Abstracts

• Biochemistry and Nutrition

EFFECT OF CHOLESTEROL FEEDING ON ARTERIAL LIPOLYTIC ACTIVITY IN THE RABBIT. J.E. Corey and D.B. Zilversmit (Div. of Nutr. Sci.; and Section of Biochem., Molecular and Cell Biol., Div. of Biol. Sci., Cornell Univ., Ithaca, N.Y.). *Atherosclerosis* 27, 201–12 (1977). Two trioleoyl glycerol hydrolases, one of lysosomal origin as determined by a high correlation with the lysosomal marker enzyme, N-acetyl-β-glucosaminidase, and one having the characteristics of lipoprotein lipase, were measured at varying stages of lesion development in the aortas of cholesterol-fed rabbits. Both lipases were greatly enhanced in atheromatous aortas and were linearly related to lesion severity as measured by total aortic cholesterol. Lipoprotein lipase activities of myocardium and of plasma of cholesterol-fed rabbits were also significantly increased relative to controls. The data suggest that lipoprotein lipase might be a factor regulating cholesterol deposition in the aorta.

LACK OF COMPETITION BETWEEN PHOSPHATIDYLCHOLINE AND PHOSPHATIDYLETHANOLAMINE SYNTHESIS IN THE MEMBRANES OF ENTODINIUM CAUDATUM. R.M.C. Dawson and A. Letcher (Biochem. Dept., A.R.C. Inst. of Animal Physio., Babraham, Cambridge CB2 4AT, England). *FEBS Letters* 77, 179–81 (1977). Recent evidence indicates that in higher plants, phosphatidylethanolamine synthesis from CDP-ethanolamine and phosphatidylcholine synthesis from CDP-choline are catalysed by a common enzyme. Studies on the kinetics of CDP-choline inhibition of ethanolamine phosphotransferase in castor bean endosperm have also suggested that a single enzyme utilizes both nucleotide substrates. During recent studies in which we have been investigating relationships between macromolecule synthesis during membrane turnover in the anaerobic protozoon *Entodinium caudatum* we have attempted to change the rate of synthesis of individual macromolecules by specific methods which would not directly affect the synthesis of other macromolecules. Thus we have markedly varied the rate of synthesis of phosphatidylcholine by altering the CDP-choline concentration without in any way affecting the synthesis of phosphatidylethanolamine. This argues strongly against a single choline (ethanolamine) phosphotransferase operating in the organism.

INTERACTION OF CHOLESTEROL ESTER AND TRIGLYCERIDE IN HUMAN PLASMA VERY LOW DENSITY LIPOPROTEIN. R.J. Deckelbaum, A.R. Tall, and D.M. Small (Dept. of Med., Boston Univ. Schl. of Med., Boston, MA 02118). *J. Lipid Res.* 18, 164–8 (1977). The properties of human plasma very low density lipoproteins (VLDL), and their extracted lipids were compared using calorimetric, X-ray scattering, and polarizing microscopy techniques. Intact LDL, and cholesterol esters isolated from LDL and VLDL each undergo reversible changes in their physical state around body temperature. These transitions are associated with ordered liquid crystalline to liquid phase changes of the cholesterol esters. In contrast to LDL, VLDL has no reversible transitions and shows no evidence of ordered liquid crystalline structures between 10 and 45°C. Therefore, unlike LDL, VLDL does not contain a separate cholesterol ester region capable of undergoing cooperative melting. Solubility studies at 37°C of cholesterol esters and triglyceride isolated from VLDL show that even at a weight ratio of 1:1, which greatly exceeds the relative amount of cholesterol esters in VLDL, cholesterol ester is completely soluble in triglyceride. Thus, the cholesterol ester in VLDL is not sequestered in a separate domain within VLDL, but is dissolved in the liquid core of the particle.

CHARACTERIZATION OF TWO TRIACYLGLYCEROL LIPASE ACTIVITIES IN PIG POST-HEPARIN PLASMA. C. Ehnholm, A. Bensadoun and W.V. Brown (Dept. of Med., Schl. of Med., Univ. of Calif., San Diego, La Jolla, CA). *Biochem. J.* 163, 347–55 (1977). Two triacylglycerol lipase activities were characterized after partial purification from pig post-heparin plasma. These two lipase activities were eluted sequentially with a NaCl gradient from columns containing Sepharose with covalently linked heparin. The first lipase activity, which was eluted at 0.75M-NaCl, was not inhibited at 28°C in the presence of 1M-NaCl and was not further activated by plasma apolipoproteins. The absence of this lipase activity from post-heparin plasma from hepatectomized pigs indicates that the liver plays a role in the synthesis of this enzyme. A second lipase activity, which was eluted at 1.2M-NaCl was inhibited when assayed in the presence of 1.0M-NaCl and was activated 14-fold by an apolipoprotein isolated from human very-low-density lipoprotein. The characteristics are identical with those of lipoprotein lipase purified from pig adipose tissue.

HEPARIN-INDUCED RELEASE OF LIPASE ACTIVITY IN THE HUMAN FOREARM. AN IMMUNOLOGICAL STUDY. C. Ehnholm, D.J. Heaf, L. Kaijser, P.K.J. Kinnunen and L.A. Carlson (King Gustaf V Res. Inst., S-104 01 Stockholm, Sweden) *Atherosclerosis* 27, 35–9 (1977). Low doses of heparin were injected into the brachial artery of three volunteers. The lipase activities in the deep vein of the same forearm, draining mainly muscle tissue, and in the artery were monitored over a 10-min. period. Lipase activity, rapidly released by heparin in the deep vein, was immunologically similar to lipoprotein lipase (E.C. 3.1.1.3.), i.e. (1) it did not react with antiserum against human post-heparin plasma hepatic lipase and (2) it was inhibited by an antiserum against bovine milk lipoprotein lipase, which cross reacts with human post-heparin plasma lipoprotein lipase. The evidence that human muscle contains lipoprotein lipase is discussed.

BENEFICIAL EFFECTS OF ARACHIDONIC ACID DURING HEMORRHAGIC SHOCK IN THE DOG. J.T. Flynn and A.M. Lefer (Dept. of Physiology, Jefferson Med. College, Thomas Jefferson Univ., Philadelphia, Pa.). *Circulation Res.* 40, 422–8 (1977). Arachidonic acid (AA), precursor of the bisenoic prostaglandins was infused at a rate of 120 μg/kg per min into the vena cava of dogs subjected to hemorrhagic shock to assess the effects of stimulation of the prostaglandin (PG) synthetase system on the shock state. Hemorrhagic shock was induced by bleeding to a mean arterial blood pressure (MABP) of 40 mm Hg for 150 minutes followed by reinfusion of all remaining shed blood. Hemorrhagic shock dogs receiving AA plus Na meclofenamate, a PG synthetase inhibitor, were not significantly different from shock dogs receiving vehicle except that the circulating PG concentrations did not increase. Thus, products of the PG synthetase system appear to prevent the plasma accummulation of lysosomal hydrolases and of MDF, and may significantly preserve MABP after hemorrhagic shock in the dog.

HEPATIC TRIGLYCERIDE LIPASE DEFICIENCY IN LIVER DISEASE. M. Freeman, L. Kuiken, J.B. Ragland and S.M. Sabesin (Div. of Gastroenterology, Dept. of Med., Univ. of Tenn, Cntr. for the Health Sci. and Veterans Admin. Hos., Memphis, Tenn.). *Lipids* 12, 443–5 (1977). The activity of post-heparin lipases in patients with alcoholic hepatitis and viral hepatitis was evaluated. Lipoprotein lipase and hepatic triglyceride lipase were differentiated by assay under high and low salt conditions and also by separation on heparin-agarose affinity chromatography columns. The mean activity of hepatic triglyceride lipase in the sera of liver disease patients was only 21–24% of the mean of controls, but lipoprotein lipase in patients' sera was not different from normal levels. Hepatic triglyceride lipase deficiency may partially account for the accumulation of a triglyceride-rich low density lipoprotein in liver disease.

BIOSYNTHESIS OF UNSATURATED FATTY ACIDS BY BACILLI. D.K. Fujii and A.J. Fulco (Dept. of Biol. Chem., UCLA Schl. of Med, Univ. of California, Los Angeles, Ca.). *J. Biol. Chem.* 252, 3660–70 (1977). Significant relationships have been established between the initiation and rate of fatty acid Δ^5-desaturase synthesis in *Bacillus megaterium* ATCC 14581 and

controlled perturbations in culture temperature, cell growth, protein synthesis, and RNA synthesis. *B. megaterium* growing from inoculum at 35° contained neither unsaturated fatty acids nor the Δ^5-desaturase responsible for their production. When the culture temperature was lowered rapidly to 20°, synthesis of desaturase began within 5 min, attained a maximum rate at about 15 min, and continued at this high rate for up to 90 min after the shift to 20°. This "hyperinduction" process, so-called because the rate of desaturase synthesis after culture transfer from 35° to 20° far exceeded the rate found in comparable cultures growing from inoculum at 20°, was dependent on protein synthesis and RNA synthesis initiated after transfer. The data were consistent with the hypothesis that the active modulator was an oligomeric protein in equilibrium with an inactive monomeric precursor and that the modulator may act at the level of transcription by selectively inhibiting the synthesis of the messenger RNA coding for the desaturase.

ENERGETIC EFFICIENCY OF DIFFERENT DIETARY FATS FOR GROWTH OF YOUNG CHICKS. H.L. Fuller and M. Rendon (Dept. of Poultry Sci., Univ. of Georgia, Athens, Ga.). *Poultry Sci.* **56,** 549–57 (1977). Two experiments were conducted to determine the energetic efficiency of diets containing different feed grade fats for the growth of broiler chicks during the finishing period. The fats were added to the basal diets replacing equicaloric amounts of glucose, based upon metabolizable energy (M.E.) thus increasing the energy and nutrient density of the diet but maintaining the same M.E.: nutrient ratios. Fats tested were corn oil, palm oil, acidulated cotton seed soapstock (A.C.S.S.), coconut oil, tallow, poultry fat, and feed grade animal fat (F.G.A.F.). In one trial all fats were tested at one level (11.6%) and in the second trial all fats except A.C.S.S. and coconut oil were tested at levels of 10 and 20%. Body balance was used to partition gross energy (G.E.) consumed in an effort to estimate the heat increment (H.I.) of the fat supplemented diets. All fats except A.C.S.S. and coconut oil improved weight gains of chicks in one trial but not in the other.

