet in the presence of ethanol for 4-5 weeks resulted in a significant decrease in arachidonate/linoleate ratios of hepatic PE, PS-PI and PC, while total phospholipid content remained constant. In the high-fat, ethanol-treated group, hepatic cholesterol content was increased 2-fold. These results suggest that the level of dietary fat plays an important role in determining the effects of chronic ethanol consumption on hepatic cholesterol content and phospholipid acyl composition.

3-HYDROXY-3-METHYLGLUTARYL COA REDUCTASE IN CULTURED HEPATOCYTES. E.F. Stange, W.E. Fleig, A. Schneider, G.Nother-Fleig, M. Alavi, G. Preclik, and H. Ditschuneit (Division of Metabolism, Nutrition and Gastroenterology, Dept. of Internal Medicine, Univ. of Ulm, Ulm (F.R.G.)) *Atherosclerosis 41*(1): 67-80 (1982). Regulation of the key enzyme of cholesterol synthesis, 3-hydroxy-3-methyl-glutaryl CoA reductase by heterologous human lipoproteins and hormones was studied in a maintenance culture of rat hepatocytes. Under control conditions total HMG CoA reductase increased by 50% after 24 h culture compared to 0 h values immediately after isolation. Thereafter a plateau of enzyme activity was reached lasting until 48 h, with a slight decline at 72 h. Concomitantly the "expressed" enzyme activity increased steadily. During the steady state period of total reductase VLDL added to the medium at concentrations up to 50 μg/ml protein had no effect on HMG-CoA reductase activity. LDL suppressed the enzyme in a

dose-dependent fashion to 40% of controls at 100 μg/ml. HDL had the opposite effect with significant induction up to 252% of controls at 50 μg/ml. Insulin also caused a comparable dose-dependent stimulation of enzyme activity at 10^{-8} and 10^{-7} M, whereas glucagon inhibited reductase activity. Compared to the insulin action, triiodothyronine and triamcinolone prompted a minor, but still significant increase of reductase activity. Insulin and triamcinolone acted synergistically, but the combination of triamcinolone and triiodothyronine was only additive. All hormonal inductions of reductase could be blocked by cycloheximide.

EFFECT OF PROTEIN, CHOLESTEROL, AND PHOSPHATIDYLGLYCEROL ON THE SURFACE ACTIVITY OF THE LIPID-PROTEIN COMPLEX RECONSTITUTED FROM PIG PULMONARY SURFACTANT. Y. Suzuki (Department of Pathology, Chest Disease Research Institute, Kyoto University, Sankyo-ku, Kyoto 606, Japan) *J. Lipid Res. 23*:62-69 (1982). Lipid-protein complexes reconstituted from pig surfactant lipids and proteins were investigated for surface adsorption, minimum surface tension, stability index, and surface compressibility. Lipid constituents remained unchanged with proecedures for the reconstitution. An apoprotein with a nominal molecular weight of 15,000 daltons significantly accelerated the lipid-protein complex to absorb the air-water interface. A 34,000-dalton apoprotein slightly modified the surface adsorption and surface activity when it was incorporated into the lipid-protein complex formed from lipids and 15,000-dalton apoprotein. No significant surface adsorption was found in lipid vesicles even with the same lipid constituents as in the lipid-protein complex. In the lipid-protein complex prepared by changing the content of cholesterol and phosphatidylglycerol, cholesterol affected both the minimum surface tension and the surface compressibility while phosphatidylglycerol had little effect on the surface activity of the complex.

EXPERIMENTAL STUDIES ON THE PULMONARY SURFACTANT. RECONSTITUTION OF SURFACE-ACTIVE MATERIAL. Y. Suzuki, E-i. Nakai, and K-i. Ohkawa (Dept. of Pathology, Chest Disease Research Institute, Kyoto University, Sakyo-ku, Kyoto 606, Japan) *J. Lipid Res. 23*:53-61 (1982). The conditions for the reconstitution of surfactant lipoprotein were investigated using pig pulmonary surfactant. Lipids of surface-active material (SAM) were extracted with ethanol-ether and the residue, containing mainly protein, was extracted first with dilute sodium borate buffer (pH 10.0) (fraction A) followed by extraction with deoxycholate solution (fraction B). The former (A) contained mainly protein having a nominal molecular weight of 34,000 daltons, albumin and globulin, and the latter (B) 34,000 and 15,000 daltons. Reconstitution of lipids and proteins using these two fractions revealed a greater affinity of fraction B to lipids than that of fraction A, when lipids and proteins were dialyzed against pH 7.4 Tris-HCl. Observation by freeze-fracture methods revealed that protein particles were incorporated into liposomes. Protein-lipid ratio of this complex (LB) could be regulated by altering the amount of lipids and protein during the dialysis. Fraction A was incorporated into LB (LBA) by dialyzing LB with fraction A at an acidic pH. With this procedure, protein having a nominal molecular weight of 34,000 daltons was selectively incorporated. In negatively stained preparations, LBA had a granular appearance in the area limited by lipid membrane. We suggest that in the lipid-protein complex of SAM, two different proteins are present; a hydrophobic one in lipids and more hydrophilic ones in the water phase that have a close association with the former.

ROLE OF SERUM IN INHIBITION OF CULTURED LYMPHOCYTES BY LYSOPHOSPHATIDYLCHOLINE. A. Takeda, R.G.E. Palfree, and D.R. Forsdyke (Dept. of Biochem., Queen's Univ., Kingston, Ontario K7L 3N6 (Canada)) *Biochim. Biophys. Acta 710* (1):87-98 (1982). Serum was heated at various temperatures to inactivate components which might be involved in the regulation of lysophosphatidylcholine (lysoPC) levels in rabbit lymph-node cell cultures. Cells cultured in medium containing serum preheated for 20 min at 66 C were inhibited much more by exogenous lysoPC than were cells cultured in medium containing control serum. This was observed over a 20 h culture period. Heating serum at 66 C caused (i) conversion of monomeric albumin to highly polymeric forms which were deficient in lysoPC-binding activity, (ii) transfer of lysoPC from albumin to lipoproteins, predominantly high density lipoproteins, and (iii) inhibition of two lysoPC metabolizing activities. Addition of albumin to cultures containing 66 C-serum decreased the toxicity of lysoPC to the same extent as did the addition of control serum with an equivalent albumin content. Thus, albumin was the major heat-labile factor protecting cells against lysoPC. Cell inhibition by lysoPC was dependent on the sequence of heating serum and lysoPC addition. Inhibition was small when lysoPC was added before heating the serum. Although radioactive labelling of cells with [^{14}C] lysoPC was increased in 66 C-serum, this did not correlate with cell inhibition. Increased labelling with [^{14}C] lysoPC occurred several hours before significant cell inhibition was evident and was not affected by the sequence of heating and lysoPC addition. It is suggested that in heated serum lysoPC generates another factor which is responsible for the cytotoxic effects observed.

INTERMEDIATE-DENSITY LIPOPROTEIN AND CHOLESTEROL-RICH VERY LOW DENSITY LIPOPROTEIN IN ANGIOGRAPHICALLY DETERMINED CORONARY ARTERY DISEASE. R. Tatami, H. Mabuchi, K. Ueda, R. Ueda, T. Haba, T. Kametani, S. Ito, J. Koizumi, M. Ohta, S. Miyamoto, A. Nakayama, H. Kanaya, H. Oiwake, A. Genda, and R. Takeda (Second Department of Internal Medicine, Kanazawa University School of Medicine, Kanazawa, Ishikawa, Japan) *Circulation 64*(6):1174-1184 (1981). The relationship between the concentrations of intermediate-density lipoprotein (IDL) and other lipoproteins and the extent of coronary artery disease (CAD) was studied in 182 consecutive patients evaluated by selective coronary cineangiography. On univariate analysis, the extent of CAD correlated significantly and positively with very low density lipoprotein (VLDL) cholesterol, IDL cholesterol and low-density lipoprotein (LDL) cholesterol, and negatively with high-density lipoprotein (HDL) cholesterol. Analysis of four subgroups divided by IDL cholesterol and LDL cholesterol levels indicated that moderately increased levels of IDL cholesterol were closely associated with a high frequency of CAD. Moreover, multivariate regression analysis demonstrated that IDL cholesterol for men, LDL cholesterol for men and women and HDL cholesterol for men were significant variable of use in the final weighting procedure. IDL cholesterol was closely associated with cholesterol-rich VLDL. This study shows that IDL and cholesterol-rich VLDL combine to contribute to the development of CAD.

HEMOLYTIC ANEMIA OF OWL MONKEYS: RED BLOOD CELL LIPID ALTERATIONS (41340). F.X. Walsh, R.J. Nicolosi, S.N. Meydani, P.K. Sehgal, and K.C. Hayes (Harvard Med. School, New England Regional Primate Research Center, Southborough, MA 01772) *Proc. Soc. Exp. Bio. Med. 169*(2):253-259 (1982). The owl monkey, a species of New World monkey represented by several different karyotypes, develops hemolytic anemia in captivity. Susceptibility to anemia varies as a function of karyotype, and the hemolytic process responds to vitamin E. Since the plasma concentration of vitamin E in these owl monkeys was normal, it was hypothesized that the anemia may reflect a lipid abnormality in the red blood cell (RBC) membrane which was stabilized by supplemental tocopherol and that the basic RBC lipids would differ as a function of owl monkey karyotype. The RBC membrane cholesterol, phospholipid, fatty acids, and free cholesterol to phospholipid ratio were compared between anemic and nonanemic owl monkeys, owl monkeys of different karyotypes, and between different primate species. The owl monkey exhibited a unique RBC phospholipid profile, having reduced proportions of phosphatidylserine (PS) and phosphatidylethanolamine (PE) and more phosphatidylcholine (PC) and sphingomyelin (Sph) when compared to other primates, including man. Owl monkeys of karyotype VI (anemia resistant) had a normal polyunsaturated fatty acid (PUFA) profile in RBC phospholipids and less RBC membrane cholesterol contributing to a normal FC/PL ratio, whereas RBCs from susceptible and overtly anemic owl monkeys revealed low levels of PUFA and increased RBC membrane cholesterol that led to an elevated FC/PL ratio. The etiology of these lipid alterations and their association with anemia remains to be elucidated.

ABNORMAL LIPOPROTEIN RECEPTOR-BINDING ACTIVITY OF THE HUMAN E APOPROTEIN DUE TO CYSTEINE-ARGININE INTERCHANGE AT A SINGLE SITE. K.H. Weisgraber, T.L. Innerarity, and R.W. Mahley (Gladstone Foundation Lab for Cardiovascular Disease, Univ. of CA, San Francisco, CA 94140) *J. Biol. Chem. 257*(5):2518-2521 (1982). Previously, we demonstrated that the human E apoprotein existed in 3 forms and that the 3 forms differed from one another by cysteine-arginine interchanges at 2 substitution sites. The E-2, E-3, and E-4 apo-E contain cysteine/cysteine, cysteine/arginine, and arginine/arginine at sites A/B, respectively. Subjects with Type III hyperlipoproteinemia, a genetic disease associated with defective plasma lipoprotein clearance, possess the E-2 form of apo-E. It was postulated that the substitution of cysteine for arginine at site B in the E-2 might be responsible for an impaired interaction of Type III apo-E with cell surface receptors. To test this possibility, the binding activities of the various forms of apo-E to the receptors on human fibroblasts were compared. The E-3 and E-4 apo-E readily bound to the receptors; however, the E-2 apo-E-binding activity was defective. Consideration was given to the possibility that a positively charged residue at site B, as occurs in both E-3 and E-4, was important for normal binding activity. To investigate this, the cysteine residues of the E-2 apo-E were converted by cysteamine treatment to a positively charged lysine analogue. This resulted in a marked increase in the binding activity of the E-2 apo-E. These studies demonstrated that the defective binding of the E-2 apo-E from

Type III hyperlipoproteinemic subjects was due, at least in part, to the cysteine-arginine interchange at site B, and they suggested the importance of a positively charged residue at this position in the sequence to mediate normal apolipoprotein-receptor interaction.

THE EFFECTS OF MEMBRANE FATTY ACID MODIFICATION OF CLONAL PHEOCHROMOCYTOMA CELLS ON DEPOLARIZATION-DEPENDENT EXOCYTOSIS. T.P. Williams and R. McGee, Jr. (Dept. of Pharmacology, Georgetown Univ., Schools of Med. and Dentistry, Washington, D.C. 20007) *J. Biol. Chem. 257*: 3491-3500 (1982). We have begun studying the role of membrane lipids in the exocytotic release process using the pheochromocytoma clone, PC12. The phospholipid fatty acid composition of the cells was modified by growth in the presence of specific fatty acids. None of the fatty acid modifications affected K^+-stimulated release of [^{3}H] norepinephrine. This observation indicates that the individual steps of the secretion process, including the extent of depolarization produced by K^+, the response of the voltage-dependent Ca^{2+} channels to depolarization, and the subsequent steps in Ca^{2+}-dependent exocytosis were unaffected by the fatty acid changes. In contrast, exocytosis evoked by stimulation of nicotinic cholinergic receptors with carbamylcholine or direct activation of action potential Na^+ channels with veratridine was diminished in cells enriched with unsaturated fatty acids. The diminished output of the release systems was observed at all concentrations of carbamylcholine and veratridine tested. Since the events of exocytosis subsequent to Ca^{2+} influx were unaffected by unsaturated fatty acids, it appears likely that the magnitude of the depolarization produced by carbamylcholine and veratridine was reduced. The loss of carbamylcholine-stimulated release did not correlate with the simple presence of the fatty acids, but paralleled closely the time and concentration-dependent changes in the phospholipid fatty acid composition. However, when oleate and arachidonate were simultaneously added to the culture medium, the inhibitory effects on carbamylcholine-stimulated release were additive, whereas the changes in fatty acid composition were antagonistic. Thus, exposure of PC12 cells to unsaturated fatty acids causes specific, reversible decreases in the activities of at least 2 stimulus/secretion systems.

DISCOVERY OF AN ARACHIDONOYL COENZYME A SYNTHETASE IN HUMAN PLATELETS. D.B. Wilson, S.M. Prescott, and P.W. Majerus (Division of Hematology-Oncology, Depts. of Internal Med. and Biol. Chem., Washington Univ. School of Med., St. Louis, MO 63110) *J. Biol. Med. 257*:3510-3515 (1982). Platelets contain small amounts of a variety of free fatty acids but essentially no free arachidonate. When free fatty acids are incubated with platelets, there is preferential incorporation of arachidonic acid and 8,-11,14-eicosatrienoic acid compared to other fatty acids. We now explain these findings by the discovery that platelets contain two long chain acyl-CoA synthetases. One shows activity with a range of different fatty acids, similar to long chain acyl-CoA synthetases studies previously. A crude platelet membrane preparation contains this enzyme that catalyzes the formation of 0.75 nmol of oleoyl-CoA/min/10^3 platelets. The other enzyme is specific for the prostaglandin precursors arachidonic acid and 8,11,14-eicosatrienoic acid. Based on the ability of fatty acids to inhibit arachidonate and 8,11,14-eicosatrienoate activation, we conclude that other fatty acids including linoleic, 5,8,11-eicosatrienoic, and oleic acids are not substrates for the enzyme. Platelet membranes catalyze formation of 2.9 nmol of arachidonoyl-CoA/min/10^9 platelets and 2.5 nmol of 8,11,14-eicosatrienoyl-CoA/min/10^9 platelets. Arachidonoyl-CoA synthetase has optimal activity at pH 8 and requires ATP (K_m=0.5 mM), Mg^{2+} (K_m=2.5 mM), CoA (K_m=0.13 mM), and arachidonic acid (K_m= 0.03 mM). We propose that the arachidonate-specific acyl-CoA synthetase may control the level of free arachidonic acid in platelets, limiting prostaglandin synthesis by the unstimulated cell and capturing free arachidonate from extracellular sources.

MOBILIZATION OF CHOLESTEROL FROM CHOLESTEROL ESTER-ENRICHED TISSUE CULTURE CELLS BY PHOSPHOLIPID DISPERSIONS. A.O. Yau-Young, G.H. Rothblat, and D.M. Small (Biophysics Institute, Depts. of Med. and Biochem., Boston Univ. Med. Center, Boston, MA 02118) *Biochim. Biophys. Acta 710*:181-187 (1982). The accumulation of cholesterol esters in foam cells of the arterial intima is an important characteristic of fatty streak lesions of atherosclerosis. Can cholesterol ester accumulations in cells be mobilized by altering their external milieu? Phospholipid dispersions were used to remove cholesterol from a cholesterol ester-enriched cell line. Rat hepatoma cells, Fu5AH, were loaded with cholesterol esters. After removing the loading medium, we incubated the cells in serum-free medium containing egg phosphatidylcholine dispersions. Unesterfied cellular cholesterol level decreased in the first 4 h and then remained at a constant level. The cholesterol esters decreased after a lag time of about 2 h and the triacylglycerol level increased after 3 h. The decrease in cellular cholesterol ester depended on the amount of phospholipid in the medium. Cellular cholesterol ester decreased with increasing concentration of medium phospholipid to 2 μmol/ml and then plateaued. The removed cellular sterols appeared in the medium as free cholesterol. Since there was no measurable cholesterol esterase activity in the medium, the cholesterol ester in the cells was hydrolyzed before it appeared in the medium. The fatty acyl composition of the cellular cholesterol esters remained unchanged after significant reduction. Sphingomyelin and dimyristoyl phosphatidylcholine dispersions, though cytotoxic, were also effective in reducing cellular cholesterol esters. These experiments demonstrate that cholesterol ester accumulations in these cells can be reduced when phospholipid dispersions are used as cholesterol acceptors in the extracellular medium.

METABOLISM *IN VIVO* OF ALL-*TRANS*-RETINOIC ACID. BIOSYNTHESIS OF 13-*CIS*-RETINOIC ACID AND ALL-*TRANS*- AND 13-*CIS*-RETINOYL GLUCURONIDES IN THE INTESTINAL MUCOSA OF THE RAT. M.H. Zile, R.C. Inhorn, and H.F. DeLuca (Department of Biochemistry, College of Agricultural and Life Sciences, University of Wisconsin-Madison, Madison, Wisconsin 53706) *J. Biol. Chem. 257*(7):3544-3550 (1982). The metabolites of all-*trans*-[^{3}H] retinoic acid appearing in the intestines of bile duct-cannulated rats were compared to those of similarly treated intact rats. 2.4% of administered radioactivity was found in the small intestines of bile duct-cannulated rats 2 h after dose, while a much larger proportion of the dose (7.2%) was found in the intestines of the intact rats. All-*trans*- and 13-*cis*-retinoic acids predominate in the intestinal mucosa of bile duct-cannulated rats shortly after dosing. Retinoyl glucuronide was the major metabolites occurring as a mixture of all-*trans* and 13-*cis* forms. Highly polar metabolites of retinoic acid appear in mucosa at all times in both intact and bile duct-cannulated rats demonstrating rapid metabolism of retinoic acid in intestine. The finding of a similar proportion of the 13-*cis* isomers in retinoic acids and retinoyl glucuronides suggests that injected all-*trans*-retinoic acid is isomerized *in vivo* probably prior to conjugation with glucuronic acid.

DIHOMO-PROSTAGLANDINS AND -THROMBOXANE. A PROSTAGLANDIN FAMILY FROM ADRENIC ACID THAT MAY BE PREFERENTIALLY SYNTHESIZED IN THE KIDNEY. H. Sprecher, M. Van Rollins, F. Sun, A. Wyche, and P. Needleman (Dept. of Pharmacology, Washington Univ. Med. School, St. Louis, MO 63110) *J. Biol. Chem. 257*:3912-3918 (1982). Arachidonic acid, the 20-carbon precursor for prostaglandin synthesis is present in membrane lipids throughout the body and its metabolic enzyme is ubiquitously distributed. It was previously shown that adrenal glands, testis, brain, and kidney medulla contain both arachidonic acid and its chain-elongated product adrenic acid. We prepared [1-^{14}C]-adrenic acid and found that the renal medulla was the only rabbit tissue tested which readily metabolized the 22-carbon fatty acid. The major renal medullary cell type that contains adrenic acid is the renomedullary interstitial cell which we found active in converting this fatty acid into 1a,1b-dihomo-prostaglandin E_2. Furthermore, the renomedullary cells possess recognition sites for the 1a,1b-dihomo-prostaglandin E_2 which results in an activation of adrenylate cyclase when added to these cells. The renal medullary conversion of adrenic acid to dihomoprostaglandins was greatly facilitated in microsomes prepared from the ureter-obstructed (hydronephrotic) kidney. The eight major products generated by the hydronephrotic kidney were purified by high performance liquid chromatography and upon analysis by gas chromatography-mass spectrometry were shown to be 1a,1b-dihomo-8-keto-prostaglandin $F_{1\alpha}$ (the dihomoprostacyclin metabolite), 1a,1b-dihomo-thromboxand B_2, 1a,1b-dihomo-prostaglandin $F_{2\alpha}$, 1a,1b-dihomo-prostaglandin E_2, 1a,1b-dihomo-prostaglandin D_2, two 14-hydroxy-nonadecatrienoic acids (the other metabolite of thromboxane synthetase), and 13-hydroxydocosatetraenoic acid. The limited distribution of adrenic acid and the demonstrated ability of the rabbit renal medulla to metabolize this fatty acid create the possibility for a family of prostaglandin metabolites largely restricted to the kidney.

7β-DEHYDROXYLATION OF URSODEOXYCHOLIC ACID BY WHOLE CELLS AND CELL EXTRACTS OF THE INTESTINAL ANAEROBIC BACTERIUM, *EUBACTERIUM* SPECIES V.P.I. 12708. B.A. White, R.J. Fricke, and P.B. Hylemon (Dept. of Microbiology, Medical College of Virginia, Virginia Commonwealth Univ., Richmond, VA 23298) *J. Lipid Res. 23*(1):145-153 (1982). Whole cells and cell extract of *Eubacterium* species V.P.I. 12708 7-dehydroxylated [^{3}H]ursodeoxycholic acid or [^{14}C] chenodeoxycholic forming lithocholic acid. 7β-Dehydroxylationspecific activity was 146 and 386 nmol hr^{-1} mg $protein^{-1}$ for cell extracts and whole cells, respectively. 7α- or 7β-Dehydroxylation activity was detected

only in whole cells or cell extracts prepared from cultures grown in the presence of cholic acid. The addition of NAD^+ (0.5 mM) to anaerobically dialyzed cell extracts stimulated 7α- and 7β-dehydroxylation activity by 5- and 40-fold, respectively. The level of 7β-dehydroxylation specific activity was approximately 3- to 5-fold lower than 7β-dehydroxylation in whole cells and 3-fold lower in cell extracts. Substrate saturation kinetics for ursodeoxycholic acid and chenodeoxycholic acid were hyperbolic and showed substrate inhibition at concentrations above 200 μM. The apparent K_m values for ursodeoxycholic and chenodeoxycholic acid were 14.5 μM and 49 μM, respectively. Both 7α- and 7β-hydroxylase activities were inactivated (60% to 70%) by heating for 6 min at 45 C. Moreover, both activities co-eluted from anaerobic Bio-Gel A 1.5-M column as a single peak at approximately 114,000 (M_r). These data show that this intestinal anaerobic bacterium has both 7α- and 7β-dehydroxylase activities which may be catalyzed by the same enzyme.

THE ACTION OF CHROMIUM ON SERUM LIPIDS AND ON ATHEROSCLEROSIS IN CHOLESTEROL-FED RABBITS. A.S. Abraham, M. Sonnenblick, and M. Eini (Dept. of Med., Shaare Zedek Hospital, Jerusalem (Israel)) *Atherosclerosis 42*(2,3):185-195 (1982). Eight rabbits, fed on a 1% cholesterol diet for 30 days, were injected daily with potassium chromate for a further 60 days. A 50% reduction in aortic intimal plaque area and in aortic total cholesterol content was observed. However, although levels of serum cholesterol and triglycerides were consistently lower and levels of high density lipoprotein fractions consistently higher in the chromium-treated as compared to the control rabbits, these differences did not reach statistical significance. A further 6 rabbits were injected with potassium chromate and fed on a 1% cholesterol diet for 12 weeks. Mean aortic cholesterol content (±SEM) was 40.23 mg/10 cm aortic length (±7.50) as compared to 66.24 mg/10 cm (±7.89) in a control group ($P<0.05$), whereas the area of aortic intima covered by macroscopic plaques was 67.5% (±2.79) and 81.1% (±3.14) ($P<0.01$) respectively.

THE EFFECT OF CHROMIUM ON CHOLESTEROL-INDUCED ATHEROSCLEROSIS IN RABBITS. A.S. Abraham, M. Sonnenblick and M. Eini (Dept. of Med., Shaare Zedek Hospital, Jerusalem (Israel)) *Atherosclerosis 41*(2/3):371-379 (1982). Rabbits fed on a 1% cholesterol diet for 30 days were injected daily with potassium chromate for a further 60 days. A 50% reduction in aortic intimal plaque area and in aortic total cholesterol content was observed. Control rabbits treated with chromium showed a significant increase in the chromium concentration of their aortas, liver and kidneys but not of the myocardium. Cholesterol-fed rabbits treated with chromium showed a significant increase in chromium concentrations in the liver and kidneys only. Serum cholesterol levels were consistently lower in the chromium-treated animals, although the differences did not reach significant levels.

CHANGES IN THE METABOLISM OF FATTY ACIDS IN ADIPOSE TISSUE IN OBESE PATIENTS WITH PRIMARY HYPERTRIACYLGLYCEROLEMIA. P. Arner, P. Engfeldt, and J. Ostman (Dept. of Medicine and the Research Center, Huddinge Hospital, Karolinska Institute, Sweden) *J. Lipid Res. 23*(3):422-427 (1982). Changes in the release and esterification of free fatty acids (FFA) in adipose tissue were looked for as a cause of moderate primary hypertriacylglycerolemia (HTG) in five obese subjects. Comparison was made with six obese normolipidemic subjects. The two groups were matched for body weight, tolerance of intravenous glucose, fat cell size, fasting levels of serum immunoreactive insulin, and serum insulin response to an intravenous glucose load. Subcutaneous adipose tissue was incubated in vitro with [1-^{14}C] palmitic acid for 30, 60, and 120 minutes. There was a significant, two-fold increase in the rate of FFA mobilization, but no change of glycerol release in HTG patients. The adipose tissue levels of mono- and diacylglycerols were similar in the two groups of subjects and did not change during incubation. Re-esterification of FFA, calculated from the net changes in medium and in tissue FFA and glycerol release, was lower in HTG patients than in the controls. In adipose tissue of HTG patients, the amount of radioactive fatty acid incorporated into triacylglycerols (TG) was 50% lower whereas that incorporated into tissue FFA was three times higher when compared with control patients. It is concluded that, in adipose tissue of obese patients with primary hypertriacylglycerolemia, the esterification of free fatty acids to triacylglycerol is decreased. As a consequence, free fatty acids are mobilized at an increased rate.

PARTIAL PURIFICATION AND CHARACTERIZATION OF 5β-CHOLESTANE-3α,7α,12α-TRIOL AND 5β-CHOLESTANE-3α,7α-DIOL 27-MONOOXYGENASE. Y. Atsuta and K. Okuda (Dept. of Biochem., Hiroshima Univ. School of Dentistry, Hiroshima 734, Japan) *J. Lipid Res. 23*(2):345-351 (1982). Hepatic mitochondrial cytochrome P-450 has been partially purified from the non-induced rat liver. The purification consisted of solubilization with cholate, polyethylene glycol fractionation, chromatographic separation using ω-amino-*n*-octyl Sepharose 4B column, and chromatography on hydroxylapatite. The overall purification of the enzyme from the solubilized extract was about 22-fold on the basis of specific content of cytochrome P-450, and 50-fold on the basis of specific activity. The partially purified enzyme was active for both 5β-cholestane-3α,7α,12α-triol and 5β-cholestane-3α,7α-diol. That the enzyme activities for these substrates were not due to two different enzymes but to the same active site of a single enzyme protein was shown by several pieces of evidence, i.e., behavior to thermal inactivation, pH-dependency of the reaction velocities, experiments with mixed substrates, and behavior towards inhibitors and activators. The lower K_m value and the higher V_{max} for 5β-cholestane-3α,7α,12α-triol compared to 5β-cholestane-3α,7α-diol seem to be important factors for the regulation mechanism that keeps the ratio of cholic acid/chenodeoxycholic acid constant in rat bile.

ENHANCED THERMOGENESIS AND DIMINISHED DEPOSITION OF FAT IN RESPONSE TO OVERFEEDING WITH DIET CONTAINING MEDIUM CHAIN TRIGLYCERIDE. N. Baba, E.F. Bracco, and S.A. Hashim (Dept. of Medicine, St. Luke's-Roosevelt Hospital Center and Institute of Human Nutrition Columbia Univ. College of Physicians and Surgeons, New York, NY) *Am. J. Clin. Nutr. 35*(4):678-682 (1982). The mechanism whereby overfeeding with diet containing medium chain triglyceride (MCT) results in diminished body weight and fat was studied. Fifteen male Sprague-Dawley rats were fitted under anesthesia with gastrostomy tubes and divided into two groups. One group was fed MCT diet, the other an isocaloric diet containing long chain triglyceride (LCT) in excess (150%) of spontaneous calorie intake. Both diets, fed for 6 wk, derived 50% of calories from fat. Basal and norepinephrine (25 μg/100 g) stimulated O_2 consumption and CO_2 production, as well as metabolic rate were measured. After the rats were killed, total dissectable fat and fat cell size and number were determined. MCT rats gained 15% less weight than LCT controls ($p<0.001$). Total dissectable fat was significantly lower ($p<0.001$) in MCT group, as was mean adipocyte size ($p<0.001$). Resting and maximal norepinephrine-stimulated O_2 consumptions were 39.7 and 22.1% higher in MCT than in LCT group, respectively. Resting and norepinephrine-stimulated metabolic rates were 38.8 and 22.2% higher in MCT than LCT fed rats, respectively. Overfeeding MCT diet results in decreased body fat related to increased metabolic rate and thermogenesis.

STUDIES ON THE BIOSYNTHESIS OF THE OOGONIOLS. S.E. Barrow, T.C. McMorris (Dept. of Chem. D-006, Univ. of Calif.-San Diego, La Jolla, CA 92093) *Lipids 17*:383-389 (1982). In feeding experiments with *Achlya heterosexualis*, [3-^{3}H] fucosterol was efficiently incorporated into oogoniols possessing an unsaturated side chain as well as those with a standard side chain (clionasterol skeleton). [23,25-^{3}H]-29-Hydroxyfucosterol was also efficiently incorporated into the oogoniols and its role as an intermediate in the biosynthesis was confirmed by a trapping experiment. This indicated the presence of a small pool of endogenous 29-hydroxyfucosterol in the mycelium. [23,25-^{3}H]-29-Oxofucosterol was also well incorporated into the oogoniols and it is probably an intermediate in the biosynthesis. It was found to be converted to 29-hydroxyfucosterol in a trapping experiment. Reduction of the C-24(28) double bond make take place after all the functional groups have been introduced, at C7, C-11, and C-15, in the tetracyclic structure.

LOW DENSITY LIPOPROTEIN METABOLISM BY CULTURED SKIN FIBROBLASTS FROM ATHEROSCLEROTIC PATIENTS. R.G. Behrman and V. Wynn (The Alexander Simpson Laboratory for Metabolic Research, St. Mary's Hospital, London, W2, Great Britain) *Atherosclerosis 42*:173-184 (1982). The aim of this study was to determine whether an abnormality in low density lipoprotein (LDL) metabolism could be demonstrated in fibroblasts cultured from normolipidaemic subjects with atherosclerosis. Seventeen male subjects aged 30-55 years with normal plasma lipid concentrations were divided into 2 groups on the basis of the presence or absence of proven coronary artery and/or peripheral vascular disease. LDL metabolism was assessed in cultured fibroblasts obtained from each of these subjects. After 6 hr incubation with ^{125}I-labeled LDL, it was found that binding, uptake and degradation of the lipoprotein were all significantly higher in cells from the atherosclerotic group of subjects than the controls. Variations in cellular LDL metabolism were also correlated with 4 risk factors for cardiovascular disease. Plasma LDL concentration in the atherosclerotic subjects was found to be inversely related to LDL binding and degradation. Subject age was inversely related to LDL degradation in both groups of subjects. No association was demonstrated in either group of subjects between LDL metabolism and glucose intolerance, or between LDL metabolsim and cigarette smoking. It is concluded from these results that cellular LDL binding may constitute a factor in determining

the rate of atheroma formation, which is independent of other cardiovascular risk factors.