EFFECTS OF FREE FATTY ACIDS ON ACTIVITY OF HEPATIC MICROSOMAL 3-HYDROXY-3-METHYLGLUTARYL COENZYME A REDUCTASE AND ON SECRETION OF TRIGLYCERIDE AND CHOLESTEROL BY LIVER. E.H. Goh and M. Heimberg (Dept. of Pharmacology, Univ. of Missouri Schl. of Med., Columbia, Mo.). *J. Biol. Chem.* **252,** 2822–6 (1977). The output of triglyceride and cholesterol, and the activity of microsomal 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA reductase) were measured following perfusion of the isolated rat liver with a medium containing free fatty acids. The activity of the enzyme and the output of cholesterol and triglyceride are regulated by the quantity and structure of the free fatty acid. The activity of HMG-CoA reductase was linearly proportional to uptake of oleic acid (18:1) by the liver. Output of triglyceride and cholesterol in the presence of oleate was also stimulated although, under these experimental conditions, the maximal secretory rate for cholesterol was observed while reductase activity was still increasing.

COMPARISON OF HYPOCHOLESTEROLEMIC ACTIVITY FOR CYCLIC ANALOGS OF CLOFIBRATE IN NORMOLIPEMIC RATS. A.P. Goldberg, W.S. Mellon, D.T. Witiak and D.R. Feller (Div. of Pharmacology and Med. Chem., College of Pharmacy, The Ohio State Univ., Columbus, Ohio). *Atherosclerosis* **27,** 15–25 (1977). Chronic administration of ethyl 2-methyl-2-(4-chlorophenoxy)-propionate [clofibrate, CPIB], ethyl 6-cyclohexylchroman-2-carboxylate, and ethyl 6-phenylchroman-2-carboxylate to normolipemic rats, in vivo, reduced serum cholesterol levels and inhibited the activity of hepatic 3-hydroxy-3-methylglutaryl Coenzyme A. Only clofibrate was found to lower liver cholesterol content after pretreatment for 4 or 18 days. The cyclic analogs, ethyl 6-chlorochromone-2-carboxylate and 9-chloro-2,3-dihydro-5H-1,4-dioxepino [6,5-b] benzofuran were ineffective as cholesterol lowering agents in normolipemic rats. These findings indicate that appropriate modification of clofibrate can lead to the development of compounds which are selective and equally effective to clofibrate as potential hypocholesterolemic agents. Results obtained in these studies are also discussed in terms of the known structural requirements of biological activity for this series of cyclic analogs in the Triton WR-1339 hyperlipemic rat model and modes of action of the parent compound.

COMPARISON OF ASSAY METHODS FOR SELECTIVE MEASUREMENT OF PLASMA LIPASE. H. Greten, V. Laible, G. Zipperle and J. Augustin (Klinisches Inst. für Herzinfarktforschung an der Medizinischen, Univ. Heidelberg, Heidelberg, West Germany). *Atherosclerosis* **26,** 563–72 (1977). Three different assays for selective measurement of plasma lipoprotein lipase (LPL) and hepatic triglyceride lipase (H-TGL) were compared. These were: an immunochemical method based on enzyme antibody precipitation (IM), a procedure in which both enzymes were separated by affinity chromatography on small heparin-Sepharose columns (HS), and an assay in which one enzyme was inhibited by protamine sulfate (PS). Good correlations were found between the immunochemical and the heparin-Sepharose method, but not between these and the protamine sulfate assay procedure. The magnitude of the LPL response was different in normals and in patients with endogenous hyperlipoproteinemia. Furthermore, in normals the maximal increase of LPL activity was already reached one week after drug treatment was begun, while in hypertriglyceridemic patients, this effect was not evident prior to four weeks of clofibrate treatment. The marked enzyme increase following clofibrate administration indicates that an increased peripheral removal rate for triglycerides is one major mechanism responsible for the lipid-lowering effect of this drug.

EFFECT OF FASTING AND FEEDING A HIGH-SUCROSE, FAT-FREE DIET ON THE SYNTHESIS OF HEPATIC GLYCEROLIPIDS IN VIVO AND IN ISOLATED HEPATOCYTES. J.E.M. Groener and L.M.G. Van Golde (Lab. of Vet. Biochem., St. Univ. Utrecht, Utrecht, The Netherlands). *Biochim. Biophys. Acta* **487,** 105–14 (1977). The synthesis of glycerolipids from a number of radioactive precursors, such as [2-^{3}H]glycerol, [^{32}P]phosphate, [*Me*-^{14}C] choline and [1,2-$^{14}C_2$]ethanolamine proceeds in enzymatically isolated hepatocytes with a specificity that agrees very well with that observed in the liver in vivo. The nutritional state of the rat has a profound influence on the glycerolipid metabolism of isolated hepatocytes. Fasting strongly decreased the incorporation of glycerol via *sn*-glycerol 3-phosphate into triacylglycerols whereas the formation of phosphatidylcholine and, particularly, phosphatidyl-ethanolamine was much less affected by food deprivation. Refeeding caused a significant increase in the formation and amount of phosphatidylcholine. The amount of phosphatidylethanolamine was even further diminished by feeding a high-sucrose, fat-free diet to 48-h-fasted rats. These results show that the alterations, induced in the in vivo metabolism of hepatic glycerolipids, by changes of the dietary state, are also reflected in the isolated hepatocytes. This finding strengthens the potential significance of isolated hepatocytes in studies on the regulation of hepatic lipid metabolism.

DETERMINATION OF CHOLESTEROL ABSORPTION IN MAN BY INTESTINAL PERFUSION. S.M. Grundy and H.Y.I. Mok (Dept. of Med., School of Med., Univ. of California, San Diego, Ca.). *J. Lipid Res.* **18,** 263–71 (1977). In this study a technique is described for estimating net absorption of total cholesterol (endogenous + exogenous) that enters the intestine. The method employs intubation of patients with a 3-lumen tube that contains a 10-cm mixing segment in the duodenum and a 100-cm absorption segment in the jejunum. A liquid formula diet containing varying amounts of exogenous cholesterol is infused continuously into the upper duodenum for a period of several hours; the formula diet stimulates constant contraction of the gallbladder and thus provides for continuous secretion of biliary cholesterol into the duodenum. Through constant infusion of β-sitosterol as a marker, the input of endogenous + exogenous cholesterol can be measured at the end of the 10-cm mixing segment. Net cholesterol absorption is estimated from the disappearance of cholesterol relative to β-sitosterol over the next 100-cm of jejunum.

INFLUENCE OF DIETARY STATUS AND DIABETES ON AORTIC ACYL-CoA HYDROLASE ACTIVITY. S. Hashimoto and S. Dayton (Res. Serv. and Med. Serv., VA Wadsworth Hosp. Center, Los Angeles, Calif. 90073) *Atherosclerosis* **26,** 289–96 (1977). We have postulated that the accelerated synthesis of cholesteryl ester in atherosclerotic microsomes may result in part from decreased acyl-CoA hydrolase activity in arterial tissue, because acyl-CoA is a common substrate for both reactions. We have now investigated the influence of nutritional status, type of diet, and diabetes on the acyl-CoA hydrolase activity of otherwise normal aortic microsomes. Aortic preparations of rats made diabetic by streptozotocin exhibited higher acyl-CoA hydrolase activity than the normal. The results show that conditions associated with human atherogenesis (diabetes and saturated fat diet) increase rather than suppress the activity of this arterial enzyme in normal arterial tissues of the rat.

INCORPORATION OF [^{14}]ARACHIDONATE IN PIG THYROID LIPIDS AND

PROSTAGLANDINS. B. Haye and C. Jacquemin (Lab. Biochem., U.E.R. Sciences, Reims-Cedex, France). *Biochim. Biophys. Acta* **487**, 231–42 (1977). In pig and sheep thyroid, the arachidonate content of phosphatidylinositol (14.3–17.5%) is much higher than in the other phospholipids. In the thyroid, phosphatidylinositol seems to play an important role in the biosynthesis of prostaglandins. In neutral thyroid lipids, the arachidonate content is much higher in diacylglycerols (15.8%) than in monoacylglycerols (2.9%) or triacylglycerols (4.2%). However, the most important pool of esterified arachidonate is triacylglycerols (1030 nmol of arachidonate/g tissue). Arachidonate represents a very small part of total free fatty acids measured in the presence of albumin and indomethacin (0.65% or 16.4 nmol/g tissue). Thyrotropin (50 munits/ml) causes after 1 h a 2-fold increase in the level of free arachidonate (37.3 nmol/g tissue). Slices and homogenates of pig thyroid weakly convert [^{14}C]arachidonate to prostaglandins E_2 and $F_{2\alpha}$ (1–2%). Thyrotropin (50 munits/ml) always diminishes the conversion of radioactivity to prostaglandins as compared with standard incubation. This result is compatible with the above-mentioned hypothesis.

BOVINE MILK XANTHINE OXIDASE, BLOOD LIPIDS AND CORONARY PLAQUES IN RABBITS. C.Y. Ho and A.J. Clifford (Dept. of Nutr., Univ. of California, Davis, Ca.) *J. Nutr.* **107**, 758–66 (1977). The effects of prolonged intravenous administration of bovine milk xanthine oxidase (EC 1.2.3.2) on blood lipids and arterial integrity were measured to determine if the administration of this enzyme produces metabolic changes conducive to plaque formation. New Zealand White rabbits were injected intravenously with bovine milk xanthine oxidase at 4-day intervals during a 13-week test period. At the end of the test period, the rabbits were killed and blood, heart, aorta, liver, and kidneys were collected and evaluated. Although xanthine oxidase activity was found in liver from all rabbits, enzyme activity was not detectable in aorta, heart or kidneys from any rabbit. The study showed that when large intravenous doses of bovine milk xanthine oxidase were given to rabbits, the enzyme was not deposited in heart, aorta, liver or kidneys. The study also showed that large intravenous doses of xanthine oxidase over prolonged periods did not deplete arterial or coronary tissue plasmalogens, and did not induce arterial plaque formation.