CHOLESTATRIENE AND ERGOSTATETRAENE AS IN VIVO AND IN VITRO MEMBRANE AND LIPOPROTEIN PROBES. R.J. Bergeron and J. Scott (Dept. of Medicinal Chemistry, J. Hillis Miller Research Center, Univ. of Florida, Gainesville, FL 32610) *J. Lipid Res. 23*(3):391-404 (1982). The fluorescent cholesterol analogues, cholesta-5,7,9(11)triene-3-β-ol (I) and ergosta-5,7,9(11)-22-tetraene-3-β-ol (II), have been shown to be readily incorporated by various tissues and lipoproteins in rabbits maintained on diets supplemented with these fluorophores. Human erythrocytes and lipoproteins were also found to incorporate I and II in vitro under physiological conditions. The thermotropic behavior of the lipoproteins and erythrocyte membranes labeled with sterols I and II was evaluated using temperature-dependent fluorescence polarization and/or fluorescence intensity spectra. Erythrocyte ghosts, fluorescently labeled in vivo (rabbit) or in vitro (rabbit and human), were found to undergo a reversible thermally induced transition at 24±2 C. A similar transition occurring at higher temperatures was also observed in fluorescently labeled human and rabbit LDL particles. Furthermore, the transition temperatures and relative microviscosities of the in vivo labeled rabbit LDL particles were found to be dependent upon the amount of sterol present in the rabbits' diet. No evidence of a similar thermotropic transition was observed in any of the HDL particles. These results are discussed in terms of a thermotropic reordering of cholesterol cluster existing in the erythrocyte membrane and of the cholesteryl ester core present within the low density lipoprotein particle.

EFFECTS OF DIABETES AND HIGH FAT-HIGH CHOLESTEROL DIET ON PLASMA LIPID LEVELS AND OR ERYTHROCYTE MEMBRANE COMPOSITION. R. Bhandaru, S.R. Srinivasan, B. Radhakrisnamurthy and G.S. Berenson (Depts. of Medicine and Biochemistry, Louisiana State Univ. Medical Center, New Orleans, LA 70112) *Atherosclerosis 42*(2,3):263-272 (1982). Erythrocyte membrane composition was studied in rats subjected to experimental hyperlipidemia and/or hyperglycemia by means of 6 weeks of high fat (40% w/w)-high cholesterol (5% w/w) diet with and without 8 weeks of streptozotocin-induced diabetes. High fat-high cholesterol diet lowered plasma glucose levels in control and in diabetic animals. While the atherogenic diet produced only hypercholesterolemia, the same diet fed to diabetic animals produced both hypercholesterolemia and hypertriglyceridemia. The membrane protein content was lower in diabetic rats than in controls, while the cholesterol and phospholipids were higher in erythrocyte membranes. Feeding the atherogenic diet increased membrane lipid levels in only nondiabetic animals. The total carbohydrate content of the membranes was greater in diabetic animals than controls. Difference in relative proportion of individual sugars, e.g., galactose, mannose, glucose, and fucose of the membranes were observed between diabetic and control groups. These observations suggest that rat erythrocyte membrane composition is altered both in hyperglycemic and hyperlipidemic conditions, and may provide a useful model for evaluating lipid-carbohydrate abnormalities of membrane structures in diabetes mellitus.

METABOLISM OF VERY LONG-CHAIN MONOUNSATURATED FATTY ACIDS (22:1) AND THE ADAPTION OF THEIR PRESENCE IN THE DIET. J. Bremer and K.R. Norum (Institute of Med. Biochem., Univ. of Oslo, Oslo, Norway) *J. Lipid Res. 23*:243-256 (1982). Unadapted rats and other animal species have a limited capacity to metabolize monounsaturated fatty acids with 22 carbons (22:1). Excess amounts in the diet of fats containing these fatty acids cause a transient accumulation (lipidosis) of triacylglycerol in the heart and other tissues but not in the liver, which seems to export the 22:1 fatty acids as very low density lipoproteins to the blood plasma. The acute lipidosis most probably is explained by a slow oxidation of 22:1 acyl-CoA by the mitochondrial acyl-CoA dehydrogenase combined with an inhibitory effect of this CoA ester on the oxidation of acyl-CoA esters of a more "normal" chain length. Other fatty acid metabolizing enzymes also show slow reaction rates with the 22:1 fatty acids. Upon continued feeding of diets with 22:1 fatty acids, an adaption takes place and the lipidosis disappears. This adaption coincides with the development of an increased capacity to chain-shorten the 22:1 fatty acids, especially in the liver, but also in the heart. The chain-shortening seems to be due to a partial β-oxidation of the 22:1 fatty acids by the peroxisomal β-oxidation enzyme system which shows an increased activity in adapted rats. In such rats, less 22:1 fatty acids circulate in the plasma very low density lipoproteins than in unadapted rats. The drug clofibrate which induces increased activity of the peroxisomal β-oxidation enzymes, provides partial protection against the lipidosis in unadapted animals. Hydrogenated fish oil is more efficient as an inducer of the chain-shortening of erucic acid in the liver than is rapeseed oil, which contains only one 22:1 fatty acid isomer and no fatty acids with *trans* bonds. The hydrogenated fish oil causes less lipidosis than does rapeseed oil when diets containing the same amount of 22:1 fatty acids are fed.

PHOSPHOLIPID SYNTHESIS IN *S. CEREVISIAE* STRAIN GL7 GROWN WITHOUT UNSATURATED FATTY ACID SUPPLEMENTS. T.M. Buttke, R. Reynolds, A.L. Pyle (Dept. of Microbiol., Univ. Med. Center, 2500 North State St., Jackson, MS 39216) *Lipids 17*:361-366 (1982). In the absence of exogenous unsaturated fatty acids (UFA), *Saccharomyces cerevisiae* strain GL7 synthesizes low levels of UFA and large amounts of decanoic and tetradecanoic fatty acids. Supplementation with hemin leads to slightly higher levels of UFA, but synthesis of the medium-chain saturated fatty acids (SFA) continues. Under these conditions of limited UFA availability, strain GL7 incorporates most of its UFA into phosphatidylethanolamine (PE), whereas phosphatidylcholine (PC) and phosphatidylserine + phosphatidylinositol (PS + PI) are enriched with the medium-chain SFA. The association of specific fatty acids with the various phospholipids is not accompanied by changes in the proportions of newly synthesized phospholipids, demonstrating that the fatty acid composition of PE can be modulated independently of the other phospholipids. The effect of sterol structure on the fatty acid composition of cells grown with limiting UFA was also examined. Yeast cells grown with either ergosterol or stigmasterol contained less UFA and more medium-chain SFA in their phospholipids than did cholesterol-grown cells, suggesting that the former sterols allow strain GL7 to grow with a lower UFA content.

COPPER(II)-CATALYZED LIPID PEROXIDATION IN LIPOSOMES AND ERYTHROCYTE MEMBRANES. P.C. Chan, O.G. Peller, and L. Kesner (Dept. of Biochem., State Univ. of New York Downstate Med. Center, Brooklyn, NY 11203) *Lipids 17*(5):331-337 (1982). Cu^{++} was uniquely capable of catalyzing the peroxidation of erythrocyte membrane lipid in the presence of 10 mM H_2O_2, whereas several other transition metal ions were without significant effect. In contrast, peroxidation of soybean phospholipid liposomes could be catalyzed with decreasing efficiency by Co^{++}, Cu^{++}, Pb^{++}, or Cr^{+++} also in the presence of H_2O_2. The effect of imidazole on Cu^{++}-catalyzed lipid peroxidation was stimulatory in liposomes and inhibitory in membrane preparations, whereas, EDTA, histidine, citrate and alanine inhibited peroxidation in both systems. EDTA could stop the peroxidation after initiation, but catalase could not, indicating that Cu^{++} alone was necessary for the propagation of the chain reaction. Competitive inhibition studies with various scavengers of hydroxyl radicals or singlet oxygen and the absence of significant reaction enhancement by D_2O indicated that neither of these reactive oxygen species was a major mediator in the Cu^{++}-H_2O_2 oxidative system. A copper-oxygen complex may be directly involved in the initiation of peroxidation. Normal erythrocyte membranes and phospholipid liposomes also differ in their sensitivities toward external oxidative stress. In the absence of H_2O_2, Cu^{++} (0.2 mM) was capable of catalyzing lipid peroxidation in liposomes, aged erythrocyte membranes from vitamin-E-deficient rats; however, freshly prepared membranes from control rats and liposomes containing α-tocopherol required H_2O_2 greater than 2 mM for the catalytic effect of Cu^{++} to be observed.

IN VIVO FLUXES OF PLASMA CHOLESTEROL, PHOSPHATIDYLCHOLINE AND PROTEIN INTO MINI-PIG AORTIC AND PULMONARY SEGMENTS. S. Christensen, S. Stender, O. Nyvad, and H. Bagger (Dept. of Physiology, Univ. of Aarhus, DK-8000 Aarhus C and Dept. of Clinical Chemistry CL, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen (Denmark)) *Atherosclerosis 41*(2/3):309-319 (1982). Levels of radioactive cholesterol found in the arterial wall after a few hours' in vivo exposure to plasma containing labeled cholesterol are so small that the contaminated plasma in the tissue may contribute significantly to the radioactivity measured in the wall. By the simultaneous use of [^{3}H]- and [^{14}C]-cholesterol the contamination was found to be less than 15 nl of plasma/cm^2 of intimal surface of the thoracic aorta in mini-pigs, and this contamination accounted for less than 5% of the total radioactivity found in the intima-media tissue 7 hr after the injection of serum with bioincorporated labeled cholesterol. The intimal clearances as calculated for labeled plasma cholesterol were about 500, 200, 100, and 50 nl cm^{-2}h^{-2} for pulmonary trunk, aortic arch, proximal and distal thoracic aorta, respectively. The concomitantly measured intimal clearances of plasma [^{32}P] phosphatidylcholine were about 1.1 times those for plasma cholesterol for the 4 segments. This suggests that the appearance of labeled plasma phosphatidylcholine and of cholesterol in the intima-media is essentially a consequence of a lipoprotein influx. Similarly, the intimal clearances of plasma [^{35}S] albumin for the same 4 segments were about 1.5 times those of the labeled lipids, suggesting a nonspecific mechanism for the transfer of plasma lipoproteins into the artery. The intimal clearances of [^{35}S] albumin were within the same order of magnitude as capillary clearance values for albumin reported for mammalian tissues.

EFFECTS OF ETHANOL METABOLISM ON OXIDOREDUCTION AND INTERMOLECULAR HYDROGEN TRANSFER AT C-17 IN STEROID 3-SULPHATES IN VIVO. Tomas Cronholm and Ulf Rudqvist (Dept. of Physiological Chem., Karolinska Institutet, S-104 01 Stockholm, Sweden) *Biochem. Biophys. Acta 711*:159-165 (1982). Steroid sulphates were infused intravenously in female rats, and metabolites were isolated from bile. Infused 3β-hydroxy-5α-androstan-17-one 3-sulphate was excreted together with 5α-androstane-3β,17β-diol disulphate, which formed a larger part after ethanol administration. Results from infusions of the 3-sulphates of 5α-[17α-^{2}H]androstane-3β,17β-diol and 3β-hydroxy-5α-[2,2,4,4-$^2H_4$]-androstan-17-one indicated that ethanol decreased the extent of transfer of the 17α-deuterium and increased the reduction of 17-oxosteroid without affecting the oxidation of 17β-hydroxysteroid. Ethanol metabolism decreased the deuterium transfer from [17α-^{2}H] estradiol 3-sulphate to C-17 of 3β-hydroxy-5α-androstan-17-one 3-sulphate. The results indicate that NADH from ethanol metabolism increased the concentration of oxidoreductase-NADH complex without affecting the corresponding complex with NAD^+. The effects of ethanol on steroid reduction were dependent on the initial redox state of the enzyme-coenzyme complex. This redox state was modified by substrates for the enzyme, indicating slow dissociation of the complex. Thus, ethanol metabolism may interfere with the interactions between steroid oxidoreductions.

CONFORMATIONAL TRANSITIONS IN SERUM HDL APOPROTEINS OF HYPERLIPIDAEMIC RABBITS. S. Dhawan, S. Nityanand, N.K. Kapoor and S. Singh (Central Drug Res. Inst., Lucknow 226 001) *Indian J. Biochem. Biophys. 18*(5):326-328 (1981). Conformational transitions in serum high desnity apoplipoproteins of normal and hyperlipidaemic rabbits have been studied by circular dichroism. The results show that these differences are at the level of secondary structure of the hyperlipemic proteins and are sensitive to the effect of pH and feeding cholesterol.

RATE OF LCAT-MEDIATED CHOLESTEROL ESTERIFICATION AND SERUM LIPIDS DURING ETIROXATE THERAPY IN HYPERLIPOPROTEINEMIA. M. Dobiasova, K. Vondra, V. Matousek and J. Valek (Institute of Nuclear Biology and Radiochemistry, Czechoslovak Academy of Sciences and Institute for Clinical and Experimental Medicine, Prague (Czechoslovakia)) *Atherosclerosis 42*(2,3):251-261 (1982). Changes in the rate of the plasma cholesterol ester production mediated by lecithin:cholesterol acyltransferase (LCAT, E.C. 2.3.1.43) were examined in 15 patients suffering from types II and IV HLP who had been treated for 14 weeks with etiroxate. Whereas the plasma cholesterol concentration decreased significantly only in the initial phase of the therapy, the rate of cholesterol esterification increased gradually and attained at the end of the study a value exceeding by 50% the initial level. The final fractional turnover rate nearly equalled that characteristic for the control group of healthy subjects, in spite of the fact that the concentration of plasma cholesterol in the diseased subjects was higher by 50-100%. Triglyceride concentration decreased only transitorily in the course of the therapy with etiroxate. It is concluded that etiroxate is likely to normalize the rate of cholesterol turnover in the endogenous pool.

COMPARISON OF BILE ACID SYNTHESIS DETERMINED BY ISOTOPE DILUTION VERSUS FECAL ACIDIC STEROL OUTPUT IN HUMAN SUBJECTS. W.C. Duane, D.E. Holloway, S.W. Hutton, P.J. Corcoran, and N.A. Haas (Dept. of Med., Veterans Administration Med. Center, Minneapolis, MN 55417) *Lipids 17*:345-348 (1982). Fecal acidic sterol output has been found to be much lower than bile acid synthesis determined by isotope dilution (*J. Lipid Res.* 17:77, 1976). Because of this confusing discrepancy, we compared these 2 measurements done simultaneously on 13 occasions in 5 normal volunteers. In contrast to previous findings, bile acid synthesis by the Lindstedt isotope dilution method averaged 16.3% lower than synthesis simultaneously determined by fecal acidic sterol output (95% confidence limit for the difference -22.2 to -10.4%). When one-sample determinations of bile acid pools were substituted for Lindstedt pools, bile acid synthesis by isotope dilution averaged 5.6% higher than synthesis by fecal acidic sterol output (95% confidence limits -4.9 to 16.1%). These data indicate that the 2 methods yield values in reasonably close agreement with one another. If anything, fecal acidic sterol outputs are slightly higher than synthesis by isotope dilution.

GLYCEROL KINASE ACTIVITY AND GLYCEROL METABOLISM OF RAT GRANULAR PNEUMOCYTES IN PRIMARY CULTURE. Aron B. Fisher and Avinash Chander (Dept. of Physiology, Schl. of Med., Univ. of Pennsylvania, Philadelphia, PA 19104, U.S.A.) *Biochim. Biophys. Acta 711*:128-133 (1982). Glycerol kinase activity and glycerol utilization by rat granular pneumocytes were determined in order to investigate the rate-limiting step for glycerol incorporation into lung lipids. Granular pneumocytes were isolated in primary culture following trypsinization of rat lungs. Glycerol kinase activity was 8.2 nmol/h per 10^6 cells. Incorporation of [1,3-^{14}C] glycerol into total cell lipids was 0.29 nmol/hr per 10^6 cells. In the presence of saturating glycerol concentrations, production of ^3H_2O from [2-^{3}H] glycerol was 13 times greater than incorporation of [^{14}C] glycerol into lipids. Glycerol phosphate dehydrogenase activity in isolated cells was approximately 10 times glycerol kinase activity. In the presence of 5.6 mM glucose, glycerol incorporation into lipids was decreased 79% and detritiation of glycerol was decreased 34%. This effect of glucose was due to a 25% increase in cell glycerol 3-phosphate content, resulting in dilution of the precursor pool and possible inhibition of glycerol phosphorylation. These results indicate that the relatively limited incorporation of glycerol into surfactant phospholipids by lung epithelial cells reflects the relatively high rate of glycerol 3-phosphate oxidation.

SERUM LOW DENSITY LIPOPROTEINS WITH MITOGENIC EFFECT ON CULTURED AORTIC SMOOTH MUSCLE CELLS. G.M. Fless, T. Kirchhausen, K. Fischer-Dzoga, R.W. Wissler, and A.M. Scanu (Dept. of Medicine, Biochem. and Pathology, Univ. of Chicago, Pritzker School of Medicine, Chicago, IL 60637) *Atherosclerosis 41*(2/3):171-183 (1982). Low density lipoprotein (LDL) subspecies of different size and lipid mass were isolated by density gradient ultracentrifugation from the serum of male rhesus monkeys (*Macaca mulatta*) fed both low fat, low cholesterol commerical primate ration, and cholesterol-supplemented high-fat diets, as well as from the serum of human donors. The mitogenic effect of these lipoproteins was examined using primary cultures of rhesus aortic smooth muscle cells. The results indicated that both hyperlipidemic and normal sera (both human and rhesus) contain mitogenic LDL species although in different amounts. LDL-III, the rhesus equivalent of human Lp(a) was not mitogenic despite its similarity in size and lipid composition to the stimulating particles. However, on the removal of most of its large sialic acid moiety, a clear mitogenic action was observed. The mechanisms responsible for the proliferative effect are unclear and may involve LDL mass, lipid composition, and surface charge although other speculations cannot at present be ruled out. Furthermore, since the small LDL subspecies of either rhesus or human origin were nonmitogenic and similar in mass to the LDL found in calf serum, the mitogenic response of the smooth muscle cells to large LDLs may depend on their early conditioning with the LDL of calf serum.

DIETARY CHOLESTEROL AND THE PLASMA LIPIDS AND LIPOPROTEINS IN THE TARAHUMARA INDIANS: A PEOPLE HABITUATED TO A LOW CHOLESTEROL DIET AFTER WEANING. M.P. McMurry, W.E. Connor, and M.T. Cerqueira (Div. of Endocrin. -Metab. -Nutr., Dept. of Med., and the Clin. Res. Ctr., Univ. of Oregon Health Sci. Ctr., Portland, OR, 97201) *Am. J. Clin. Nutr. 35*(4):741-744 (1982). Eight Tarahumara Indian men participated in a metabolic study to measure the responsiveness of their plasma cholesterol levels to dietary cholesterol. They were fed isocaloric cholesterol-free and high cholesterol diets containing 20% fat, 15% protein, and 65% carbohydrate calories. On admission to the study, the Tarahumaras had a low mean plasma cholesterol concentration (120 mg/dl), reflecting their habitual low cholesterol diet. After 3 wk of a cholesterol-free diet their cholesterol levels were 113 mg/dl. The men were then fed a high cholesterol diet (1000 mg/day) which increased the mean total plasma cholesterol to 147 mg/dl ($p<0.01$) and also increased the low-density lipoprotein cholesterol concenteation. Tarahumaras, habituated to a low cholesterol diet after weaning, had the typical hypercholesterolemic response to a high cholesterol diet that has been previously observed in subjects whose lifelong diet was high in cholesterol content.

DIURNAL VARIATION OF CHOLESTEROL PRECURSORS SQUALENE AND METHYL STEROLS IN HUMAN PLASMA LIPOPROTEINS. T.A. Miettinen (Second Dept. of Med., Univ. of Helsinki, 00290 Helsinki 29, Finland) *J. Lipid Res. 23*(3)466-473 (1982). Animal cholesterol synthesis shows a marked diurnal variation, a phenomenon, at the moment, not known to occur in man. Since cholesterol precursors in serum reflect overall cholesterol synthesis in many conditions, a 24 hr profile of squalene and methyl sterols was studied in plasma lipoproteins in order to demonstrate whether these cholesterol precursors could exhibit a diurnal cycling in healthy human subjects. It was found that for different methyl sterols the mean diurnal variation was 3.5- to 6.9-fold in LDL, 2.0- to 4.5-fold in HDL, and 2.6- to 3.6-fold in the density class < 1.006 g/ml. The respective values for squalene were 2.2, 1.4, and 2.9. Esterified methyl sterols varied slightly in the density class < 1.006 g/ml only, and the percentage esterification exhibited a diurnal fluctuation that was the reciprocal of that of free methyl sterol levels. The rapid and marked diurnal fluctuation of squalene and free methyl sterols in plasma lipoproteins suggests that these precursors are metabolized on and off lipoproteins. The variation is most likely caused by changed in cholesterol synthesis, inferring that circadian

rhythm also regulates human cholesterol production.

SIDE-CHAIN OXIDATION OF LIPOPROTEIN-BOUND [24,25-^{3}H] CHOLESTEROL IN THE RAT: COMPARISON OF HDL AND LDL AND IMPLICATIONS FOR BILE ACID SYNTHESIS. L.K. Miller, M.L. Tiell, I. Paul, T.H. Spacet, and R.S. Resenfeld (Institute for Steroid Res. and the Div. of Hematology, Montefiore Hosp. and Med. Center and Dept. of Biochem., Albert Einstein College of Med., Bronx, NY 10467) *J. Lipid Res. 23*(2):344-355 (1982). The purpose of the study was to test the hypothesis that high density lipoprotein (HDL) cholesterol would be more easily oxidized in vivo than low density lipoprotein (LDL) cholesterol. Homologous plasma was incubated with [24,25-^{3}H] cholesterol and fractionated by ultracentrifugation to obtain HDL and LDL each labeled with [^{3}H] free sterol. HDL and LDL labeled with [24,25-^{3}H] cholesteryl esters were prepared by ultracentrifugation of plasma from donor rats injected 24 hr previously with [24,25-^{3}H] cholesterol in propylene glycol. These four labeled lipoproteins were administered to recipient rats. It was found that more tritium oxide (^3H_2O) was produced after the HDL doses than after the corresponding LDL doses, from 2-3 -fold more when lipoprotein free cholesterol was labeled and from 2-6 -fold more when lipoprotein cholesteryl esters were labeled. More ^3H_2O was produced from free cholesterol-labeled lipoproteins than from cholesteryl ester-labeled lipoproteins. Since oxidation of cholesterol is measure of bile acid formation, it is concluded that under the conditions of the study HDL-cholesterol is a better precursor of the bile acids than the LDL-cholesterol.

FATTY ACID OXIDATION OF RAT BRAIN MICROVESSELS IN HYPERTENSION, AGING AND EXPERIMENTAL DIABETES. N. Morisaki, Y. Saito, A. Kumagai (Second Dept. of Internal Med., Schl. of Med., Chiba Univ., Chiba, Japan) *Atherosclerosis 42*:221-227 (1982). Microvessels were prepared from rat brain and their fatty acid oxidation was investigated. This activity was much higher in brain microvessels than in other vessels or organs, suggesting that brain microvessels have a high capacity for energy production. The activity was decreased in some pathological conditions, such as hypertension, aging and diabetes mellitus. The relationship between changes in fatty acid oxidation activities and injuries of brain microvessels is discussed.

CHARACTERIZATION AND QUANTITATIVE DETERMINATION OF GANGLIOSIDES AND NEUTRAL GLYCOSPHINGOLIPIDS IN HUMAN LIVER. O. Nilsson and L. Svennerholm (Dept. of Psychiatry and Neurochemistry, St. Jörgen's Hospital, Univ. of Göteborg, S-422 03 Hisings Backa, Sweden) *J. Lipid Res. 23*(2): 327-334 (1982). The neutral and acidic glycolipids from the liver of an 11-year-old male were quantitatively isolated and characterized. The total concentration of gangliosides was also determined in samples from five other human livers. Lipid-bound sialic acid varied between 190-248 nmol/g with a mean value of 212 nmol/g. The major ganglioside was G_{M3}, which represented 91.6% of the sialic acid. Besides G_{M3} and G_{M1}, a wide variety of other minor monosialogangliosides of the gangliotetraose series with up to four sialic acids were demonstrated in human liver for the first time. The composition of the ceramide portion of the gangliotetraose gangliosides was considerably different from that of the "visceral" gangliosides, G_{M3}, G_{D3}, and L_{M1} (sialosyl-lactonerotetrasyl-ceramide), which suggests that these two groups of gangliosides are biosynthesized in two different pools. The concentration of the neutral glycolipids was approximately the same as that of the gangliosides. Lactosylceramide was the largest fraction closely followed by galactosylceramide, glucosylceramide, and globotriaosylceramide. The ceramide composition of the neutral glycolipids resembled that of the "visceral" gangliosides, suggesting that they are metabolically related. 2-Hydroxy fatty acids were found in glucosyl-, galactosyl, and lactosylceramides as well as in ganglioside G_{M3}.

DOSE-RESPONSE STUDY OF THE EFFECT OF CIPROFIBRATE ON SERUM LIPOPROTEIN CONCENTRATIONS IN HYPERLIPOPROTEINAEMIA. A.G. Olsson, L. Oro (King Gustaf V Res. Inst. and Depts. of Med. at Karolinska Hosp. and Ersta Hosp., Stockholm, Sweden) *Atherosclerosis*, 42:229-243 (1982). The effect of ciprofibrate, 2[*p*-(2,2-dichlorocyclopropyl)-phenoxyl]-2-methyl propionic acid, in daily doses of 50, 100 and 200 mg was studied in 50 patients with hyperlipoproteinaemia (21 type IIA, 10 type IIB and 19 type IV). Ciprofibrate was convenient to take and was without subjective side effects. The greatest hypolipidaemic effects were reached for all lipoproteins with 200 mg daily. In type IIA and IIB, mean low density lipoprotein (LDL) cholesterol was normalized on the 200 mg dose. The effect was highly dependent on initial LDL cholesterol concentrations, decreases being observed above 4 mmol/l and increases below that concentration. Mean very low density lipoprotein (VLDL) triglyceride concentrations decreased on 200 mg per day by 48-59%. HDL cholesterol increased in all types of hyperlipoproteinaemia by 6-19%, the change being unrelated to changes in VLDL lipids. With a dosage of 200 mg daily the effects were maintained for the following period of 6 months. It is concluded from this study that it would be appropriate to start patients on 100 mg daily and then titrate their dose according to response. The optimal dosage for ciprofibrate seems to be 200 mg daily.

DIFFERENT KINETIC FATES OF APOLIPOPROTEINS A-I AND A-II FROM LYMPH CHYLOMICRA OF NONHUMAN PRIMATES. EFFECT OF SATURATED VS. POLYUNSATURATED DIETARY FAT. J.S. Parks and L.L. Rudel (Dept. of Comparative Medicine, Bowman Gray School of Med., Wake Forest Univ. Winston-Salem, NC 27103) *J. Lipid Res. 23*(3):410-421 (1982). Monkeys fed polyunsaturated fat had lower plasma cholesterol and high density lipoprotein (HDL) mass concentrations than animals fed saturated fat. Plasma apoA-I and apoA-II concentrations also were lower in the group fed polyunsaturated fat. In vivo reinjection studies, using thoracic duct lymph chylomicra labeled with ^{131}I and HDL labeled with ^{125}I, were done in order to study the mechanism of plasma HDL-lowering by polyunsaturated dietary fat. The peak specific activity (SA) of HDL apoA-I derived from ^{131}I-labeled chylomicra occurred at 3 hr after injection and then an exponential decay occurred indicative of a precursor-product relationship between chylomicron apoA-I and HDL apoA-I. HDL apoA-II derived from ^{131}I-labeled chylomicra had no early SA increase and began to die away immediately after injection. Labeled apoA-I from chylomicron and HDL origin had similar plasma fractional catabolic rates; apoA-II from chylomicron or HDL origin also had similar FCR, which were significantly shorter than those for HDL apoA-I. There was a consistent trend toward a higher FCR for HDL apoA-I or A-II of polyunsaturated fat-fed recipients. Chylomicron apoA-I/triglyceride and apoA-II/triglyceride mass ratios were lower in polyunsaturated fat-fed animals vs. saturated fat-fed animals. It was concluded that: dietary polyunsaturated fat lowered plasma cholesterol, HDL and apoA-I concentrations; the HDL-lowering effect of the dietary polyunsaturated fat may be due to the combined effects of decreased apoprotein production by the intestine and increased HDL catabolism; and in the blood, chylomicron apoA-I and A-II differ in their fates.

DISTRIBUTION OF 25-HYDROXYCHOLESTEROL IN PLASMA LIPOPROTEINS AND ITS ROLE IN ATHEROGENESIS. A STUDY IN SQUIRREL MONKEYS. S.K. Peng, C.B. Taylor, E.H. Mosbach, W.Y. Huang, J. Hill, and B. Mikkelson (Lab. Service and the Res. Service, Albany VA Med. Center and Dept. of Pathology, Albany Med. College, Albany, NY 12208) *Atherosclerosis 41*(2/3):395-402 (1982). Oxidation products of cholesterol have been shown to be potent inhibitors of cholesterol biosynthesis and also highly toxic to cultured aortic smooth muscle cells. In rabbit experiments, these compounds produced arterial injury resulting in arteriosclerosis. Purified cholesterol only minimally inhibited cholesterol biosynthesis and had no effect on cultured aortic smooth muscle cells. This raises the possibility that plasma lipoproteins containing β-apoprotein (i.e. LDL and VLDL), which are considered to be atherogenic, may carry more oxidation products than HDL which is not atherogenic [^{3}H]-25-hydroxycholesterol and [^{14}C] cholesterol were given orally to 10 squirrel monkeys (*Saimiri sciureus*) and blood samples were collected via femoral puncture 24 hr after administration. Lipoproteins were separated by ultracentrifugation and the radioactivity in each fraction was counted. Results show that the distribution of labeled cholesterol in VLDL, LDL, and HDL was almost identical to that of unlabeled cholesterol. Most of the radio-activity of 25-hydroxycholesterol was located in LDL & VLDL (55.1% and 34.7%, respectively), only 10.2% was present in HDL. If the radioactivity of 25-hydroxycholesterol were calculated on the basis of the apoprotein content of the lipoprotein micelle, the relative capacity of VLDL and LDL to carry 25-hydroxycholesterol was even greater and more significant than that of HDL (90 X and 42X respectively).

LINKAGE OF THE ISOPRENOID BIOSYNTHETIC PATHWAY WITH INDUCTION OF DNA SYNTHESIS IN MOUSE LYMPHOCYTES. EFFECTS OF COMPACTIN ON MITOGEN-INDUCED LYMPHOCYTES IN SERUM-FREE MEDIUM. Sherrie L. Perkins, Suzanne F. Ledin and John D. Stubbs (Program in Cell and Molecular Biol., Dept. of Biol. Science, San Francisco State Univ., San Francisco, CA 94132, U.S.A.) *Biochim. Biophys. Acta 711*:83-89 (1982). Concanavalin A induction of DNA synthesis in mouse spleen lymphocytes cultured in serum-free medium was shown to be very sensitive to inhibition by compactin (ML-236B), a specific competitive inhibitor of hydroxymethylglutaryl-CoA reductase. As low as 0.1 μM compactin could give 98% inhibition of mitogen induction of a $5 \cdot 10^6$ cells/ml culture. This inhibition could be reversed completely by addition of exogenous mevalonate, but could not be reversed by either exogenous cholesterol or isopentenyladenine. Oxygenated sterol inhibition of mitogen-induced DNA synthesis could be reversed by cholesterol or by mevalonate, whereas cyclic AMP inhibition could not be reversed by either compound. These results

suggest that endogenous cholesterol production is a necessary but not sufficient factor co-ordinated with mitogen-induced DNA synthesis, and that the presence of some additional product of mevalonate metabolism is involved also. Isopentenyladenine, though, did not have a significant effect on alleviating any of the above inhibitions. Since mevalonate could not relieve cyclic AMP inhibition, but couls overcome compactin inhibition, cyclic AMP inhibition cannot be explained as due only to blockage of mevalonate production.

ACYL AND PHOSPHORYL MIGRATION IN LYSOPHOSPHOLIPIDS: IMPORTANCE IN PHOSPHOLIPID SYNTHESIS AND PHOSPHOLIPASE SPECIFICITY. A. Plüchthun and E.A. Dennis (Dept. of Univ. of California at San Diego, La Jolla, CA 92093) *Biochemistry 21*(8):1743-1750(1982). Three isomeric lysophosphatidylcholines have been prepared by the action of phospholipase A_2 or lipase on 1,2-di-palmitoyl-*sn*-glycero-3-phosphorylcholine or phospholipase A_2 on 1,3-dipalmitoyl-*sn*-glycero-2-phosphorylcholine. The structures of the lyso compounds have been confirmed by a complete assignment of the polar head groups using ^{1}H NMR spectroscopy. The product of phospholipase A_2 action on phosphatidylcholine is 1-acyl-*sn*-phorylcholine. Acyl migration between this compound and the 2-acyl isomer and 2-phosphoryl isomer were followed by ^{31}P NMR. The acyl migration was found to be first order in both lysophospholipid and acid or base with a base-catalyzed second-order rate constant of about 4×10^{-4} $M^{-1} s^{-1}$. At alkaline pHs, the equilibrium mixture contains about 90% of the 1-acyl and about 10% of the 2-acyl isomer. A slow acyl migration also occurs in organic solvents, most notably in the presence of basic catalysts used in common acylation procedures for the synthesis of phospholipids from lysophospholipids. At alkaline pHs, no phosphoryl migration was detected in the time scale of acyl migration and hydrolysis. ^{31}P NMR could also directly demonstrate the positional specificity of phospholipase A_2 and lipase, which acts as a phospholipase A_1, by direct observation of the products formed under conditions where migration was slow. While it is well-known that phospholipase A_2 is specific for the *sn*-2 positiosn of phospholipids in micelles and bilayer membranes, it was demonstrated by this technique that this specificity also holds for the monomeric phospholipid dibutyrylphosphatidylcholine.