DESATURATION OF BILE AND CHOLESTEROL GALLSTONE DISSOLUTION WITH CHENODEOXYCHOLIC ACID. A.F. Hofmann (Mayo Clinic and Mayo Foundation, Rochester, Minn.). *Am. J. Clin. Nutr.* **30**, 993–1000 (1977). The feeding of one of the major biliary bile acids, chenodeoxycholic acid, at a dose of 10 to 15 mg/kg per day causes the circulating bile acid pool to become greatly enriched in this bile acid. When chenodeoxycholic acid composes more than 70% of the biliary bile acids, the amount of cholesterol secreted in bile falls, and bile becomes unsaturated in cholesterol. If cholesterol gallstones are present and are exposed to this unsaturated bile, they will dissolve in 4 to 24 months in the majority of patients. Extensive clinical experience indicates that such medical therapy is safe, despite unequivocal toxicity of chenodeoxycholic acid in several nonhuman primates. When therapy is stopped, bile resaturates, and stones may recur. Since cholecystecomy is a rapid, safe, effective, and usually permanent treatment for all gallstones, the value of medical therapy remains uncertain at present, except for patients in whom surgery is inadvisable. Nonetheless, the demonstration that chenodeoxycholic acid ingestion will desaturate bile and induce gallstone dissolution would appear to be an important pharmacological advance.

CELLULARITY OF PORCINE ADIPOSE TISSUE: EFFECTS OF GROWTH AND ADIPOSITY. R.L. Hood and C.E. Allen (CSIRO, Div. of Food Res., North Ryde, New South Wales, Australia). *J. Lipid Res.* **18**, 275–84 (1977). Adipose tissue, from two depots in pigs of three breeding groups with different propensities to fatten, was characterized in terms of weight of the adipose tissue organ, adipose cell number, and mean cell volume as determined by electronic counting of adipose cells fixed with osmium tetroxide. Perirenal and extramuscular adipose tissue growth was accompanied by progressive adipose cell enlargement along with an increase in cell number. By approximately 18–20 weeks of life, adipose tissue growth in both lean Hampshire × Yorkshire and fat Minnesota 3 × 1 pigs occurred exclusively by cellular hypertrophy. By 24 weeks of life (37 kg), hyperplasia was complete in Hormel Miniature pigs, which contained about one-third as many extramuscular adipose cells as the conventional pigs. In young animals (28 and 54 kg), growth rate was positively correlated with adipose cell number. However, growth rate was unrelated to the total number of cells in the more mature animals (83 and 109 kg). Therefore a slow, normal growth rate may delay but not alter the final cell number.

INFLUENCE OF ELAIDATE AND ERUCATE ON HEART MITOCHONDRIA. C.M.L. Hsu and F.A. Kummerow (Burnsides Res. Lab., Univ. of Illinois, Urbana, IL). *Lipids* **12**, 486–94 (1977). Male, weanling rats were fed, for up to six weeks, corn oil (CO), rapeseed oil (RSO), partially hydrogenated fat (HF), or a mixture of partially hydrogenated fat and corn oil (HF + CO). The respiratory activity of their isolated heart mitochondria, their hormone-sensitive lipase activity, and the fatty acid compositions of the phospholipids of the mitochondria were determined. The results indicated that heart mitochondria isolated from the rats which had been fed corn oil (CO) had a higher rate of oxygen uptake, showed higher respiratory control ratios, higher ADP/O ratios and a higher rate of ATP synthesis than those fed rapeseed oil or hydrogenated fats. The substrate preference for lipase activity in myocardium was corn oil-triglycerides > trierucin > trielaidin > tripalmitin. However, cardiac lipid accumulation did not seem related to lipase activity in the myocardium.

INFLUENCE OF DIETARY TRANS-FATTY ACIDS ON SWINE LIPOPROTEIN COMPOSITION AND STRUCTURE. R.L. Jackson, J.D. Morrisett, H.J. Pownall, A.M. Gotto, Jr., A.K. Kamio, H. Imai, R. Tracy, and F.A. Kummerow (Dept. of Med., Baylor Coll. of Med. and the Methodist Hosp., Houston, TX 77030). *J. Lipid Res.* **18**, 182–90 (1977). Four groups of 20 weanling swine each were fed either (a) basal diet, (b) basal plus hydrogenated fat (13% *trans*), (c) basal plus hydrogenated fat (13% *trans*) and 0.4% cholesterol, or (d) basal plus beef tallow (all *cis*). After six months of feeding, the animals were killed and the blood and aortas were removed. Very low density, low density, and high density lipoproteins were then isolated from the plasma by ultracentrifugal flotation. Although the fatty acid composition of the basal diet was different from the diets supplemented with either hydrogenated fat containing *trans*-fatty acid or beef tallow containing all *cis*, the lipid and fatty acid compositions of each of the isolated lipoprotein classes for the four groups of animals were remarkably similar. These studies demonstrate that a diet containing a substantial amount of *trans*-fatty acid leads to a small but defenite incorporation into the swine lipoproteins. However, such changes had relatively little effect on lipoprotein structure or the presence of atherosclerotic lesions in these 6-month-old swine.

INTERRELATIONSHIP BETWEEN THE DIETARY REGULATION OF FATTY ACID SYNTHESIS AND THE FATTY ACYL-CoA DESATURASES. R. Jeffcoat and A.T. James (Basic Studies Unit, Biosciences Div., Unilever Res., Colworth/Welwyn Lab., Sharnbrook, Bedford, U.K.) *Lipids* **12**, 469–74 (1977). In this paper we present further evidence for the close control of fatty acid synthetase and stearoyl-CoA desaturase. Furthermore, we have established that whereas dietary palmitic acid may influence the activity of this desaturase but not of fatty acid synthetase, dietary linoleic acid appears to control both these enzymes. Finally, we have studied the influence of dietary fat and carbohydrate on the activities of the Δ^6 and Δ^5 desaturases. The former is only slightly affected by these dietary components. The Δ^5 desaturase activity is stimulated as the dietary fat content rises but is unaffected by dietary carbohydrate. The control of these enzymes is therefore independent of the control of fatty acid synthetase and stearoyl-CoA desaturase. From the data presented, the magnitude of the controlling effect of polyunsaturated fatty acids on fatty acid synthetase and stearoyl-CoA desaturase activity is determined and its relevance to lipogenesis in man based on daily intake of carbohydrate and linoleic acid is discussed.

INTERACTION OF HUMAN AND BOVINE A-I APOLIPOPROTEINS WITH L-α-DIMYRISTOYL PHOSPHATIDYLCHOLINE AND L-α-MYRISTOYL LYSOPHOSPHATIDYLCHOLINE. A. Jonas and D.J. Krajnovich (Dept. of Biochem., Schl. of Basic Med. Sci., and Schl. of Chem. Sci., Univ. of Illinois, Urbana, Il). *J. Biol. Chem.* **252**, 2194–9 (1977). The major protein components from human and bovine high density serum lipoproteins (apo-A-I proteins) were investigated in their interactions with L-α-myristoyl lysophosphatidylcholine and L-α-dimyristoyl phosphatidylcholine. Complex formation was followed at 25° by observing changes in fluorescence polarization, rotational relaxation times (*ph*), and CD spectra of the proteins, covalently labeled with fluorescent dimethylaminonaphthalene sulfonyl groups. With

L-α-dimyristoyl phosphatidylcholine the complexes are different from those formed with the lysophospholipid. They have limiting *ph* values of 250 ± 50 and 280 ± 60 ns with the human and bovine proteins, respectively. These *ph* values are consistent with particles of the general size of human high density lipoprotein rather than of liposomes and indicate the formation of distinct, relatively small structures upon interaction of the self-associated lipid with the apo-A-I proteins.

DIETARY CONTROL OF THE CHAIN ELONGATION OF PALMITYL-COA IN RAT LIVER MICROSOMES. Y. Kawashima, Y. Suzuki and Y. Hashimoto (Pharmaceutical Institute, Tohoku Univ., Aobayama, Sendai, Japan). *Lipids* 12, 434–7 (1977). The rate of chain elongation of palmityl-CoA to stearyl-CoA in rat liver microsomes was studied in connection with the nutritional status of the rats. The microsomal chain elongation activity, which had been decreased by starvation for 48 hr, was rapidly increased to a high level on refeeding. The apparent Km value for malonyl-CoA in both normal and refed rats was the same, 1.2×10^{-4} M. Both cycloheximide and actinomycin D prevented the induction of microsomal chain elongation activity which was associated with refeeding. In addition, the activity of acyl-CoA hydrolase and the rates of esterification of acyl-CoA into phospholipids and neutral lipids in microsomes were not changed by the dietary alteration. These results support the conclusion that changes of the activity of microsomal chain elongation of palmityl-CoA in various nutritional status result from a rapid synthesis of new enzyme(s).

THE EFFECTS OF SUPPLEMENTAL DIETARY CHOLESTEROL AND EXERCISE ON BLOOD CHOLESTEROL AND ATHEROSCLEROSIS IN THE GOAT. M.D. Kenealy, N.L. Jacobson, and K.D. Wiggers (Dept. of Animal Sci., Iowa State Univ., Ames, Iowa). *Atherosclerosis* 27, 65–9 (1977). The objective of this experiment was to determine the effects of supplemental dietary cholesterol and treadmill exercise on blood plasma cholesterol and development of atherosclerosis in young goats. Eighteen two-week-old goats, assigned to four groups for 22 weeks, were fed 100 g whole milk and, after 14 weeks, 50 g corn and cob meal daily/kg body weight. The four groups received, respectively, 250, 175, 100 and 25 mg cholesterol/kg body weight daily in the milk. From week 10 to week 22 of the experiment half of the goats in each group were exercised on a motorized treadmill at a rate of 6.4 km/h for 15 min daily, five days per week. Six males, three exercised and three nonexercised, were sacrificed; all had extensive aortic sudanophilia. Histological preparations from sudanophilic areas of all aortas showed areas of intimal thickening composed of foam cells. These same areas stained strongly for lipid with Oil Red 0. No histological evidence of calcium deposition or fibrous plaques was found.