CHARACTERIZATION OF UNUSUAL INTERMEDIATE DENSITY LIPOPROTEINS. D.L. Puppione, S.T. Kunitake, R.L. Hamilton, M.L. Phillips, V.N. Schumaker and L.D. Davis (Dept. of Chem. an the Molecular Biology Institute, Univ. of California, L.A., CA 90024). *J. of Lipid Res. 23*(2):283-290 (1982). We report on the physicochemical properties of unusual lipoproteins isolated from both lymph and blood of ruminating cattle. The densities of most of these particles fall within the range between 1.006 and 1.020 g/ml, although densities of 0.97-0.99 g/ml are calculated from chemical composition, assuming a liquid core. The triglycerides of these particls have a high content of saturated fatty acids. The major apoprotein has a mobility on polyacrylamide-SDS gels consistent with a molecular weight of 40,000. The negatively-stained particles appear flattened and asymmetric in electron micrographs. The particles are very large, with molecular weights in the 20 to 250 millions dalton range, and they scatter light strongly. The hydrodynamic frictional ratio is about 1.4, consistent with oblate ellipsoids with axial ratios of about 8 to 1. The flat appearance, asymmetric shape, and anomalous densities of the particles would be explained if these lipoproteins consisted of a core of crystallized triglycerides encapsulated within a phospholipids monolayer. Crystallization of the saturated triglycerides could occur during routine lipoprotein isolation, in which temperatures much lower than the melting points of their core lipids are employed. When protocols are done entirely at 37 C, the unusual structures are not observed in the intermediate density class. Although the saturated fats in these bovine lipoproteins are derived from ruminal fermentation, we feel that any triglyceride-rich lipoprotein highly enriched in saturated fats will behave similarly if isolation temperatures are well below the melting points of the core lipids.

PHYSICOCHEMICAL CHARACTERIZATION OF TEN FRACTIONS OF BOVINE ALPHA LIPOPROTEINS. D.L. Puppion e, S.T. Kunitake, M.L. Toomey, E. Loh, and V.N. Schumaker (Dept. of Chem. and the Molecular Biol. Inst., and the Sch. of Public Health, Univ. of Calif. at Los Angeles, CA 90024) *J. Lipid Res. 23*(3):371-379 (1982). With the onset of milk production, serum concentrations of alpha lipoproteins in the dairy cow steadily increase, frequently attaining values greater than 1.5 g/dl. Since these lipoproteins comprise a highly polydisperse system, we have carried out studies to explore differences among bovine alpha lipoproteins in the density interval between 1.05 to 1.21 g/ml. Separation into ten fractions was achieved ultracentrifugally in an isopycnic gradient. Agarose gel electrophoresis showed that all but the bottom fraction contained alpha lipoproteins as either the major or sole lipoprotein class. Compositional analyses revealed an increasing percentage of both protein and phospholipid and a decreasing percentage of cholesterol with increasing fraction density. The esterified to unesterified cholesterol ratio ranged from 3 to 8 from the top to the bottom of the gradient.

THE INFLUENCE OF THYROID FUNCTION ON SERUM LIPID PROFILE. A. Raziel, B. Rosenzweig, V. Botvinic, I. Beigel, B. Landau, and I. Blum (Depts. of Internal Med. B, Endocrinology, and The Lipids Lab. of the Inst. of Cardiac Rehab., Beilinson Med. Center, Petah Tiqva) *Atherosclerosis 41*(2/3):321-326 (1982). Serum triglycerides, cholesterol, HDL-C and LDL-C levels as well as the LDL/HDL cholesterol ratio were determined in 11 patients suffering from hyperthyroidism and 7 patients suffering from hypothyroidism, and compared with those of 19 sex- and age-matched controls. In hypothroidism cholesterol and LDL-C values were reduced while those of the triglycerides and HDL-C were unchanged as compared with controls. The LDL/HDL cholesterol ratio in either group of patients was lower than in controls, the lowest being observed in thyrotoxicosis.

ISOLATION AND CHARACTERIZATION OF FILIPIN-RESISTANT LM CELL VARIANTS NOT AUXOTROPHIC FOR STEROL. D.A. Rintoul, N. Neungton, and D.F. Silbert (Dept. of Biological Chemistry, Washington Univ. School of Medicine, 660 S. Euclid Ave., St. Louis, MO 63110) *J. Lipid Res. 23*(3):405-405 (1982). A series of LM cell variants resistant to filipin, but not auxotrophic for sterol, was isolated by plating mutagenized, filipin-treated cells on soft agar medium containing no sterol. Cloned variants were assayed for growth in the presence and absence of sterol or unsaturated fatty acid. Filipin-resistant clones whose growth rate was unaffected by the addition of sterol to the medium were further analyzed. Variants were cultured in minimal medium, and plasma membranes prepared from these cultures were analyzed for sterol content, phospholipid head group composition, and unsaturated fatty acyl content. All variants examined showed a decrease in membrane sterol in conjunction with an increase in unsaturated fatty acyl chains in the membrane phospholipids. In addition, several variants exhibited alterations in phospholipid head group composition, including changes in the phosphatidylcholine/phosphatidylethanolamine ratio, or a decrease in sphingomyelin content. These observations imply that several different metabolic lesions can give rise to decreased plasma membrane sterol content (and hence to filipin resistance). The range of phospholipid alterations observed in these sterol prototrophs emphasizes the complex interrelationship between membrane sterol and phospholipid structure.

RETINOL ESTERIFICATION BY MAMMARY GLAND MICROSOMES FROM THE LACTATING RAT. A.C. Ross (Dept. of Physiology and Biochem. and Dept. of Pediatrics, The Med. College of Pennsylvania, Philadelphia, PA 19129) *J. Lipid Res. 23*(1):133-144 (1982). Because vitamin A in milk is largely present as esterified retinol while blood plasma predominantly contains unesterified retinol, experiments were conducted to determine whether membranes from the lactating mammary gland are able to synthesize retinyl esters in vitro. When microsomes from rats lactating for 7 to 14 days were incubated with [^{3}H] retinol dispersed in dimethylsulfoxide, some [^{3}H] retinol esterification was observed (147 pmol/5 min per 0.5 mg protein). However, 3- to 7-fold increases in retinyl ester synthesis could be achieved by supplying either a fatty acyl CoA-generating system or preformed fatty acyl CoA thioesters; thus, the major activity in vitro has the characteristics of a fatty acyl CoA: retinol acyltransferase. Both long-chain and medium-chain fatty acyl CoA esters stimulated [^{3}H]-labeled retinyl ester synthesis in vitro. Concordantly, analysis of the retinyl ester pattern of rat milk demonstrated the presence of eight different esters of retinol ranging in fatty acyl chain length from 8 to 18 carbons. Retinol esterification by microsomes was maximal at neutral pH (7.1) in the presence of approximately 50 μM palmitoyl CoA, and was linear with time of incubation for at least 5 min. Retinyl ester synthesis increased with the apparent concentration of [^{3}H] retinol to approximately 200 nmol/ml, but was also dependent on the ratio of retinol relative to total microsomal protein in the incubation mixture. These experiments demonstrate for the first time retinol esterification by mammary gland membranes and point to the hypothesis that free retinol from plasma is esterified in this organ before secretion of retinyl esters in milk.

FURTHER VALIDATION OF THE PLASMA ISOTOPE RATIO METHOD FOR MEASUREMENT OF CHOLESTEROL ABSORPTION IN MAN. P. Samuel, D.J. McNamara, E.H. Ahrens, Jr., J.R. Crouse, and T. Parker (Rockefeller Univ., New York, nY 10021) *J. Lipid Res. 23*(3):480-489 (1982). Recently we evaluated an isotope ratio method (IRM) for measurement of cholesterol absorption in 14 patients hospitalized in the metabolic ward by comparing it to simultaneous measurements with a fecal radioactivity method (FRM) and found good to excellent agreement between two procedures. Various procedural modifications of the IRM were studied in outpatients. The measurement of isotope ratios in a single blood sam-

ple on the third day gave identical results to those obtained from six to eight daily blood samplings. Blood samples drawn during the day gave cholesterol absorption values similar to those obtained from samples drawn following an overnight fast. Absorption tests carried out before and 1 hr after breakfast, lunch, or dinner, or giving the oral isotope in three divided daily doses all yielded identical results with tests carried out in the AM in the fasting state. Cholesterol absorption was reduced when the oral radiolabeled cholesterol was administered in orange juice vs. liquid formula, milk or a solution of glucose and amino acids, consistent with the well-known fact that gallbladder contraction is a critical requirement of cholesterol absorption. A meal high in cholesterol consumed on the day of the test did not influence the results of the absorption measurements. Addition of three eggs per day for 3 weeks to a low-cholesterol polyunsatured fat diet caused no significant change in percent cholesterol absorption in any of eight patients. We conclude that the isotope ratio method accurately and precisely measures cholesterol absorption in man, and that it is suitable not only for in- but also for out-patient studies.

EFFECT OF ETHANOL ON TRANSPORT FROM RAT INTESTINE DURING HIGH AND LOW RATES OF OLEATE ABSORPTION. D.R. Saunders, J. Sillery, G.B. McDonald (Dept. of Med., Univ. of Wash., Seattle, WA 98195) *Lipids 17*:356-369 (1982). Long-chain fatty acids (LCFA) are transported predominantly in the intestinal lymph when rates of LCFA absorption are high, and oral ethanol has been shown to enhance this lymphatic transport. A greater proportion of absorbed LCFA is transported via portal blood when rates of LCFA absorption are low. We tested the hypothesis in unanesthetized lymph-fistula rats that ethanol might also enhance the mucosal absorption and lymphatic transport of oleic acid when oleate absorption and transport from the intestine when 360 μmol, but not when 8 μmol of [^{14}Cp oleate was infused intraduodenally over 4 hr. There were major differences in intestinal mucosal metabolism of high and low loads of oleic acid. After the high load, the proportion of intestinal [^{14}C] phospholipid to [^{14}C] neutral lipid was 8:92. This ratio changed to 37:63, and the percentage of neutral ^{14}C as triglyceride decreased from 87 to 68% when the low load of oleate was infused. We suggest that a portion of absorbed LCFA is incorporated into phospholipid and transported as high-density lipoproteins in portal blood. This portal pathway for LCFA was uninfluenced by ethanol in the present experiments.

PHOSPHATIDYLCHOLINE FORMATION FROM EXOGENOUS LYSOPHOSPHATIDYLCHOLINE IN ISOLATED HAMSTER HEART. Jeannine D. Savard and Patrick C. Choy (Dept. of Biochemistry, Faculty of Medicine, Univ. of Manitoba, Winnipeg, Manitoba, R3E 0W3 (Canada)) *Biochim. Biophys. Acta 711*:40-48 (1982). The formation of phosphatidylcholine in hamster heart by reacylation and transacylation of exogenous lysophosphatidylcholine was investigated. Isolated hamster hearts were perfused with labeled lysophosphatidylcholine in Krebs-Henseleit buffer. Uptake of total radioactivity by the heart was maximum at 30 min of perfusion and was also linear from 5-20 μM of lysophosphatidylcholine in the perfusate. About 17 ± 3% of total radioactivity taken up by the heart was recovered in phosphatidylcholine. Perfusion of the isolated heart with 1-[^{14}C] palmitoylglycerophospho[*methyl*-^{3}H] choline indicated that labeled phosphatidylcholine was formed by reacylation of lysophosphatidylcholine with acyl-CoA and not by transacylation with another molecule of lysophosphatidylcholine. From the pool size of total cardiac lysophosphatidylcholine, the amount of phosphatidylcholine formed via the reacylation process was estimated to be 6.6 nmol/min per g heart.

ANTIBACTERIAL EFFECTS OF BUTYLATED HYDROXYANISOLE (BHA) AGAINST *BACILLUS* SPECIES. L.A. Shelef and P. Liang (Division of Food Sci. and Human Nutr., Dept. of Family and Consumer Resources, Wayne State Univ., Detroit, MI 48202) *J. Food Sci. 47*(3):796-799 (1982). The antibacterial effect of butylated hydroxyanisole (BHA) was evaluated in laboratory media and in two foods. In nutrient broth growth of *Bacillus* species (three strains of *B. cereus*, two of which were enterotoxigenic, and one strain each of *B. subtilis* and *B. megaterium*) was inhibited by 75 ppm of BHA. In tests with food systems growth inhibition of vegetative cells of these organisms required 1000 ppm in cooked rice and 5000 ppm in strained chicken. The effect of BHA was bacteriostatic at the tested levels (≤200 ppm in laboratory media and ≤10,000 ppm in the food systems), and viable cells were recovered from all samples. Bacterial growth resumed in samples which contained bacteriostatic levels of BHA after dilution with antioxidant free broth or food.

METABOLISM OF MALONALDEHYDE IN VIVO AND IN VITRO. G.M. Siu, H.H. Draper (Dept. of Nutr., Coll. of Biol. Sci., Univ. of Guelph, Guelph, Ontario, Canada N1G 2W1) *Lipids 17*:349-355 (1982). The metabolism of malonaldehyde (MA) was investigated in vivo using male Wistar rats and in vitro using rat liver mitochondria. Twelve hr after intubation with [1,3-^{14}C] MA, 60-70%, 5-15%, and 9-17% of administered radioactivity was recovered in expired CO_2, feces and urine, respectively. In rats intubated with [1,2-^{14}C] acetate, the corresponding values were 68-82%, 1-2% and 2-3%. $^{14}CO_2$ evolution was initially slower after ^{14}C-MA administration than after ^{14}C-acetate administration and more radioactivity was excreted in the feces and urine. In vitro experiments using [1,3-^{14}C] MA showed that MA is metabolized primarily in the mitochondria via reactions involving O_2 utilization and $^{14}CO_2$ production. The apparent K_m and V_{max} were 0.5 mM and 9.3 nmol/min/mg protein for O_2 uptake, respectively, and 2.0 mM and 2.4 nmol/min/mg protein for $^{14}CO_2$ production. Addition of malonic acid to mitochondrial incubates at concentrations inhibitory to succinate dehydrogenase did not affect MA induced O_2 uptake but enhanced $^{14}CO_2$ production from ^{14}C-MA. ^{14}C-Acetate appeared to be the major accumulating metabolite in rat liver mitochondrial preparations following a 120-min incubation with ^{14}C-MA. A probable biochemical route for MA metabolism involves oxidation of MA by mitochondrial aldehyde dehydrogenase followed by decarboxylation to produce CO_2 and acetate.

THE CHARACTERIZATION OF LIPOPROTEINS IN THE HIGH DENSITY FRACTION OBTAINED FROM PATIENTS WITH FAMILIAL LECITHIN:CHOLESTEROL ACYLTRANSFERASE DEFICIENCY AND THEIR INTERACTION WITH CULTURED HUMAN FIBROBLASTS. A.K. Soutar, B.L. Knight, and N.B. Myant (MRC lipid Metabolism Unit, Hammersmith Hospital, London W12 0HS, England) *J. Lipid Res. 23*(3):380-390 (1982). Lipoproteins of density 1.063-1.21 g/ml were isolated from the palsma of thee sisters of Irish origin with familial LCAT deficiency. Fractionation of the lipoproteins on the basis of particle size by chromatography on Sephacryl S-300 permitted partial separation of two major and at least three other minor components which differed in their lipid:protein ratio and their apolipoprotein content. One of the major components was a small spherical lipoprotein whose sole apolipoprotein was apoA-I; the second major component contained predominantly apoA-I, together with apoE, and in addition an apolipoprotein of molecular weight of 46,000 that was not cleaved by reduction of disulfide bonds, and which was identified as apoA-IV. This apoprotein has not previously been detected in the lipoproteins of LCAT-deficient patients. A second apoE-containing lipoprotein, which contained apoA-I and apo E in a ratio of approximately 2:1, was also present as a minor component, together with two or more minor components whose apoproteins were comprised of apoA-I and apoC. The apoE-containing lipoproteins competed efficiently with ^{125}I-labeled LDL for binding to high affinity LDL-receptor sites on the surface of cultured human skin fibroblasts. The ability to bind to the LDL receptor was directly proportional to the apoE content of the lipoproteins, even when other apoproteins, with the exception of apoB, were present in relatively large proportions. ApoE-containing ^{125}I-labeled lipoproteins from an LCAT-deficient subject were also taken up and degraded by the cultured cells.

STEROL COMPOSITION OF BOVINE RETINAL ROD OUTER SEGMENT MEMBRANES AND WHOLE RETINAS. Steven J. Fliesler and George J. Schroepfer, Jr. (Depts. of Biochem. and Chem., Rice University, Houston, TX 77001, U.S.A.) *Biochim. Biophys. Acta 711*:138-148 (1982). The sterol composition of bovine retinal rod outer segment membranes and whole retinas was studied by detailed chromatographic analyses. Cholesterol represented at least 98% of the total 3β-monohydroxy sterols of rod outer segment membranes, accounting for 1.68±0.15% of the dry weight. Whole retinas contained 1.76±0.29% cholesterol by dry weight, representing at least 99% of the total 3β-monohydroxy sterols. Trace amounts of a component having the chromatographic properties of 5α-cholestan-3β-ol were found in rod outer segment membranes and whole retinas. Very small amounts of a component having the chromatographic properties of 5α-cholest-7-en-3β-ol were found in whole retinas, but not in rod outer segment membranes. The molar ratio of cholesterol to rhodopsin in bovine rod outer segment membranes was approximately 4.7. Cholesterol accounted for only 5-7 mol% of total rod outer segment membrane lipids.

GENETIC MEDIATION OF CHOLESTEROL METABOLISM IN THE BABOON (*PAPIO CYNOCEPHALUS*). B.L. Flow and G.E. Mott (Dept. of Pahology, Univ. of Texas Health Sci. Center at San Antonio, San Antonio, TX 78284) *Atherosclerosis 41*(2/3):403-414 (1982). Genetic effects of serum cholesterol concentration and measure of cholesterol metabolism were investigated in 83 normocholesterolemic juvenile baboons (*Papio cynocephalus*), the progeny of 6 sires. Sire effects (P 0.05) were observed for serum cholesterol production rate, and several cholesterol pool parameters derived from a two-pool model. The estimates heritability (h^2) for the half-time of the first (t1/2 A) and second exponentials (t1/2 B) derived from serum [^{14}C] cholesterol decay curves and the cholesterol turnover rate were 0.67, 0.73 and 0.71, respectively. These heritabilities

and those for serum cholesterol concentration (h^2=0.44) and cholesterol production rate (h^2=0.56) indicate these characters are moderately to highly heritable. Serum cholesterol concentration was correlated genetically with cholesterol turnover rate (r_g=-0.56), production rate (r_g=-0.41), t1/2 A (r_g=0.53), and t1/2 B (r_g=0.39). Correlations among observed values, or phenotypic correlations, were low. Path analyses revealed that the low phenotypic (r_p=0.02) between serum cholesterol concentration and cholesterol turnover rate was due to genetic and environmental contributions of similar magnitude but opposite in sign. The low phenotypic correlations of serum cholesterol with cholesterol production rate, t1/2 A, and t1/2 B (r_p=-0.24, 0.23, and 0.19, respectively) were due primarily to the genetic contribution since environmental contributions were near zero. Application of similar genetic and path analytic techniques to human populations should enhance our understanding of the low phenotypic relationships previously observed between serum cholesterol and parameters of cholesterol metabolism.

LYSOPHOSPHOLIPASE ACTIVITY OF BOVINE ADRENAL MEDULLA: A REEVALUATION. Richard C. Franson and Henk Van Den Bosch (The Laboratory of Biochemistry, Padualaan 8, De Uithof, 3508 TB Utrecht, Netherlands) *Biochim. Biophys. Acta 711*:75-82 (1982). 1. Chromaffin granule preparations isolated from bovine adrenal medulla hydrolyzed endogenous lysophosphatidylcholine (lyso-PC) and generated lysophosphatidylethanolamine when dialyzed at pH 7.5. 2. Undialyzed granule preparations hydrolyzed exogenously added [1-^{14}C] palmitoyl-lyso-PC maximally (12-16 nmol/min per mg) at pH 7.5. At a given concentration of protein, activity increased with increasing concentrations of substrate lyso-PC to a maximum beyond which substrate inhibited activity up to 95%. 3. More than 95% of the lysophospholipase activity of fresh granule preparations toward exogenously added lyso-PC was inactivated irreversibly by dialysis. 4. By contrast, fresh microsomal preparations from adrenal medulla had similar substrate requirements for maximal lysophospholipase activity, but more than 35% of the activity was retained at high substrate concentrations or after extensive dialysis. 5. We conclude that adrenal organelles, other than microsomes, contain potent membrane-associated lysophospholipase activity that is inactivated preferentially by high detergent-substrate concentrations and/or dialysis. These observations suggest that lysophospholipase activity (and perhaps phospholipase A activity) is more widely distributed in organelle membranes of the adrenal medulla than was reported previously.

EFFECT OF RATIO OF BASAL DIET FAT TO TEST FAT ON THE TRUE METABOLIZABLE ENERGY OF THE TEST FAT. H.L. Fuller and N.M. Dale (Dept. of Poultry Sci., Univ. of Georgia, Athens, GA 30602) *Poultry Science 61*(5):914-918 (1982). Experiments were conducted to evaluate the influence of basal dietary fat on the true metabolizable energy (TME) of test fats differing in composition and physical properties. Two samples of blended fats and one sample of tallow were tested using a simplified corn-soy basal diet with all of the fat extracted and with the extracted fat added back in increasing increments up to 10% of the diet. The test fats were added at levels of 5 to 15%, resulting in ratios of basal fat to test fat of 0:15 to 10:5. The TME of tallow and one of the blends was improved as the ratio of basal fat:test fat was increased from 1:4.5 up to 7.5:7.5, at which point there were no significant differences in TME among the fats. Even at a more narrow ratio (5:10), the TME of the tallow was equal to or higher than that of either blend. Fatty acid absorption was determined using the fat-free diet to determine endogenous fat excretion. Absorption of 18:0 and, to a lesser extent, 16:1 was improved as the ratio of basal fat:test fat was increased from 0:15 to 7.5:7.5. The TME of the tallow was the same when fed with extracted (fat-free) basal as with unextracted basal suggesting involvement of two separate mechanisms.

BIOTRANSFORMATION OF 16α-HYDROXYPROGESTERONE BY *EUBACTERIUM* SP. 144: NON-ENZYMATIC ADDITION OF L-CYSTEINE TO Δ^{16}-PROGESTERONE. T.L. Glass, J. Winter, V.D. Bokkenheuser, and P.B. Hylemon (Dept. of Microbiol., Med. College of Virginia, Virginia Commonwealth Univ., Richmond, VA 23298) *J. Lipid Res. 23*(2):352-356 (1982). *Eubacterium* sp. 144 dehydroxylated 16α-hydroxy-progesterone; however, the expected intermediate, Δ^{16}-progesterone, did not accumulate to significant concentrations in the culture medium. Moreover, the final end product of this biotransformation, 17α-progesterone, was produced at a very slow rate. It was discovered that, under our culture conditions, Δ^{16}-progesterone reacted chemically with L-cysteine to form a highly water-soluble derivative. The ability of Δ^{16}-progesterone to react with L-cysteine in culture media was considerably reduced when L-cysteine was autoclaved in the presence of complex medium components. Δ^{16}-progesterone also reacted chemically with D-cysteine, L-homocysteine, glutathione, and 2-mercaptoethylamine. The reaction was favored by alkaline pH (≥pH 8.0) and required both an unhindered thiol group and a proximal amino group on the mercapto compound. Chromatography of the putative Δ^{16}-progesterone L-[U-^{14}C]-cysteine reaction product by HPLC showed a single UV-absorbing, radioactive peak (RT 4.31 min).

CHARACTERIZATION OF NEUTRAL AND ACID ESTER HYDROLASE IN WOLMAN'S DISEASE. Jeffrey M. Hoeg, Stephen J. Demosky, Jr. and H. Bryan Brewer, Jr. (Molecular Disease Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Building 10, Room 7N117, Bethesda, MD 20205 (U.S.A.)) *Biochim. Biophys. Acta 711*:59-65 (1982). Wolman's disease is characterized by diffuse cellular accumulation of cholesteryl ester and triacylglycerol, steatorrhea, and death in infancy. Although lysosomal acid ester hydrolase has been reported to be absent in tissues from affected infants, full evaluation of the intracellular ester hydrolases in hepatic and nonhepatic tissues has not been performed previously. Studies on ester hydrolase activity in human liver and skin fibroblasts have permitted the following conclusions. (1) The ester hydrolase activity of cholesteryl oleate and triolein are parallel in human liver and skin fibroblasts. (2) There is a significant loss of activity for both of these substrates at pH 4 in both liver and skin fibroblasts in a subject with Wolman's disease. (3) At pH 7, however, ester hydrolase activity for both substrates in both liver and skin fibroblast preparations from a patient with Wolman's disease is preserved. (4) The patient's mother, an obligate heterozygote, does not demonstrate any loss of activity for either substrate at pH 4. These data are consistent with the concept that acid and neutral ester hydrolases are different enzymes.

LONG-TERM EFFECTS OF SEMIPURIFIED DIETS CONTAINING CASEIN OR SOY PROTEIN ISOLATE ON ATHEROSCLEROSIS AND PLASMA LIPOPROTIENS IN RABBITS. M.W. Huff, D.C.K. Roberts, and K.K. Carroll (Dept. of Biochem., Univ. of Western Ontario, London, Ontario N6A 5C1 (Canada)) *Atherosclerosis 41*(2/3):327-336 (1982). Long-term feeding trials of male New Zealand White rabbits were carried out with low-fat cholesterol free semipurified diets containing casein or soy protein isolate as the source of protein. Young rabbits fed the casein diet from 6 to 8 weeks of age for 10 months rapidly become hypercholesterolemic and maintained high cholesterol levels throughout the experiment. At autopsy, all rabbits showed extensive aortic lesions. In young rabbits fed the soy protein diet, low plasma cholesterol levels were maintained for the 10-month period, and aortic lesions were minimal. Analysis of plasma midway through these experiments, showed the excess cholesterol in the casein-fed animals was present mainly in the intermediate density fraction (d=1.006-1.019, although the cholesterol content of very low density and low density lipoproteins was also increased. Mature rabbits fed the casein diet from 6 months of age did not become significantly hypercholesterolemic until they had been on the diet for 6 months and the final cholesterol level achieved after 9 months on diet was less than that seen in the young rabbits. Those fed the soy protein isolate diet maintained low plasma cholesterol levels throughout the 9-month period.

ELEVATED LEVELS OF CELLULAR AND EXTRACELLULAR PHOSPHOLIPASES FROM PATHOGENIC *NAEGLERIA FOWLERI*. Robert M. Hysmith and Richard C. Franson (Depts. of Pathology, Biophysics and Biochemistry, Medical College of Virginia, Richmond, VA 23298 (U.S.A.)) *Biochim. Biophys. Acta 711*:26-32 (1982). Phospholipase A, sphingomyelinase and lysophospholipase activities were examined in cell homogenates and cell-free culture media of virulent and virulent-attenuated *Naegleria fowleri* and nonpathogenic *Naegleria gruberi*. Homogenates of virulent *N. fowleri* contained from 3 to 250 times the lipolytic activity of virulent-attenuated and nonpathogenic *Naegleria* spp. Similarly, the cell-free media of virulent *N. fowleri* cultures contained large quantities of phospholipase A, lysophospholipase and sphingomyelinase while comparable activities in the cell-free media of virulent-attenuated and nonpathogenic *Naegleria* spp. were only slightly, if at all, detectable. Lipolytic enzymes accumulated in the media of virulent *N. fowleri* cultures at various stages during growth but not in virulent-attenuated and nonpathogenic *Naegleria* cultures. In general, phospholipase A and sphingomyelinase accumulated during the log phase of growth with lysophospholipase appeared only in the late stationary phase. We conclude that pathogenic *Naegleria* contain potent lipolytic enzymes that are released selectively into the media during growth. These enzymes could contribute to the pathogenesis of *Naegleria*-induced primary amoebic meningoencephalitis.

CHYLOMICRON CATABOLISM DIFFERS BETWEEN HOODED AND ALBINO LABORATORY RATS. F. Jeffery and T.G. Redgrave (Dept. of Physiology, Univ. of Melbourne, Parkville, Victoria 3052, Australia) *J. Lipid Res. 23*(1):154-160 (1982). To extend

previous reports that some aspects of lipid metabolism are different between Hooded and albino strains of laboratory rats, thoracic duct lymph chylomicrons were collected and their composition and metabolism were compared in this study. Chylomicrons from Hooded rats had more core components and fewer surface components than albino rats. After adding 1% cholesterol to the diet the ratio of cholesterol:phospholipid was higher in Hooded rat chylomicrons. Nascent lymph chylomicrons from Hooded rats contained less apolipoprotein A-IV, but after incubation with serum there was a gain of apolipoprotein A-IV and a loss of A-I from both types of chylomicron. The ratio of apoC to apoE was higher in Hooded than in albino rats. The metabolism of injected chylomicrons was slower in Hooded rats. Twenty minutes after a single injection, only 1-3% of chylomicron triacylglycerol and 8-13% of chylomicron cholesteryl ester remained in the plasma of albino rats, compared with 6-12% of triacylglycerol and 30-33% of cholesteryl ester in Hooded rats. At 30 min, in the Hooded rats, the uptake of injected chylomicron cholesterol into the liver was decreased whereas uptake into other tissues, notably adipose tissue and muscle, was increased. During the steady intravenous injection of chylomicrons from the same strain, the fractional clearance rate of chylomicron triacylglycerol was about three-fold faster in albino rats than in Hooded rats, and the fractional clearance rate of chylomicron cholesteryl ester was 70% faster in albino rats. When chylomicrons were allowed to circulate for 30 min after injection into functionally hepatectomized rats, with or without heparin, the remnant formation and chemical composition were similar in Hooded and albino rats.

INTESTINAL VERY LOW DENSITY LIPOPROTEIN SECRETION IN RATS FED VARIOUS AMOUNTS OF FAT. Athina-Despina Kalopissis, Sabine Griglio and Xavier Le Liepvre (Groupe de Recherches sur la Physiopathologie de la Nutrttion, INSERM U.177, Institut Biomédical des Cordeliers, 15, 21 rue de l'Ecole de Médecine, 75270 Paris (France)) *Biochim. Biophys. Acta 711*:33-39 (1982). 1. The effect of a high-fat diet (30% fat by wt.) on intestinal very low density (VLDL) secretion was studied in male rats after specific inhibition of hepatic VLDL secretion by dietary orotic acid. Total VLDL secretion (from liver to intestine) was measured in animals not receiving orotic acid. 2. Fat-feeding resulted in a 32% decreased post-Triton secretion of total serum VLDL triglycerides as compared to control (low fat) diet. Concomitantly, a large stimulation of post-Triton intestinal VLDL triacylglycerols secretion was measured in fat-fed rats. Thus, the major part (64%) of circulaing triacylglycerols transported as VLDL originated from the intestine in these animals, leading presumably to an increased secretion of intestinal apolipoproteins. 3. Intestinal VLDL and chylomicron secretion rates increased with the amount of fat in the diet (7, 13, 20 or 30% by wt.). Whereas the chylomicron secretion was linearly related to the dietary fat content, the relationship between intestinal VLDL secretion and fat content of the diet was sigmoidal. The highest stimulation of intestinal VLDL formation was observed within a narrow range of dietary fat content (between 10 and 20%).

PANCREATIC ENZYMES, BILE ACIDS AND CHOLESTEROL LEVELS IN MICE FED RAW OR HEATED EGG ALBUMEN. S.G. Kirschenmann and B.O. Scheeman (Dept. of Nutr., Univ. of Calif., Davis, CA 95616) *J. Food Sci. 47*(3):714-715. Mice were fed semipurified diets which contained either 20% unheated egg albumen (UEA) or heat-treated egg albumen (HTEA) for 15 days. After consuming a meal, the intestinal contents contained similar activities of trypsin, chymotrypsin, amylase and lipase in the two groups, but bile acid levels were greater in the UEA group. Relative to fasted animals, enzyme activities, measured in the pancreata, were present in greater amounts in the UEA group compared to those in the HTEA group following consumption of a meal. Liver cholesterol levels were lower in the UEA group than in the HTEA group; however, plasma cholesterol levels did not differ significantly. These results indicate that the feeding of unheated egg albumen can stimulate synthesis of pancreatic enzymes and enhance conversion of liver cholesterol to bile acids.