EFFECTS OF TEMPERATURE AND BOVINE SERUM ALBUMIN ON LYSIS OF ERYTHROCYTES INDUCED BY DILAUROYLGLYCEROPHOSPHOCHOLINE AND DIDECANOYLGLYCEROPHOSPHOCHOLINE. T. Kitagawa, Y. Tanaka, K. Inoue and S. Nojima (Dept. of Health Chem., Faculty of Pharmaceutical Sci., Univ. of Tokyo, Bunkyo-ku, Tokyo). *Biochim. Biophys. Acta.* 467, 137–45 (1977). The effects of the incubation temperature and bovine serum albumin on hemolysis induced by short-chain phosphatidylcholine were examined. The rate of hemolysis of human, monkey, rabbit, and rat erythrocytes by dilauroylglycerophosphocholine showed biphasic temperature-dependence: hemolysis was rapid at 5–10°C and above 40°C, but slow at around 25°C. In contrast, the rate of lysis of cow, calf, sheep, pig, cat, and dog erythrocytes did not show biphasic temperature-dependence, but increased progressively with increase in the incubation temperature. Bovine serum albumin increased the hemolysis of human erythrocytes induced by dilauroylglycerophosphocholine or didecanoylglycerophosphocholine: it shortened the lag time of lysis and reduced the amount of phosphatidylcholine required for lysis. A shift-down of the incubation temperature from 40 to below 10°C also shortened the lag time of lysis of human erythrocytes induced by dilauroylglycerophosphocholine and reduced the amount of phosphatidylcholine required for lysis.

EXPERIMENTAL ATHEROSCLEROSIS IN RABBITS FED CHOLESTEROL-FREE DIETS. PART 7. INTERACTION OF ANIMAL OR VEGETABLE PROTEIN WITH FIBER. D. Kritchevsky, S.A. Tepper, D.E. Williams and J.A. Story. (The Wistar Inst. of Anatomy and Bio., 36th Str. at Spruce, Philadelphia, Pa.). *Atherosclerosis* 26, 397–402 (1977). Rabbits were maintained for 10 months on a semipurified, cholesterol-free atherogenic regimen. All diets contained sucrose (40%) and hydrogenated coconut oil (14%). The protein (25%) was either casein or soya protein and the fiber (15%) was either wheat straw, alfalfa, or cellulose. Within either protein group the order for induction of cholesteremia was cellulose-wheat straw > alfalfa. For atherogenesis, the effect was cellulose > wheat straw > alfalfa. Soya-wheat straw or soya-cellulose diets were less cholesteremic and atherogenic than their casein counterparts. When alfalfa was the fiber, the two types of protein were almost equivalent. Our results show that casein may be more cholesteremic and atherogenic than soya protein under certain conditions (cellulose or wheat straw as fiber) but the addition of alfalfa to the diet renders the two proteins equivalent.

A SIMPLE METHOD FOR THE PREPARATION OF HOMOGENEOUS PHOSPHOLIPID VESICLES. Y. Barenholz, D. Gibbes, B.J. Litman, J. Goll, T.E. Thompson and F.D. Carlson (Dept. of Biochem., Univ. of Virginia Schl. of Med., Charlottesville, Va.). *Biochemistry* 16, 2806–10 (1977). A new method is described for the preparation of homogeneously sized, single-lamellar phospholipid vesicles. This method, which is based on differential high-speed ultracentrifugation, has the advantages of a higher vesicle yield without dilution and rapidity of preparation when compared to the molecular-sieve technique. The homogeneity of vesicle dispersions, prepared by this new method, is examined by several physical techniques and found to be comparable to the best samples prepared by molecular-sieve chromatography.

INDUCTION OF A RELATIVELY FAST TRANSBILAYER MOVEMENT OF PHOSPHATIDYLCHOLINE IN VESICLES. A ^{13}C NMR STUDY. B. De Kruijff and K.W.A. Wirtz (Institute of Molecular Biol., Dept. of Biochem., State Univ. of Utrecht, Transitorium III, Padualaan 8, Utrecht, The Netherlands). *Biochim. Biophys. Acta* 468, 318–26 (1977). [N^{13}-CH_3]Phosphatidylcholines are introduced into the outer monolayer of phosphatidylcholine vesicles with the phosphatidylcholine exchange protein from bovine liver. The transbilayer distribution of the [N-$^{13}CH_3$] phosphatidylcholine is measured with ^{13}C NMR. The transbilayer movements of [N-$^{13}CH_3$]dioleoyl phosphatidylcholine and [$N^{13}CH_3$]dimyristoyl phosphatidylcholine at 30°C in vesicles composed of these phosphatidylcholines are extremely slow processes with estimated half-times of days. [N-$^{13}CH_3$]Dioleoyl phosphatidylcholine introduced into dimyristoyl phosphatidylcholine vesicles migrates from the outer to the inner monolayer with a half-time of less than 12h. The data suggest that differential changes in the lateral packing of the two monolayers might be a driving force for transbilayer transport of phospholipids.

CONFIGURATIONS OF FATTY ACYL CHAINS IN EGG PHOSPHATIDYLCHOLINE-CHOLESTEROL MIXED BILAYERS. C. Huang (Dept. of Biochem., Univ. Virginia, Schl. of Med., Charlottesville, Virginia). *Chem. Phys. Lipids* 19, 150–8 (1977). Based on the structural properties of cholesterol and egg phosphatidylcholine, and on the assumption than the van der Waals' type attractive interaction between the steroid nucleus and the fatty acyl chains provides a stabilizing force for the cholesterol-egg phosphatidyl-choline complex, some specific orientation and configurations of the fatty acyl chains around the steroid nucleus in the interacting system are proposed in terms of an optimal packing. The proposed model suggests that the saturated chains are largely facing the flattened (α) surface of the steroid nucleus of cholesterol, while the unsaturated chains can interact with both the α and β surfaces of the steroid nucleus. It is also suggested that the angular methyl groups on the β surface of the steroid nucleus lock the unsaturated fatty acyl chain in a relatively immobile configuration. Experimental evidence which provides support for the proposed sterochemical model is presented.

FATTY ACIDS AND THEIR PROSTAGLANDIN DERIVATIVES: INHIBITORS OF PROLIFERATION IN AORTIC SMOOTH MUSCLE CELLS. J.J. Huttner, E.T. Gwebu, R.V. Panganamala, G.E. Milo, D.G. Cornwell, H.M. Sharma and J.C. Geer (Dept. of Physiol. Chem., Ohio State Univ., Columbus, OH). *Science* 197, 289–91 (1977). Prostaglandins are synthesized from eicosa-8,11,14-trienoic acid and eicosa-5,8,11,14-tetra-enoic acid by smooth muscle cell cultures from guinea pig aorta. Production is inhibited by indomethacin. The precursor fatty acids and their prostaglandin derivatives inhibit proliferation of the cell cultures. The relative availability of fatty acids for prostaglandin biosynthesis may represent a control mechanism for cell proliferation.

FURTHER STUDIES OF MODE OF ACTION OF LIPOLYTIC ENZYMES. J. Rietsch, F. Pattus, P. Desnuelle, and R. Verger (Centre de

Biochimie et de Biologie Moleculaire du Centre National de la Recherche Scientifique, Marseille, Cedex 2, France). *J. Biol. Chem.* 252, 4313–8 (1977). Pancreatic lipase and phospholipase A_2 have been shown by the monomolecular film technique to be progressively inactivated when adsorbed at the interface of their respective substrates. This inactivation is faster for lipase than for phospholipase. It is also enhanced by low film pressures and film transfer. The use of radioactive phospholipase and lipase samples offered the possibility to measure the amount of enzyme adsorbed at a monomolecular film with a reasonable accuracy. This adsorption was found to be relatively slow under the conditions of the assays. The main conclusion drawn from these data is that the enzyme kinetics in presence of a substrate film, and probably also under bulk conditions, is controlled by an adsorption flux responsible for an initial lag period and an inactivation flux tending to decrease the reaction time. The kinetics are linear only when both fluxes equilibrate.

A NUCLEAR MAGNETIC RESONANCE STUDY OF SPHINGOMYELIN IN BILAYER SYSTEMS. C.F. Schmidt, Y. Barenholz, and T.E. Thompson (Dept. of Biochem., Univ. of Virginia Schl. of Med., Charlottesville, Va.). *Biochemistry* 16, 2649–56 (1977). The physical properties of small single-walled vesicles composed of the zwitterionic phospholipid sphingomyelin have been studied using ^1H and ^{31}P nuclear magnetic resonance spectroscopy. The temperature variation of proton line widths and spin-lattice relaxation times and the chemical shift behavior for sphingomyelin vesicles are compared with results previously determined for phosphatidylcholine vesicles. Differences between the two systems are interpreted as indications of the presence of both inter- and intramolecular hydrogen bonding in sphingomyelin bilayers.

THE INFLUENCE OF EGG CONSUMPTION ON THE SERUM CHOLESTEROL LEVEL IN HUMAN SUBJECTS. F.A. Kummerow, Y. Kim, Hull, J. Pollard, P. Ilinov, D.L. Dorossiev, and J. Valek (Burnsides Res. Lab., Univ. Illinois, Urbana, IL). *Am. J. Clin. Nutr.* 30, 664–73 (1977). The influence of whole fresh eggs on the serum cholesterol level in men and women was studied independently in hospitalized patients in Sofia, Prague and Urbana-Champaign. The patients were fed two eggs or the equivalent to two eggs in a custard base or milk shake in addition to the foods that were consumed in their diet pattern. The serum cholesterol level was determined before and at periods varying from 5 hr to 54 days after the consumption of the eggs. The mixed fatty acid composition of the total lipids in the serum and the erythrocytes was also determined. A comparison of the mixed fatty acid composition of the total serum lipids obtained from men and women who had received treatment for other reasons than cardiovascular disease with those that had been treated for cardiovascular disease indicated that the serum from both groups contained a substantial amount of polyunsaturated fatty acids. The lipids extracted from the red blood cells obtained from patients in Urbana-Champaign and Sofia did not differ significantly in linoleic and arachidonic acid content.