IDENTIFICATION OF MULTIPLE SUBCLASSES OF PLASMA LOW DENSITY LIPOPROTEINS IN NORMAL HUMANS. R.M. Krauss and D.J. Burke (Donner Laboratory, Lawrence Berkeley Laboratory, Univ. of California, Berkeley, CA 94720) *J. Lipid Res. 23*(1):97-104 (1982). Density gradient ultracentrifugation of low density lipoproteins (LDL) from 12 normal subjects showed multiple distinct isopycnic bands. Densitometric scanning of the gradient tubes revealed that each band could be assigned to one of four density intervals and that the boundaries of these intervals were consistent among all the subjects. Analytic ultracentrifuge flotation (S_f°) rates were assigned to the four density intervals, and there was a strong correlation between peak S_f° rate and peak isopycnic banding position (R_f) of the LDL in the 12 subjects. Further delineation of distinct subspecies of LDL was afforded by electrophoresis in 2-16% gradient polyacrylamide gels. Densitometric scans of protein-stained gels revealed multiple peaks, and particle diameters were assigned to these peaks using calibration markers. Use of lipid-staining procedure allowed identification of electrophoretic bands in whole plasma which corresponded to those seen in isolated LDL, eliminating the possibility that ultracentrifugation was responsible for formation of the subspecies detected by the gradient gel procedure. The application of density gradient ultracentrifugation and gradient gel electrophoresis provides a means of characterizing LDL from normal humans in terms of multiple distinct subpopulations which may also prove to have differing metabolic and pathologic properties.

EXPERIMENTAL ATHEROSCLEROSIS IN RABBITS FED CHOLESTEROL-FREE DIETS. D. Kritchevsky, S.A. Tepper, G. Bises, and D.M. Klurfeld (The Wistar Inst. of Anatomy and Biol., 36th Street at Spruce, Philadelphia, PA 19104) *Atherosclerosis 41*:279-284 (1982). Rabbits were fed a semipurified, cholesterol-free atherogenic diet containing 40% sucrose, 25% casein, 14% fat, 15% fiber, 5% salt mix and 1% vitamin mix. The fats were corn oil (CO), palm kernel oil (PO), cocoa butter (CB), and coconut oil (CNO). The rabbits were bled at 3, 6, and 9 months and killed at 9 months. Serum lipids of rabbits fed CO were unaffected. Serum cholesterol levels (mg/dl) at 9 months were: CO—64; PO—436; CB—220; and CNO—474. HDL-cholesterol (%) was: CO—37; PO—8.6; CB—25.1; and CNO—7.0. Average atherosclerosis (arch + thoracic/2) was: CO—0.15; PO—1.28; CB—0.53; and CNO—1.60. Cocoa butter (iodine value 33) is significantly less cholesterolemic and atherogenic than palm oil (iodine value 17) or coconut oil (iodine value 6). The difference between the atherogenic effects of cocoa butter and palm oil may lie in the fact that about half of the fatty acids of palm oil are C_{16} or shorter, whereas 76% of the fatty acids of cocoa butter are C_{18} or longer.

REDUCTION OF MYOCARDIAL NECROSIS IN MALE ALBINO RATS BY MANIPULATION OF DIETARY FATTY ACID LEVELS. J.K.G. Kramer, E.R. Farnworth, B.K. Thompson, and A.H. Corner (Animal Res. Centre and Engineering and Statistical Res. Inst., Agriculture Canada, Ottawa, Ontario K1A 0C6, Canada) *Lipids 17*(5):372-382 (1982). A comprehensive statistical analysis has shown a significant correlation between the incidence of myocardial lesions in male albino rats and the concentration of certain dietary fatty acids. To test this result under controlled conditions, male rats were fed for 16 weeks diets containing 20% by weight soybean oil or a low erucic acid rapeseed (LEAR) oil. Both oils contained substantial amounts of linolenic acid, and both groups developed a high incidence of myocardial necrosis. Addition of dietary saturated fatty acids to the oil significantly lowered the incidence of heart lesions in both groups. Addition of cocoa butter resulted in increased absorption of saturates and increased growth. Replacement of the cocoa butter by at least an equal amount of synthetic triolein resulted in no significant changes, thus ensuring that the reduction in heart lesions associated with the addition of cocoa butter was not due to dilution of cardiopathogenic compounds in the original vegetable oils. These results support the hypothesis that myocardial lesions in male rats are related to the balance of dietary fatty acids and not to cardiotoxic contaminants in the oils. Changes in the dietary fatty acids did not appear to influence the proportion of the cardiac phospholipids, but their fatty acid composition was markedly influenced. Dietary linolenic acid affected the C22 polyunsaturated fatty acids (PUFA) and dietary saturates increased the level of saturates in cardiac phospholipids. The level of arachidonic acid and total C22 PUFA did not appear to be affected by diet.

EFFECT OF SATURATED AND UNSATURATED FAT DIETS ON LIPID PROFILES OF PLASMA LIPOPROTEINS. A. Kuksis, et al. (Banting and Best Dept. of Med. Res., Univ. of Toronto, Canada) *Atherosclerosis 41*(2/3):221-240 (1982). Four to five healthy normolipidemic men were maintained on controlled diets containing 40% of calories from either unsaturated or saturated fat, with a period of ad lib diet in between. The effect of the diets on the total lipid profiles of the very low (VLDL), low (LDL) and high (HDL_3) density lipoproteins was determined by high temperature gas-liquid chromatography. When compared with the saturated, the unsaturated fat diet caused a decrease in the protein content in HDL_3 and to a lesser extent in LDL, which were compensated for by an increase in all lipid classes, resulting in similar lipid class proportions on both diets. There were no significant alterations induced by the diet in the neutral lipid/polar lipid ratios, so that the radii of the particles calculated on the basis of the surface and core component content gave comparable values for corresponding lipoprotein classes on both diets. There was an increase in triacylglycerols and a decrease in cholesteryl esters in the LDL fractions from the unsaturated fat diet. The opposite effect was observed for VLDL, while the HDL_3 showed no change. The dietary varia-

tions resulted in changes in the molecular weight or carbon number profiles of the cholesteryl esters, phosphatidylcholines and triacylglycerols. There was a decrease in the lower molecular weight species and an increase in the higher molecular weight species on the unsaturated fat diet and vice versa on the saturated fat diet. The ad lib diet produced a lower free cholesterol/total phospholipid ratio in VLDL and of sphingomyelin/phosphatidylcholine ratio in LDL. The results suggest that the decreases in plasma cholesterol and triacylglycerols are due to a decrease or plasma lipoprotein particles.

PLASMA HIGH DENSITY LIPOPROTEINS HDL_2, HDL_3, AND POSTHEPARIN PLASMA LIPASES IN RELATION TO PARAMETERS OF PHYSICAL FITNESS. T. Kuusi, E.A. Nikkila, P. Saarinen, P. Varjo, and L.A. Laitinen (Third Dept. of Med., Univ. of Helsinki; Military Academy of Helsinki: and Naval Res. Unit. of Finland, Helsinki, Finland) *Atherosclerosis 41*:209-219 (1982). A number of studies has shown that the plasma levels of high density lipoprotein (HDL) are increased by regular aerobic exercise. The plasma HDL, particularly HDL_2, is regulated by the activity of 2 endothelial lipases, viz. lipoprotein lipase (LPL) and hepatic lipase (HL), which both can be assayed in postheparin plasma. In the present study the plasma levels of HDL_2 and HDL_3 cholesterol and postheparin plasma lipase activities were related to parameters of physical fitness obtained from a pulse conducted maximal bicycle ergometer test. There was a significant positive correlation between HDL_2 cholesterol and physical fitness ($r=0.52$, $P<0.01$). On the other hand, the postheparin plasma hepatic lipase activity showed a significant negative correlation to physical fitness ($r=-0.57$, $P<0.01$). The HDL_2 cholesterol was inversely correlated with the HL activity ($r=-0.69$, $P<0.001$). Application of partial correlation analysis to the data showed that the relationship between HDL_2 cholesterol and fitness disappeared by keeping the HL activity constant whereas the correlation between HDL_2 and HL was not influenced by fitness. The relation of HDL_2 to fitness was independent in body fat and basal plasma insulin level; in addition the relationship between HL and fitness was not accounted for by body fatness. No relationship was found between physical fitness and LPL activity or between HDL_3 and fitness. The results support the hypothesis that hepatic endothelial lipase has a role in the regulation of plasma HDL_2 cholesterol and that the activity of this enzyme decreases upon increase of physical fitness.

DECREASED PROSTAGLANDIN PRODUCTION IN CULTURED SMOOTH MUSCLE CELLS FROM ATHEROSCLEROTIC RABBIT AORTA. J. Larrue, C. Leroux, D. Daret, and H. Bricaud (Unite de Recherches de Cardiologie, U8 I.N.S.E.R.M., Avenue du Haut-Leveque, 33600 Pessac (France)) *Biochim. Biophys. Acta 710*(3): 257-263 (1982). Prostaglandin synthesis in aortic smooth muscle cells originating from healthy and atherosclerotic rabbits was studied by incubating [^{14}C] arachidonic acid with intact confluent cells and cell homogenates. In spite of a reduced 6-keto prostaglandin $F_{1\alpha}$ formation, no potentiating effect on the prostaglandin E_2 generation occurred. Indeed, both cyclooxygenase and prostaglandin I_2 synthetase activities appear to be reduced. These results suggest that an impaired arachidonic acid utilization in aortic smooth muscle cells may be involved in the course of the atherosclerotic process.

SPECIFICITY IN THE ACTION OF HYPOLIPIDEMIC DRUGS: INCREASE OF PEROXISOMAL β-OXIDATION LARGELY DISSOCIATED FROM HEPATOMEGALY AND PEROXISOME PROLIFERATION IN THE RAT. P.B. Lazarow, H. Shio, and M.A. Leroy-Houyet (Rockefeller Univ., New York, NY 10020) *J. Lipid Res. 23*(2):317-326 (1982). Hypolipidemic drugs increased 3- to 4-fold the activity of the peroxisomal β-oxidation system in rat liver, with modest or no effects on catalase activity, liver weight, or peroxisome abundance. This specificity of action was observed in two experimental models: 1) bezafibrate treatment of male rats (25 mg/kg body wt., p.o.) and 2) clofibrate treatment of female rats (5 g/kg chow). Bezafibrate had no effect on the liver content of protein, catalase, or cytochrome oxidase, and little or no effect on mitochondrial β-oxidation. The results indicate that the hypotriglyceridemic mechanism of action of these drugs involves an induction of the peroxisomal β-oxidation system, but this mechanism does not obligatorily include gross hepatomegaly or other alterations of peroxisomes that are often caused by hypolipidemic compounds. This dissociation of specific biochemical changes from other effects demonstrates a precise regulation of organelle biogenesis. Peroxisomes synthesized under the influence of bezafibrate or clofibrate have a different enzymatic composition than do normal peroxisomes. These results have several implications. 1) Side effects of clofibrate that are of current clinical concern may be unrelated to its lipid-lowering effects. 2) Measurement of peroxisomal β-oxidation should be a sensitive and specific tool for screening for new hypotriglyceridemic compounds. 3) Peroxisome proliferation or lack thereof is not central to efficacy. 4) Other new drugs may be discovered that are highly discriminating in elevating specific enzymes of fatty acid catabolism while causing even less or no hepatomegaly and other side effects.

THE FATTY ACIDS OF ERYTHROCYTES OF MYOCARDIAL INFARCTION PATIENTS. E.J.A. Lea, S.P. Jones, and D.V. Hamilton (Membrane Lab., School of Biological Sciences, Univ. of East Anglia, Norwich, NR4 7TJ, and Addenbrooke's Hospital, Cambridge (Great Britain)) *Atherosclerosis 41*(2/3):363-369 (1982). Arachidonic acid (C20:4ω6) and eicosapentaenoic acid (C20:5ω3) are precursors of two different series of prostaglandins important in homeostasis of the cardiovascular system. The levels of these and other fatty acids have been measured in a group of 20 patients who had suffered myocardial infarction (samples taken within 12 h of infarction) and a group of 17 healthy age-matched controls using the erythrocyte as a lipid probe. There was no significant difference between the level of C20:4ω6 in patients and controls. There was however a highly significant difference in the level of the peak containing C20:5ω3 i.e. 6.60% ± 0.29 (mean and SE of mean) for controls; 3.91 ± 0.36 (mean and SE of mean) for patients with myocardial infarction. In each of the two groups the relationship between the levels of the two fatty acids arachidonic acid, eicosapentaenoic acid and their essential fatty acid precursors has been investigated. No significant functional relationship was found except between C18:3ω3 and C20:5ω3 in the control group. These results are discussed in relation to homeostasis and recent evidence that levels of these fatty acids can be altered by dietary manipulation.

PROBUCOL: EFFECTS ON THE METABOLISM OF LOW DENSITY LIPOPROTEINS IN MODERATE HYPERCHOLESTEROLAEMIA. P. Magill, C. Whiting, F. Hammett, I. Glick, N.E. Miller, and B. Lewis (Dept. of Chem. Pathology and Metabolic Disorders, St. Thomas' Hospital, London, England) *Artery 10*:88-94 (1982). Seven patients with primary hypercholesterolaemia (baseline levels 7.5 to 13.1 mmol/1), and with no evidence of xanthomas, were treated with probucol 1g daily. Plasma LDL-cholesterol decreased by 20% due to reduced LDL apo B synthetic rate. HDL-cholesterol also decreased; this fall was confined to the HDL_3 subclass, while HDL_2-cholesterol was unchanged.

IN VITRO UPTAKE AND TRANSFER OF CHLORINATED HYDROCARBONS AMONG HUMAN LIPOPROTEINS. B.P. Maliwal and F.E. Guthrie (Toxicology Program, Dept. of Entomology, North Carolina State Univ., Raleigh, NC 27650) *J. Lipid Res. 23*(3):474-479 (1982). The uptake, distribution, and exchange of chlorinated hydrocarbon insecticides (dieldrin and chlordecone) and biphenyls (2,4,5-2',4',5'-hexachlorobiphenyl and 3-chlorobiphenyl) among human lipoproteins was examined by fluorescence quenching, gel filtration and ultrafiltration. The chlorinated hydrocarbons were rapidly taken up from solution or silica particles by lipoproteins. The distribution of chlorinated hydrocarbons among the lipoproteins was independent of the amount taken up by the lipoproteins. The partition coefficient for each lipoprotein and the serum concentration of individual lipoproteins determined the distribution pattern of chlorinated hydrocarbons among lipoproteins. The chlorinated hydrocarbons attached to albumin or one of the lipoproteins were rapidly transferred to all other lipoproteins. The exchange was complete in less than one minute. The role of rapid exchange of chlorinated hydrocarbons among lipoproteins in removal of these chemicals from blood and distribution to other tissues is discussed.

APOPROTEIN S, A FAMILY OF HUMAN SERUM LIPOPROTEIN POLYPEPTIDES. C.L. Malmendier and J.P. Ameryckx (Research Unit on Atherosclerosis, Laboratory of Chemical Pathology, Faculty of Med., and Dept. of Clinical Chemistry, St-Pierre University Hospital, University of Brussels, Brussels, Belgium) *Atherosclerosis 42*:161-172 (1982). Glucose infusions given to neurological and postsurgical patients in the absence of oral feeding were found to increase the amount of new polypeptides in high density lipoproteins from 3 to 40% of total proteins as compared to 0.1% in normal subjects fed a regular diet. This increase was observed in HDL_2 as well as in HDL_3 and even in VLDL. Eight polymorphic forms were detected by chromatography, polyacrylamide gel electrophoresis and isoelectric focusing. The partial amino acid sequence of one of these forms is given: the first 26 NH_2-terminal residues are identical to the amphipathic helical segment of SAA protein, theoretically responsible for the lipid binding. The role of glucose as the major factor involved in the production of these apoproteins is discussed.

OPTIMIZING EFFECT OF PLANT STEROLS ON CHOLESTEROL ABSORPTION IN MAN. F.H. Mattson, S.M. Grundy and J.R. Crouse (Dept. of Med., Schl. of Med., Univ. of Calif. San Diego, and Veterans Administration Med. Ctr., San Diego,

Calif.) *Am. J. Clin. Nutr. 35*(4):697-700 (1982). During three experimental periods, nine adults were hospitalized on a metabolic ward and fed a meal containing 500 mg of cholesterol as a component of scrambled eggs. In addition, the meal contained: 1) no additive, 2) 1 g β-sitosterol, or 3) 2 g β-sitosteryl oleate. Stools for the succeeding 5 days were analyzed to determine the percentage of the cholesterol in the test meal that was absorbed. The addition of β-sitosterol resulted in a 42% decrease in cholesterol absorption; the β-sitosteryl oleate caused a 33% reduction. These results indicate that the judicious addition of β-sitosterol or β-sitosteryl oleate to meals containing cholesterol-rich foods will result in a significant decrease in cholesterol absorption, with a consequent decrease in plasma cholesterol.