HYPOLIPIDEMIC ACTIVITY OF IN VITRO INHIBITORS OF HEPATIC AND INTESTINAL SN-GLYCEROL-3-PHOSPHATE ACYLTRANSFERASE AND PHOSPHATIDATE PHOSPHOHYDROLASE. R.G. Lamb, S.D. Wyrick and C. Piantadosi (Depts. of Pharmacology and Med., The Med. College of Virginia, Virginia Commonwealth Univ., Richmond, Va.). *Atherosclerosis* 27, 147–54 (1977). A number of agents including a series of 1,3-bis (substituted phenoxy)-2-propanones were screened in vitro for their ability to inhibit hepatic and intestinal microsomal sn-glycerol-3-phosphate acyltransferase and phosphatidate phosphohydrolase. Effective inhibitors reduced in vivo hepatic and intestinal glycerolipid production and with one exception also lowered serum triglyceride levels, suggesting that agents which inhibit potential rate-limiting steps of glycerolipid biosynthesis may be effective hypolipidemic agents. Two compounds, 1-methyl-4-piperidyl bis (p-chlorophenoxy) acetate (Sah 42-348) and 1,3-bis (p-methylphenoxy)-2-propanone were the best inhibitors of glycerolipid biosynthesis and lipid-lowering agents. The lipid-altering effects of both drugs were compared to chlorophenoxyisobutyrate during high fructose intake in rats. Each agent reduced fructose induced glycerolipid biosynthesis and serum triglyceride levels to similar degrees.

FATTY ACID PROFILES OF PHOSPHOLIPIDS IN RABBIT AND BOVINE DENTAL PULP. L.R. Larson, J.S. Ellingson (Dept. of Biochem., West Virginia Univ., Schl. of Dent., Morgantown, W. Va.). *Biochim. Biophys. Acta* 486, 437–43 (1977). The fatty acid profiles of purified phospholipids were similar in dental pulp from rabbit and bovine teeth. The characteristic fatty acid profile of each phospholipid was similar to that found in several other mammalian tissues. The ethanolamine phosphoglycerides had high levels of arachidonic acid and docosapolyenoic acids. Phosphatidylserine and phosphatidic acid contained high amounts of stearic acid and low levels of polyunsaturated fatty acids. Phosphatidylcholine and sphingomyelin contained high amounts of palmitic acid and low levels of C_{20} and C_{22} unsaturated fatty acids, and sphingomyelin contained C_{24} fatty acids. Phosphatidylinsitol contained mainly stearic, oleic, and arachidonic acids. The fatty acid compositions of the purified pulp phospholipids are markedly different from those reported for dentin lipids which have been reported to contain little or no arachidonic acid and docosapolyenoic acids. The possible significance of the polyunsaturated fatty acids and phospholipids in tooth formation and maintenance is discussed.

BILE ACID SYNTHESIS IN MAN. II. DETERMINATION OF 7α-HYDROXYCHOLESTEROL, (22R)-22-HYDROXYCHOLESTEROL, AND 26-HYDROXYCHOLESTEROL IN HUMAN MECONIUM. U. Lavy, S. Burstein, M. Gut, and N.B. Javitt (Gastroenterology Div., Dept. of Med., Cornell Univ. Med. College-New York Hosp., New York, NY 10021) *J. Lipid Res.* 18, 232–8 (1977). 7α-Hydroxycholesterol, (22R)-22-hydroxycholesterol and 26-hydroxycholesterol have been quantitated in human meconium. The method used tetrahydrofuran for extraction and solvolysis of the sulfate esters, liquid partition chromatography for the separation of the hydroxysterols, gas-liquid chromatography for quantitation, gas-liquid chromatography-mass spectrometry for identification, and tritiated and ^{14}C-labeled tracers for overall recovery standards. (22R)-22-Hydroxycholesterol and 26-hydroxycholesterol were present almost entirely, (> 93%) in the sulfate fraction at concentrations of 3.8–6.4 and 0.4–0.8 mg per 100 g meconium, respectively. Since free tritiated (22R)-22-hydroxycholesterol was used as the tracer to assess recovery of this hydroxysterol, the concentrations found for this compound may be minimal. Tritiated 26-hydroxycholesterol 3, 26-disulfate was used as tracer to determine the levels of this compound, and the solvolysis procedure was optimized for recovery of 26-hydroxycholesterol and least decomposition of 7α-hydroxycholesterol. No significant amounts of 7α-hydroxycholesterol were found based on the tracer-free hydroxysterol as recovery standard.

EFFECT OF LYSOLECITHIN ON THE STRUCTURE AND PERMEABILITY OF LECITHIN BILAYER VESICLES. Y. Lee and S.I. Chan (Noyes Lab. of Chem. Phys., Calif. Inst. of Tech., Pasadena, CA). *Biochem. J.* 16, 1303–9 (1977). In order to elucidate the role of lysolecithin in membranes, we have examined the effect of lysolecithin on the structure and permeability of lecithin bilayer membranes. Small L-α-dimyristoyllecithin (DML) vesicles with myristoyllysolecithin (MLL) incorporated as well as small L-α-dipalmitoyllecithin (DPL) vesicles with palmitoyllysolecithin (PLL) were studied by nuclear magnetic resonance (NMR) methods at temperatures both above and below the α-gel ⇌ liquid crystalline phase transition temperature (T_c) and as a function of the concentration of the incorporated lysolecithin. Europium (III) ion was used as a probe to measure the permeability of the vesicular bilayer membrane. At temperatures below T_c, these vesicles were found to be extremely permeable to europium (III) ions. The ion translocation was found to be too fast to be measured by the NMR method under these conditions. These lysolecithin clusters are presumably long-lived under these conditions and are sufficiently structurally perturbed or disordered to serve as channels for rapid ion permeation.

EFFECT OF LIPOPROTEIN-X ON HEPATIC CHOLESTEROL SYNTHESIS. M. Liersch, G. Baggio, C.C. Heuck and D. Seidel (Med. Univ. Hos. (Ludolf-Krehl-Klinik) and Gastroenterology Dept., Univ. of Heidelberg, Bergheimerstrasse 58, D-6900 Heidelberg, West Germany). *Atherosclerosis* 26, 505–4 (1977). The effect of different lipoproteins (lipoprotein-X and lipoprotein-B; LP-X and LP-B) on hepatic cholesterol synthesis was studied *in vivo* in rats. Lipoproteins were continuously infused into rats for 16 hours so that 25 mg cholesterol/100 g body weight were applied. Serum cholesterol level was nearly doubled after the infusion period. The effect of LP-X on liver cholesterol synthesis is similar to that of lecithin:cholesterol dispersions. The failure of LP-X to exert a feedback inhibition on cholesterol synthesis may therefore contribute to the mechanism of hypercholesterolemia in obstructive jaundice.

FATTY ACID COMPOSITIONS OF LIPID FRACTIONS FROM VEGETATIVE CELLS AND MATURE SOROCARPS OF THE CELLULAR SLIME MOLD DICTYOSTELIUM DISCOIDEUM. B.H. Long and E.L. Coe (Biochem. Dept., Northwestern Univ. Med. and Dental Schls., Chicago, IL). *Lipids* 12, 414–7 (1977). A wild-type strain of *Dictyostelium discoideum* was grown upon *Aorobacter aerogenes*. Fatty acid compositions of lipid fractions and of total lipids obtained from vegetative amoebae and mature sorocarps were compared. Fatty acids isolated from vegetative cells were found to include large quantities of 17- and 19-carbon cyclopropane fatty acids while straight-chain, saturated fatty acids represented only 10% (w/w) of total fatty acids. These cyclopropane fatty acids appear to be derived from ingested bacteria and are preferentially incorporated into neutral lipids of the slime mold. Development of amoebae to mature sorocarps is accompanied by a substantial decrease in cyclopropane fatty acid content and a concomitant increase in unsaturated fatty acids, mostly as octadeca-5,11-dienoic acid. The Δ-22 stigmastenyl ester fraction is the richest source of this acid. Fully 65% of the fatty acids in this fraction are the octadecadienoate.

ALTERATIONS OF THE PLASMA LIPOPROTEINS AND APOPROTEINS FOLLOWING CHOLESTEROL FEEDING IN THE RAT. R.W. Mahley and K.S. Holcombe (Comparative Athero. and Arterial Metabolism Sec., Lab. of Experimental Athero., Natl. Heart, Lung, and Blood Inst., Natl. Inst. of Health, Bethesda, Md.). *J. Lipid Res.* 18, 314–24 (1977). The feeding of cholesterol to rats resulted in marked alterations in the type and distribution of the plasma lipoproteins and their apoproteins. The hyperlipoproteinemia was characterized by an increase in the $d < 1.006$ lipoproteins (B-VLDL and VLDL), and increase in the intermediate and low density lipoproteins (LDL), and the appearance of HDL_c. Associated with these lipoproteins was a prominence of the arginine-rich apoprotein. The high density lipoproteins (HDL) were decreased. A two-dimensional immunoelectrophoretic procedure was adapted to quantitate the changes in distribution of the arginine-rich apoprotein in the plasma and various ultracentrifugal fractions obtained from control and cholesterol-fed rats. Significant alterations in the arginine-rich apoprotein quantitation notwithstanding, the observations of increased arginine-rich apoprotein in the B-VLDL, intermediate fraction, and HDL_c following cholesterol feeding remained valid. However, precise quantitation awaits refinements in lipoprotein isolation techniques.