TRIACYLGLYCEROL TURNOVER IN LARGE AND SMALL RAT ADIPOCYTES: EFFECTS OF LIPOLYTIC STIMULATION, GLUCOSE, AND INSULIN. J.M. May (Dept. of Medicine, Medical College of Virginia, Richmond, VA 23298) *J. Lipid Res. 23*(3):428-436 (1982). Rates of lipolysis and reesterification were determined under various conditions in adipocytes from epididymal fat pads of old, spontaneously obese rats and compared to cells from younger, leaner animals. No differences were observed in lipolytic responsiveness to several concentrations of the β-adrenergic agent ritodrine compared to cells from younger, leaner rats. The large cells showed diminished rates of lipolysis, reesterification, and glyceride-glycerol synthesis from glucose of submaximal but not maximal insulin concentrations, probably reflecting decreased large cell receptor numbers. In both cell types reesterification measured in the presence of ritodrine progressively rose with increasing concentrations of glucose in the medium. At each glucose concentration rates of reesterification were similar in each cell type. When maximal concentrations of insulin were also added, at low glucose concentrations there was a similar increase in reesterification in large and small cells. No insulin effect in either cell type was observed at high concentrations of glucose. Although fatty acid synthesis from glucose in the large cells was markedly diminished, glyceride-glycerol synthesis was well maintained, correlating well with calculated reesterification rates. In fact, reesterification was found to be quantitatively very important in determining total triacylglycerol turnover in both cell types. High rates of reesterification might not only allow maintenance of triacylglycerol stores, but could also increase metabolic sensitivity to changes in hormonal or substrate concentrations.

THE METABOLISM OF FATTY ACIDS IN HEPATOCYTES ISOLATED FROM TRIIODOTHYRONINE-TREATED RATS. Jacob A. Stakkestad and Jon Bremer (Inst. of Med. Biochem., Univ. of Oslo, Oslo, Norway) *Biochim. Biophys. Acta 711*:90-100 (1982). 1. The effect of triiodothyronine on the metabolism of palmitate, oleate and erucate in isolated rat heptocytes was studied. 2. In triiodothyronine-treated rats increased oxidation and decreased triacylglycerol formation from palmitate and oleate was observed. For erucate triiodothyronine caused increased oxidation, but had no significant effect on esterification 3. Glucagon had no effect on the fatty acid metabolism in hepatocytes from triiodothyronine-treated rats, whereas it stimulated the oxidation in hepatocytes from normal rats. Still, after treatment with triiodothyronine, the oxidation of fatty acids was significantly higher than in glucagon-stimulated normal hepatocytes. 4. In isolated rat liver mitochondria triiodothyronine raised the activity of the outer carnitine palmitoyltransferase (EC 2.3.1.21). The activity of the total carnitine palmitoyltransferase was elevated only slightly in isolated mitochondria from triiodothyronine-treated rats. These effects were similar to those seen in fasted rats. 5. Triiodothyronine had no significant influence on the concentration of long-chain acyl-CoA or α-glycerophosphate in isolated rat hepatocytes.

ION-PAIR HIGH-PRESSURE LIQUID CHROMATOGRAPHY OF *CIS-TRANS* ISOMERS OF RETINOIC ACID IN TISSUES OF VITAMIN A-SUFFICIENT RATS. P.R. Sundaresan and P.V. Bhat (Div. of Toxicology, Bureau of Foods, Food and Drug Administration, Washington, DC 20204) *J. Lipid Res. 23*(3):448-455 (1982). Naturally occurring retinoids were separated by reversed-phase high-pressure liquid chromatography on an octadecylsilane column eluted with acetonitrile-potassium phosphate buffer mixtures. The order of elution from a mixture of 500 ng each of the following standards was 4-oxo retinoic acid (RA), retinyl phosphate (RP), 13-*cis* RA, all-*trans* RA, retinol, retinal, retinyl acetate, anhydroretinol, and retinyl palmitate. This method was employed to investigate the *cis-trans* isomerization of RA and its metabolism in vitamin A-sufficient male rats. Rats were injected intraperitoneally with 50 μCi of either [10-^{3}H]-all-*trans* RA or [11-^{3}H]-13-*cis* RA and killed after 0.5 hr and 3 hr. Blood, liver, kidney, small intestines, and testes were removed and lyophilized. All-*trans* RA was converted at 0.5 hr after injection to 13-*cis* RA in all the tissues examined, with the exception of the small intestine; the conversion ranged from 2.4 to 6.9% of the total radioactivity. In addition, all-*trans* RA was converted to metabolites of greater polarity than 4-oxo RA. After 3 hr, most of the radioactivity was found in the highly polar metabolites. 13-*cis* RA was also partially isomerized to the all-*trans* RA and to the highly polar metabolites by 0.5 and 3 hr after injection. Appreciable radioactivity still resided in the 13-*cis* RA fraction after 3 hr. These results indicate that 13-*cis* RA is partially isomerized to all-*trans* RA and that all-*trans* RA is rapidly metabolized to highly polar compounds in tissues of vitamin A-sufficient rats.

EFFECT OF CLINOFIBRATE, A NEW HYPOLIPIDEMIC AGENT, ON BILIARY AND SERUM LIPIDS IN PATIENTS WITH HYPERLIPIDEMIA. N. Takeuchi, H. Kukita, G. Kajiyama, M. Fujiyama, K. Ishikawa, H. Miki, T. Mishima, K. Murata, and T. Asano (Central Laboratory, Ehime Univ. Hospital, Shigenobucho, Ehime 791-02, Japan) *Atherosclerosis 42*:129-139 (1982). Clinofibrate was given to 15 patients with hyperlipidemia, for 6-8 weeks at the daily dose of 600 mg, and its effect on 3 biliary lipid components and on the lithogenic index was investigated. After clinofibrate treatment, 6 of the patients were given 1.5 g/day clofibrate for 6-8 weeks to compare the effect of clofibrate with that of clinofibrate. The molar percentages of biliary cholesterol and phospholipids to the total mol number of the 3 biliary lipid components decreased, and that of bile acids increased during clinofibrate administration. In this way, the molar ratio of bile acids to cholesterol increased during treatment. Neither the lithogenic index calculated by the formula of Admirand and Small nor that of Hegardt, Dam and Holzbach was altered significantly by the treatment. There was no apparent relationship between the effect of the drug on the lithogenic index and any of the factors initial lithogenic index, rate of decrease of serum lipids, or type of hyperlipidemia. Although clofibrate had no significant effect on the maximum solubility of cholesterol in the bile, the molar percentage of biliary cholesterol was elevated and the lithogenic index increased as compared with the control and clinofibrate period. No significant influence of bile acid composition in the bile was observed, with either clinofibrate or clofibrate.

IN VITRO CATABOLISM OF HUMAN PLASMA LOW DENSITY LIPOPROTEINS. EFFECTS OF VLDL CONCENTRATION ON THE INTERCONVERSION OF HIGH DENSITY LIPOPROTEIN SUBFRACTIONS. M.R. Taskinen, M.L. Kashyap, L.S. Srivastava, M. Ashraf, J.D. Johnson, G. Perisutti, D. Brady, C.J. Glueck and R.L. Jackson (Div. of Lipoprotein Res., Depts. of Pharmacology and Cell Biophysics, Biological Chem., Med. and Pathology, Univ. of Cincinnati Med. Center, Cincinnati, OH 45267) *Atherosclerosis 41*(2/3):381-394 (1982). The effect of lipolysis of human plasma very low density lipoproteins (VLDL) on the distribution of high density lipoprotein subfractions was studied in an in vitro system consisting of purified bovine milk lipoprotein lipase and albumin. The distribution of lipids and apoproteins (apoC-II and apoC-III) within the lipoprotein fractions corresponding to HDL_2 (d=1.063-1.120 g/ml) and HDL_3 (d=1.120-1.210 g/ml) was dependent upon the concentration of VLDL in the incubation mixture. After lipolysis of an incubation mixture containing VLDL-triglyceride (0.6 mg triglyceride/ml) and HDL_3 (0.1 mg protein/ml), most of the lipid and apoproteins were recovered in HDL_3. At higher concentrations of VLDL-triglyceride relative to HDL_3-protein (1.8 or 2.4 mg of VLDL-triglyceride and 0.1 mg of HDL_3-protein) the amount of lipid and apoprotein isolated in the HDL_3 density fraction decreased after lipolysis and there was an increase in the amount isolated between d 1.063-1.120 g/ml. These results provide additional evidence for the conversion of HDL_3 to HDL_2 during lipolysis. Furthermore, they suggest that the relative distribution of plasma HDL_2 and HDL_3 is related to the rate of catabolism of triglyceride-rich lipoproteins.

EFFECT OF PANTETHINE ON LIPOPROTEIN PROFILES AND HDL SUBFRACTIONS IN EXPERIMENTALLY HYPERCHOLESTEROLEMIC RABBITS. M. Tomikawa, T. Nakayasu, K. Tawara, K. Kameda, and Y. Abiko (Lab. of Biochem., Res. Inst., Daiichi Seiyaku Co., Ltd., Edogawa-ku, Tokyo 132, Japan) *Atherosclerosis 41*:267-277 (1982). A high-cholesterol diet caused in rabbits a great increase in β-migrating VLDL and a significant decrease in HDL_2 (43% of normal) and HDL_3 masses (64% of normal), without significant changes in HDL cholesterol values. Chemical analysis of the HDL subfractions indicated an abnormal lipid-protein composition in the hypercholesterolemic rabbits, an increase in cholesterol and a decrease in the contents of triglycerides and phospholipid. When these rabbits were treated for about 1 month with pantethine, an intermediate precursor of coenzyme A, the increase in cholesterol levels was effectively prevented in the β-VLDL (11%) and LDL fractions (43%) but, conversely, HDL-cholesterol was significantly increased (151%). In a separate experiment, HDL_2 and HDL_3 masses were calculated to be increased to 186% and 193%, respectively, by pantethine treatment, when compared with those in control cholesterol-fed rabbits. Serum apolipoprotein AI antigen

levels were also significantly increased by the treatment.

THE TURNOVER OF MOLECULAR SPECIES OF PHOSPHATIDYLINOSITOL IN EHRLICH ASCITES TUMOR CELLS. K. Waku, T. Shibata, H. Kato, K. Tsutsui and Y. Nakazawa (Faculty of Pharmaceutical Sciences, Teikyo University, Tsukuigun, Sagamiko, Kanagawa 199-01) *Biochim. Biophys. Acta 710*:39-44 (1982). It has been shown previously that $^{32}P_i$ is incorporated into phosphatidylinositol 30 times faster than into the other phospholipid classes in Ehrlich ascites tumor cells, whereas [1-^{14}C] glycerol is incorporated at almost the same rate. It was therefore suggested that there is a recirculating system (phosphatidylinositol→diacylglycerol→phosphatidic acid→CDP-diacylglycerol→phosphatidylinositol) of phosphatidylinositol in Ehrlich ascites tumor cells. In this work, $^{32}P_i$ or [1-^{3}H] glycerol was injected into the periotoneal cavity of mice bearing Ehrlich ascites tumor cells from which the lipids were extracted after selected periods. Phosphatidylinositol was prepared and fractionated in the form of dimethylphosphatidic acid into six molecular species by $AgNO_3$-impregnated TLC. The specific radioactivities of the fractionated species were determined. $^{32}P_i$ was incorporated into diene molecular species and [1-^{3}H]-glycerol into monoene species with a higher rate than the other species and both precursors were incorporated into tetraene species rather slowly. $^{32}P/^3H$ values appeared to be at almost the same for each molecular species, although monoene species showed slightly lower values. These results suggest that there could be a recirculating of the phosphorylinositol moiety in each of the molecular species of phosphatidylinositol.

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LECITHIN:CHOLESTEROL ACYL TRANSFERRASE AND HIGH DENSITY LIPOPROTEIN LEVEL IN CORONARY ARTERY DISEASE. L. Wallentin and B. Moberg (Dept. of Internal Medicine, Linkoping University Medical School, S-581 85 Linkoping (Sweden)) *Atherosclerosis 41*(2/3):155-165 (1982). The lecithin:cholesterol acyl transfer (LCAT) reaction occurs in connection with the high density lipoproteins (HDL) and might have importance for the development of atheromatosis. The LCAT rate and the lipoprotein concentrations in plasma were determined in 82 patients, 40-60 years old, with incapacitating angina pectoris and significant lesions at coronary angiography. 38 cases were normolipidemic and 22 had type IV hyperlipidemia while the others had different types of hypercholesterolemia (n=7) or were pharmacologically treated for previously diagnosed hyperlipidemia (n=11) or diabetes mellitus. The normolipidemic group and the type IV group with coronary artery disease were separately compared to one normolipidemic (n=44) and one type IV hyperlipidemic (n=29) control group of healthy subjects of about the same age. The fractional LCAT rate was lower in patients compared to controls both regarding the normolipidemic and type IV subjects. The molar LCAT rate did not differ between normolipidemic cases and controls while it was lower in type IV patients with coronary artery disease than in the type IV controls. The HDL total cholesterol (TC) concentration and the HDL-TC/TC ratio were lower in normolipidemic cases than in normolipidemic controls while both cases and controls with type IV hyperlipidemia showed equally low levels of these parameters. In conclusion, both a reduced fractional LCAT rate and a decreased HDL-TC/TC ratio might be indicators of disturbances of the cholesterol ester metabolism and might contribute to the development of the coronary atheromatosis.

EFFECTS OF INSULIN ON PLASMA LIPOPROTEINS IN DIABETIC KETOACIDOSIS: EVIDENCE FOR A CHANGE IN HIGH DENSITY LIPOPROTEIN COMPOSITION DURING TREATMENT. S.W. Weidman, J.B. Ragland, J.N. Fisher, A.E. Kitabchi, and S.M. Sabesin (Divisions of Gastroenterology and Endocrinology and Metabolism, Dept. of Medicine, Univ. of Tennessee Center for the Health Sciences, Memphis, TN 38163) *J. Lipid Res. 23*(1):171-182 (1982). To determine the acute effects of insulin on lipoprotein metabolism, we have followed the plasma lipoprotein lipid and apolipoprotein levels during insulin therapy for the first 24 hr in 13 patients with diabetic ketoacidosis. Corrections were made for plasma volume changes during treatment. Before insulin treatment, mean plasma triglyceride and cholesterol levels were 574 mg/dl and 212 mg/dl respectively. Insulin therapy resulted in rapid decreases in triglyceride-rich lipoproteins, chylomicrons, and very low density lipoproteins (VLDL). Mean basal levels of intermediate density lipoproteins (IDL) and low density lipoproteins (LDL)-cholesterol were low and were statistically invariant with therapy. Mean basal levels of high density lipoprotein (HDL) cholesterol were also low and were invariant during the first 12 hr and increased significantly by the 24th hr. Plasma lipoprotein (apo) B levels were in the upper normal range before treatment and decreased with therapy due to significant decreases in VLDL but not IDL or LDL apoB. VLDL appeared to have a normal apoprotein composition which did not change with treatment. Mean apoA-I levels which were near normal in plasma and HDL before therapy, decreased significantly by 12 hr and subsequently increased towards basal levels between 12 and 24 hr. The ratio of apoA-I to cholesterol in HDL also fell significantly during the entire 24 hr. Density gradient ultracentrifugal analysis of the d>1.006 g/ml fractions of HDL-apoA-I during treatment. These results provide evidence that insulin may decrease the secretion of apoA-I into plasma or increase catabolism.

ARTERIAL CHOLESTEROL AND DNA CONTENTS IN RELATION TO SERUM LIPIDS AND APOLIPOPROTEINS. O. Wiklund, J.G. Kral, L. Lindblad, S. Olefsson, T. Schersten, L. Sjostrom, and G. Bondjers (Arterial Biol. Group, Dept. of Med. I and Dept. of Med. Biochem. and Dept. of Surgery, Sahlgren's Hospital, Univ. of Goteborg, Goteborg, Sweden) *Atherosclerosis 41*:247-253 (1982). Though various relationships between serum lipoprotein levels and risk for atherosclerotic disease have been shown there are only a few studies on the relationships between serum lipoprotein levels and the lipid contents of the arterial wall. This study presents cholesterol and DNA contents of arterial tissue from biopsies of the cystic artery in 23 patients with uncomplicated cholecystolithiasis. Serum levels of cholesterol, triglycerides, alphalipoprotein cholesterol, apoA-I, A-II and B were determined, and the relationships between artery and serum variables were calculated. There was a positive correlation between serum apoB and the arterial cholesterol, normalized to the DNA contents (r=0.43, $P<0.05$). There was a tendency towards an inverse correlation between the *q*-lipoprotein cholesterol levels and the arterial cholesterol (r=0.39, $P<0.10$). There were no significant correlations between serum apoA-I or A-II and the arterial cholesterol contents. These data indicate that deposition of cholesterol in the arterial wall is related to the serum level of apoB, with higher levels of arterial cholesterol at higher serum levels of apoB. Earlier observations of an inverse correlation between alphalipoprotein cholesterol and arterial cholesterol could, however, not be conclusively confirmed.

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