INTERACTION OF CANINE AND SWINE LIPOPROTEINS WITH THE LOW DENSITY LIPOPROTEIN RECEPTOR OF FIBROBLASTS AS CORRELATED WITH HEPARIN/MANGANESE PRECIPITABILITY. R.W. Mahley and T.L. Innerarity (Lab. of Experimental Athero., Natl. Heart, Lung, and Blood Inst., Bethesda, Md.). *J. Biol. Chem.* 252, 3980–6 (1977). Canine HDL_1 and canine and swine HDL_c were fractionated into several lipoprotein subpopulations by heparin/manganese precipitation. The ability of the various subfractions of HDL_1 or HDL_c to compete with ^{125}I-labeled low density lipoproteins (LDL) for binding and degradation by human fibroblasts was compared. The HDL_1 or HDL_c which precipitated at the lowest concentration of heparin (a concentration which precipitates LDL) were the most effective in competing with ^{125}I-LDL for binding, internalization, and degradation. A striking characteristic of these lipoproteins was the occurrence of a prominence of the arginine-rich apoprotein. Specific lipoprotein interaction with heparin and with the cell surface receptors may occur by a common mechanism; namely, through a positively charged region on the lipoprotein surface which may reside with the B and arginine-rich apoproteins.

INTERACTION OF MEMBRANE AMINOPHOSPHOLIPIDS OF E. COLI WITH FLUORODINITROBENZENE AND TRINITROBENZENESULFONATE. G.V. Marinetti and R. Love (Dept. of Biochem., Univ. of Rochester School of Med. and Dentistry, Rochester, N.Y.). *Chem. Phys. Lipids* 18, 170–80 (1977). *E. coli* cells were reacted with TNBS and FDNB in bicarbonate-NaCl buffer, pH 8.5 (buffer A) and in phosphate-NaCl buffer, pH 7.0 (buffer B). In buffer A, DNP-GPE is the major product when FDNB is used. DNP-PE and DNP-LPE are formed in lesser amounts. Phospholipase A activity is high in buffer A. When TNBS is used, the labeling of the lipid components is less than with FDNB and more TNP-PE is formed relative to TNP-GPE. *E. coli* cells were incubated with exogenous DNP-GPE or TNP-GPE in buffer A. The DNP-GPE and TNP-GPE were rapidly hydrolyzed by a phosphodiesterase to DNP-ethanolamine and TNP-ethanolamine. An orange derivative was formed which was provisionally identified as a derivative of DNP-ethanolamine or TNP-ethanolamine in which a nitro group has been reduced to an amino group by nitroreductase. The phospholipases and acylating enzymes present in the cell wall of *E. coli* are active on the dinitrophenyl and trinitrophenyl derivatives of PE and LPE and may act in concert to model and repair the plasma membrane.

ENHANCED SYNTHESIS AND ACCUMULATION OF COLLAGEN IN CHOLESTEROL-AGGRAVATED PIGEON ATHEROSCLEROSIS. K.G. McCullagh and L.A. Ehrhart (Research Div., Cleveland Clinic Found., 9500 Euclid Ave., Cleveland, Ohio 44106). *Atherosclerosis* 26, 341–52 (1977). Atherosclerotic segments of pigeon aorta synthesized collagen at four times the rate found in normal aorta (Athero = 2071 ± 1339 ng/g/h; Control = 497 ± 192 ng/g/h; $P < 0.025$). Similar results were obtained when synthesis was expressed per mg DNA. Ultrastructural studies revealed the accumulation of large amounts of dense fibrillar collagen in the sub-endothelial region of the plaque. Plaque cells contained multiple vacuoles, an extensive rough endoplasmic reticulum and many mitochondria, suggesting active protein synthesis. It is concluded that increased collagen biosynthesis and deposition is an important metabolic derangement *in lipid-rich* atherosclerotic lesions which promotes their gradual conversion to fibrous plaques.

CONTROL OF FATTY ACID COMPOSITION OF ACHOLEPLASMA LAIDLAWII MEMBRANES. D.L. Melchior and J.M. Steim (Dept. of Chem., Brown Univ., Providence, R.I.) *Biochim. Biophys Acta* 466, 148–59 (1977). The temperature-dependent pattern of incorporation of palmitate and oleate from the growth medium into *Acholeplasma laidlawii* membrane lipids correlates with the physical state of the membrane defined by calorimetry. Both the pattern and the state can be changed at will by changing the fatty acid composition of the membrane lipids. The ratio of palmitate to oleate incorporated is independent of temperature when the membrane bilayer is below its transition and fully ordered, but becomes temperature dependent upon the onset of the transition and continues to be temperature dependent when the membrane is above its transition and fully fluid. This behavior is mimicked by the physical binding of palmitate and oleate to bilayers of extracted membrane lipids and to bilayers of lecithin. Selective binding by membranes may provide a means for controlling lipid fatty acid composition without invoking an enzymatic mechanism.

CRYSTALLINE PATTERNS OF MYELIN LIPIDS VISUALIZED BY FREEZE FRACTURE. R.G. Miller and P. Torreyson (The Salk Inst. for Bio. Studies, P.O. Box 1809, San Diego, Calif.). *Biochim. Biophys. Acta* 466, 325–35 (1977). Freeze fracture of rat optic nerve reveals smooth, particle-free regions on the lammeller fracture faces of myelin when prepared by standard procedures. When the fixed, glycerin-impregnated tissue is incubated at 6°C for two or more days, crystalline patterns indicative of a phase transition can be seen in the particle-free regions. The crystalline patterns can be destroyed by subsequent incubation at 37°C and are not seen when the initial incubation is at room temperature or 37°C. Butylated hydroxytoluene has no effect on the formation of the crystalline patterns. The time course of the formation of the crystalline patterns suggest that the rate-limiting step in the process is not the phase transition itself. We propose that the lipids associated with the particles *in vivo* are involved in the formation of the crystalline patterns.

THE EFFECT OF CHOLESTYRAMINE ON THE FECAL EXCRETION OF BILE ACIDS AND NEUTRAL STEROIDS IN FAMILIAL HYPERCHOLESTEROLAEMIA. C.D. Moutafis, L.A. Simons, N.B. Myant, P.W. Adams and V. Wynn (Med. Res. Council Lipid Metabolism Unit, Hammersmith Hosp., London, W12 OHS). *Atherosclerosis* 26, 329–34 (1977). The fecal excretion of total bile acids was measured in two normal subjects and in seven patients with familial hypercholesterolaemia (four heterozygotes and three homozygotes) in the untreated state and during treatment with near-maximal doses of cholestyramine. There were no significant differences between the three groups. The increase in bile-acid excretion in response to cholestyramine was as great in the homozygotes as in the normal subjects. It is concluded that familial hypercholesterolaemia is not generally due to an inherited defect in the mechanism for catabolizing cholesterol to bile acids.

FATTY ACID SYNTHETASE COMPLEX FROM THE INSECT CERATITIS CAPITATA. A.M. Municio, M.A. Lizarbe, E. Relaño and J.A. Ramos (Dept. of Biochem., Complutensis Univ., Madrid, Spain). *Biochim. Biophys. Acta* 487, 175–88 (1977). Fatty acid synthesis capacity of the insect *Ceratitis capitata* has been

investigated in vitro from [1-^{14}C]acetyl-CoA using homogenates at different stages of development. A maximum activity was observed after 5–6 days of larval development. But homogenates of the pharate adult insect did not show synthetic capacity of fatty acids. Amino acid analysis, general properties, stability and kinetic constants (V and K_m) for the substrates are reported. The fatty acid synthetase complex from the insect contains 42 ± 1-SH residues and one phosphonpantetheine moiety per 5.2×10^5. Activity was dependent on the presence of NADPH; FMN strongly inhibited the enzyme activity promoted by NADPH. The enzyme complex synthesized a range of fatty acid (10 : 0–18 : 0), palmitate being the predominant end product. The proportions of fatty acids synthesized varied with substrate concentrations. Fatty acids released from the complex were almost completely in the free form.

CHOLESTEROL 7α-HYDROXYLASE. N.B. Myant and K.A. Mitropoulos (Med. Res. Council Lipid Metabolism Unit, Hammersmith Hospital, London, W12 OHS, United Kingdom). *J. Lipid Res.* **18**, 135–53 (1977). A 7α-hydroxyl group is present in cholic acid and chenic (chenodeoxycholic) acid, the two primary bile acids synthesized from cholesterol in the livers of most mammals. A proportion of the primary bile acids reaching the lumen of the small intestine is modified by intestinal micro-organisms to form secondary bile acids lacking a 7α-hydroxyl group, with deoxycholate arising from cholic acid and lithocholate from chenic acid. The primary and secondary bile acids are partially reabsorbed, reaching the liver via the portal vein. In rats, the secondary bile acids are hydroxylated in the 7α position by hepatic enzymes and are then secreted into the intestine, together with re-absorbed and newly-synthesized primary bile acids. The enzymes responsible for the 7α-hydroxylation of secondary bile acids and of certain steroid hormones are almost certainly different from cholesterol 7α-hydroxylase and are not dealt with systematically in this review.

THE EFFECT OF BILE SALTS ON THE FORMATION AND HYDROLYSIS OF CHOLESTEROL ESTERS BY RAT LIVER ENZYMES. V.J. Neelon and L. Lack (Dept. of Physio. and Pharma., Duke Univ. Med. Ctr., Durham, NC). *Biochim. Biophys. Acta* **487**, 137–44 (1977). To determine the effects of different bile salts on the enzymic esterification of cholesterol and the hydrolysis of cholesterol esters rat liver homogenates and rat liver microsomes were incubated with varying amounts of different bile salts. Bile salts inhibited the formation of radioactive cholesterol esters in incubations of either rat liver homogenates or rat liver microsomes containing [^{14}C]cholesterol. Chenodeoxycholate, glycochenodeoxycholate and taurochenodeoxycholate were more potent inhibitors than their comparable cholate analogues. Since cholesterol esterification was also inhibited under these conditions a direct inhibitory effect (not attributable to enhanced hydrolase activity) of the bile salts on the formation of cholesterol esters by the microsomes was established. Furthermore, this inhibition takes place at the transacylation step involving the fatty acyl-CoA ester and the sterol.

EFFECTS OF THIAMINE AND PYRIDOXINE ON THE LIPID COMPOSITION OF SACCHAROMYCES CARLSBERGENSIS 4228. Y. Nishikawa, I. Nakamura, T. Kamihara and S. Fukui (Dept. of Indust. Chem., Kyoto Univ., Kyoto, Japan). *Biochim. Biophys. Acta* **486**, 483–9 (1977). The lipid composition of *Saccharomyces carlsbergensis* 4228 cells grown aerobically in the presence of thiamine and absence of pyridoxine was markedly different from that of cells grown without addition of both of the growth factors. In addition to the previous observations showing a reduction in the levels of unsaturated fatty acids, the thiamine-grown cells were found to contain low levels of total lipids, sterols (especially in the form of esters), triacylglycerols and total phospholipids. However, relative contents of triacylglycerols and phospholipids to total lipids were higher than those of control cells. It was found that unsaturated fatty acid contents were low in all lipid esters tested. The effect of thiamine was particularly noteworthy in the case of sterol esters. Concomitant addition of pyridoxine with thiamine to the medium brought about a normal lipid composition in the yeast cells.

THE EFFECT OF DIETARY FATS ON THE PLASMA LIPID COMPOSITION OF SHEEP. R.C. Noble, R.G. Vernon, W.W. Christie, J.H. Moore, and A.J. Evans (The Hannah Research Institute, Aye, Scotland). *Lipids* **12**, 423–33 (1977). This study reports on the plasma lipid compositions of sheep fed either a control diet (C), a control diet supplemented with tallow (A) or polyunsaturated fatty acid (B) that had been protected against hydrolysis and hydrogenation in the rumen, or a control diet supplemented with maize oil (D). Diet B increased considerably the proportion of triglyceride found in association with the very low density fraction and the concentrations of 18:2 within all the lipoprotein fractions; these increases in the concentrations of 18:2 were not confined to any particular lipid fraction of the lipoproteins. In contrast, the increases in the concentrations of 18:2 produced as a result of feeding diet D were confined to the low and high density lipoproteins. The effect of feeding diet A was confined to fatty acid changes within the triglycerides of the low and very low density lipoproteins.

INVOLVEMENT OF NADPH-CYTOCHROME C REDUCTASE IN THE RAT LIVER SQUALENE EPOXIDASE SYSTEM. T. Ono, S. Ozasa, F. Hasegawa and Y. Imai (Dept. of Biochem., Schl. of Med., Hokkaido Univ. Sapporo 060, Japan). *Biochim. Biophys. Acta* **486**, 401–7 (1977). Microsomal squalene epoxidase has previously been solubilized with Triton X-100 and resolved into fractions, F_A and F_B, by DEAE-cellulose chromatography. It has now been found that F_B is identical with NADPH-cytochrome *c* reductase (denoted F_{PT}, EC 1.6.2.3). Although both NADPH and NADH served as electron donors, the former was preferred for squalene epoxidase activity in the reconstituted system of F_A and F_B. F_B is characterized by its ability to reduce cytochrome *c* by NADPH. Rabbit antisera preparations to the purified F_{PT} solubilized with trypsin were shown to inhibit concomitantly F_{PT} activity and squalene epoxidase activity. These observations support the concept that squalene epoxidation is primarily mediated via a flavoprotein, NADPH-cytochrome *c* reductase, and a terminal oxidase, squalene epoxidase, which is distinct from cytochrome *P*-450.

ACTIVATION OF (Na^+ + K^+)-DEPENDENT ATPASE BY LIPID VESICLES OF NEGATIVE PHOSPHOLIPIDS. P. Palatini, F. Dabbeni-Sala, A. Pitotti, A. Bruni and J.C. Mandersloot (Inst. of Pharmacology, Univ. of Padova, Largo Meneghetti 2, 35100 Padova, Italy). *Biochim. Biophys. Acta.* **466**, 1–9 (1977). Kidney (Na^+ + K^+)-stimulated ATPase was depleted of phospholipids by extraction with lubrol and inserted in lipid structures of known composition. Both ouabain-sensitive ATPase and phosphatase reactions could be partially restored by lipid replacement. Lipid vesicles of natural and synthetic negative phospholipids proved to be effective. The low activity of uncharged liposomes was increased when negative charges were included into the bilayer structure. It is concluded that reassembly of lipid-deficient (Na^+ + K^+)-stimulated ATPase requires the addition of diacylphospholipids with fluid acyl-chains and negatively charged polar heads able to assemble in an expanded lamellar configuration.

EFFECTS OF PROPRANOLOL, MINOXIDIL, AND CLOFIBRATE ON CHOLESTEROL-INDUCED ATHEROSCLEROSIS IN STUMPTAIL MACAQUES (MACACA ARCTOIDES). R. Pick and G. Glick (Cardiovascular Inst., Dept. of Med., Michael Reese Hosp. and Med. Center, and the Univ. of Chicago Pritzker Schl. of Med., Chicago, IL). *Atherosclerosis* **27**, 71–7 (1977). Propranolol, minoxidil, and clofibrate, three different classes of pharmacological agents used clinically in various conditions related to atherosclerosis, were shown not to have any intrinsic potentiating effects on the development of atherosclerosis in stumptail macaque fed an atherogenic diet. We did obtain, however, some results that suggest that clofibrate and propranolol may exert some beneficial actions.

ACTIVATABLE CHOLESTEROL ESTERASE AND TRIACYLGLYCEROL LIPASE ACTIVITIES OF RAT ADRENAL AND THEIR RELATIONSHIP. R.C. Pittman and D. Steinberg (Div. of Metabolic Disease, Dept. of Med., Univ. of California, San Diego Schl. of Med., La Jolla, Ca.). *Biochim. Biophys. Acta* **487**, 431–44 (1977). Activatable cholesterol esterase and triacylglycerol lipase of rat adrenal were 58–69% recovered in the 100,000 × *g* supernatant fraction. Activatable triacylglycerol lipase activity was differentiated from the activity of acid lipase and lipoprotein lipase also found in this fraction. Cholesterol esterase was activated 39.7 ± 13.6% (S.D.) and triacylglycerol lipase 11.9 ± 2.9% in a reaction dependent on ATP, cyclic AMP, and protein kinase. The two activities were shown by differential inhibition by an organophosphate, and by partial separation on salting out, to be largely due to separate enzymes. The two enzymes bound tightly to substrate emulsions with quantitatively similar distribution between com-

peting emulsions, suggesting concerted binding. Coinciding gel filtration patterns reinforced, the hypothesis of a lipase complex. Cholesterol esterase comprised a major component of higher apparent K_m for substrate and molecular weight $3 \cdot 10^5$—$6 \cdot 10^5$ by gel filtration, and a minor component of lower apparent K_m and heterogeneous molecular weight above 1 million, which was found mostly in complex with lipid.

DILUTE BLOOD CLOT LYSIS TIME AND ELECTROPHORETIC LIPOPROTEIN FRACTIONS IN A POPULATION SAMPLE OF HEALTHY ROMANIANS. T.A. Popescu, C. Stef, G. Moraru and M.P. Cucuianu (Med. Clinic N.1, Cluj-Napoca, Romania). *Atherosclerosis* 27, 155–63 (1977). Serum total lipids and cholesterol, electrophoretically determined lipoprotein concentrations, serum pseudocholinesterase and dilute blood clot lysis time were determined in 630 healthy subjects (297 men and 343 women) aged 20–60, working in the food industry. A high incidence of overweight was noted ranging from 22.4% in women aged 20–40 to 58.7% in men aged 41–60. Over-weight subjects presenting higher levels of serum cholesterol, total lipids and of the pre-beta electrophoretic fraction also had a higher pseudo-cholinesterase activity and a more delayed clot lysis time than normal-weight subjects matched as to age and sex. When the material was divided into quintiles for pre-beta- and beta-lipoproteins, a highly significant delay of fibrinolysis was noted in the fouth and fifth quintiles for pre-beta-lipoproteins, but no significant changes of lysis time occurred with increasing concentrations of beta-lipoproteins. Possible explanations of the abovementioned findings are briefly discussed.

DYNAMIC MECHANICAL PROPERTIES OF ATHEROSCLEROTIC AORTA. A CORRELATION BETWEEN THE CHOLESTEROL ESTER CONTENT AND THE VISCOELASTIC PROPERTIES OF ATHEROSCLEROTIC AORTA. T.I. Pynadath and D.P. Mukherjee (Dept. of Chem., Kent St. Univ., Kent, Ohio 44242). *Atherosclerosis* 26, 311–8 (1977). The effect of cholesterol and cholesterol ester content of aortas on the dynamic mechanical properties of these tissues was studied in rabbits during development of atherosclerosis. The disease was induced by feeding a 1.5% cholesterol diet for six weeks. At two week intervals, an equal number of control and experimental animals were sacrificed and their aortas were collected. The results showed that cholesterol feeding had no effect on the longitudinal dynamic Young's modulus of the aortas. On the other hand, the tangential dynamic Young's modulus of the aortas was found to be very much influenced by the cholesterol diet.

THE EFFECT OF PHOSPHATIDYLCHOLINE AND LYSOPHOSPHATIDYLCHOLINE ON THE ABSORPTION AND MUCOSAL METABOLISM OF OLEIC ACID AND CHOLESTEROL IN VITRO. A.J. Rampone and L.R. Long (Dept. of Physio., Schl. of Med., Univ. Oregon Health Serv. Ctr., Portland, OR). *Biochim. Biophys. Acta* 486, 500–10 (1977). The absorption and mucosal metabolism of [^{14}C]oleic acid and [^{3}H]Cholesterol were studied using everted sacs of rat jejunum in an in vitro incubation system. The labeled compounds were present in the incubation mixture either singly or together as mixed micelles with bile salt and monoacylglycerol and in the presence or absence of phosphatidylcholine or lysophosphatidylcholine. Lysophosphatidylcholine had only a minimal effect on cholesterol absorption and no effect on cholesterol acylation. Evidence is presented showing that lysophosphatidylcholine is itself well absorbed and variously metabolized. We conclude that phosphatidylcholine and lysophosphatidylcholine have quite divergent effects on lipid absorption but the full elucidation of their mechanisms of action must await further study.

EFFECT OF ESTROGENS ON THE CONCENTRATION AND COMPOSITION OF ARTERIAL STEROLS AND STERYL ESTERS IN MALE WHITE CARNEAU PIGEONS. M.T. Ravi Subbiah and B.A. Dicke (Cardiovascular Res. Unit, Mayo Clinic and Mayo Fd., Rochester, Minn). *Atherosclerosis* 27, 59–64 (1977). The effect of short-term (6 months) administration of conjugated equine estrogen (Premarin) on the content and composition of the aortic sterols in male White Carneau pigeons while they were on a cholesterol-free grain diet was investigated. Estrogen treatment resulted in a 38% increase ($P < 0.05$) in free sterol concentration, with a 28.8% concomitant decrease ($P < 0.05$) in the percent of cholesteryl esters. The total sterol concentration remained unchanged. This finding suggests that estrogens might influence the synthetic or hydrolytic (or both) processes that control the concentration of cholesteryl esters in the aorta. Fatty acid composition of steryl esters did not change significantly. The cholesterol content of plasma showed a mild reduction (14%) whereas the triglycerides increased significantly (30%).

A CORRELATIVE STUDY OF HEPATIC SELENIUM LEVELS AND DEPLETION RATES WITH THE ONSET OF SELENIUM-VITAMIN E DEFICIENCY DISEASE IN THE CHICK. A.H. Rebar and J.F. Van Vleet (Dept. of Microbiol., Pathology and Public Health, School of Veterinary Med., Purdue Univ., West Lafayette, Ind.). *Poultry Sci.* 56, 797–800 (1977). Two experiments were conducted to determine the correlation between time of onset of selenium-vitamin E (Se-E) deficiency disease and hepatic selenium (Se) levels in young chicks. Hepatic Se depletion occurred more rapidly in chicks with higher initial hepatic stores. By the end of the second week of the depletion period mean hepatic Se levels among the three groups were comparable (approximately 0.20 p.p.m.). Clinical signs of Se-E deficiency were seen after 18 to 20 days when mean hepatic Se levels had dropped to 0.11–0.17 p.p.m. These results suggest that Se supplementation of breeding hens would appear to be an inefficient and probably ineffective method when used alone as a preventative measure against the development of Se deficiency disease in chicks.

FECAL BILE ACIDS AND CHOLESTEROL METABOLITES OF PATIENTS WITH ULCERATIVE COLITIS, A HIGH-RISK GROUP FOR DEVELOPMENT OF COLON CANCER. B.S. Reddy, C.W. Martin and E.L. Wynder (Naylor Dana Inst. for Disease Prevention, Am. Health Fd., Valhalla, New York). *Cancer Res.* 37, 1697–701 (1977). Patients with chronic ulcerative colitis are at increased risk of developing carcinoma of the colon. It has been shown that the concentration of fecal bile acids and neutral sterols was higher in cancer patients than in the comparable healthy controls. Fecal neutral steriods and bile acids were measured in patients with ulcerative colitis, family controls who were immediate relatives of patients, patients with other digestive diseases, and healthy unrelated controls. The fecal excretion of cholesterol, coprostanol, and cholestane-3β,5α,6β-triol was higher in patients with ulcerative colitis than in other groups. Patients with other diseases, family controls, and unrelated controls excreted comparable levels of neutral sterols. Patients with ulcerative colitis excreted levels of bile acids in their feces comparable to those excreted by other groups. These findings suggest that possible interactions between cholesterol metabolites and colonic epithelial cells may be relevant in colon carcinogenesis.

EFFECT OF ORAL ALANINE LOADS ON THE SERUM TRIGLYCERIDES OF ORAL CONTRACEPTIVE USERS AND NORMAL SUBJECTS. D.P. Rose, J.E. Leklem, L. Fardal, R.B. Baron, and E. Shrago (Division of Clinical Oncology, Wisconsin Clin. Cancer Center, and Dept. of Nutr. Sci., Univ. of Wis., Madison, Wis.). *Am. J. Clin. Nutr.* 30, 691–4 (1977). The effect of orally administered L-alanine loads on serum triglycerides, and plasma insulin and glucose, was studied in 23 women using an estrogen-containing oral contraceptive and 13 healthy female controls. Oral contraceptive users had significantly higher fasting serum triglycerides than the controls. Serum triglyceride concentrations underwent little change in the controls after alanine ingestion, whereas the oral contraceptive users showed increases which were maintained throughout the 3-hr sampling period. The two groups had similar elevations in plasma insulin after alanine loading; the glucose concentrations were unchanged. The changes in serum triglycerides may have resulted from increased metabolism of alanine to pyruvate, and its incorporation into lipids under the stimulus of elevated insulin levels.

CHYLOMICRON REMNANT CHOLESTERYL ESTERS AS THE MAJOR CONSTITUENT OF VERY LOW DENSITY LIPOPROTEINS IN PLASMA OF CHOLESTEROL-FED RABBITS. A.C. Ross and D.B. Zilversmit (Section of Biochem., Molec. and Cell Biol., Div. of Biological Scis., and Div. of Nutr'l. Sciences, Cornell Univ., Ithaca, NY 14853). *J. Lipid Res.* 18, 169–81 (1977). Feeding rabbits 500 mg of cholesterol daily for 4 to 15 days greatly increased the concentration of esterified cholesterol in lipoproteins of $d < 1.006$ g/ml. The origin of hypercholesterolemic very low density lipoproteins was investigated by monitoring the degradation of labeled lymph chylomicrons administered to normal and cholesterol-fed rabbits. Normal rabbits rapidly removed from plasma both labeled cholesteryl and retinyl esters, whereas cholesterol-fed rabbits retained nearly 50% of doubly labeled remnants in plasma 25 min after chylomicron injection. Apparently, nearly two-thirds of the esterified cholesterol in total very low density lipoproteins from moderately hypercholesterolemic rabbits is of dietary origin.

CHARACTERIZATION OF PLASMA LOW DENSITY LIPOPROTEINS OF NONHUMAN PRIMATES FED DIETARY CHOLESTEROL. L.L. Rudel, L.L. Pitts, II, and C.A. Nelson (Dept. of Comparative Med.,

Arteriosclerosis Research Center, Bowman Gray School of Med. of Wake Forest Univ., Winston-Salem, NC 27103) J. Lipid Res. 18, 211–22 (1977). LDL from animals of three nonhuman primate species, *Macaca mulatta, Macaca fascicularis,* and *Cercopithecus aethiops,* were studied. A standard preparation of ^{125}I-LDL was added to isolated lipoprotein mixtures just prior to separation of plasma lipo-proteins by agarose gel chromatography. The increase in LDL molecular weight was associated with a large increase in cholesteryl ester content and concomitant smaller increases in protein, phospholipid, and free cholesterol. As molecular weight increased, these components appeared to be added to LDL particles together as discrete increments of fixed composition. The data are consistent with a spherical model of LDL structure with a core of cholesteryl ester and triglyceride and a 21.3 Å-thick coat of phospholipid, free cholesterol, and protein.

EXPERIMENTAL DIABETES REDUCED CIRCULATING 1,25-DIHYDROXYVITAMIN D IN THE RAT. L.E. Schneider, H.P. Schedl, T. McCain and M.R. Haussler (Gastroenterology Res. Labs., Dept. of Med., Univ. of Iowa, Iowa City, IA). *Science* 196, 1452–3 (1977). Duodenal calcium absorption and a vitamin D-dependent duodenal calcium-binding protein are depressed in rats with alloxan- or streptozotocin-induced diabetes. To test for possible abnormal vitamin D metabolism in diabetes we measured serum concentrations of 25-hydroxyvitamin D and 1,25-hydroxyvitamin D in control, streptozotocin diabetic, and insulin-treated diabetic rats. The serum concentration of 1,25-dihydroxyvitamin D was depressed in untreated diabetic rats to one-eighth of the level in controls and was restored to control levels by insulin treatment. The serum concentration of 25-hydroxyvitamin D was the same in all three groups. Hence, effects of diabetes on duodenal calcium transport can be explained by reduced concentrations of 1,25--dihydroxyvitamin D resulting either from failure of renal 1-hydroxylation of 25-hydroxyvitamin D or increased catabolism of 1,25-dihydroxyvitamin D.

CYCLIC AMP METABOLISM IN CHOLESTEROL-RICH PLATELETS. A.K. Sinha, S.J. Shattil and R.W. Colman (Dept. of Med., Univ. of Pa. Sch. of Med., Philadelphia, PA). *J. Biol. Chem.* 252, 3310–14 (1977). The incorporation of cholesterol in human platelets by means of incubation with cholesterol-rich lecithin dispersions is associated with a decreased fluidity in the phospholipid hydrocarbon core of platelet membranes and an increased sensitivity of platelets to aggregating agents. We examined whether the platelet membrane enzyme, adenylate cyclase is influenced by changes in phospholipid fluidity. These studies demonstrate that incorporation of cholesterol into platelet membranes is associated with a diminished inhibitory effect of prostaglandin E_1 on platelet aggregation. This appears to be related to the inability of prostaglandin E_1 to stimulate adenylate cyclase and therefore adenosine 3′:5′-monophosphate production in these platelets. The loss of hormone and fluoride responsiveness as well as the increased basal activity of adenylate cyclase in cholesterol-rich platelets may be due to the physical effects of cholesterol on platelet membrane phospholipid.

DESTRUCTION OF ENDOGENOUS LOW DENSITY LIPOPROTEIN IN INCUBATED INTIMA. E.B. Smith and I.B. Massie. (Dept. of Chem. Pathology, Univ. of Aberdeen, Foresterhill, Aberdeen, Great Britain). *Atherosclerosis* 26, 427–39 (1977). The effect of incubation on the content of endogenous intact plasma lipoprotein (LP) has been examined in minced samples of normal intima and lesions from 38 patients. Both the electrophoretically mobile and the immobilized LP fractions decreased on incubation, and the rate of destruction was proportional to LP concentration ($r = 0.832, P <, < 0.001$). Mincing the intima with EDTA before incubation increased the rate of destruction about 4-fold in fibrous lesions, but not in lesions containing numerous fat-filled cells. The destruction of LP was highly dependent on pH; the rate was highest below pH 5.5 and destruction was almost completely inhibited above pH 6.4. In standard cathepsin assays haemoglobin substrate was hydrolysed at a rate comparable to the rate of destruction of LP. The results suggest that LP may be degraded by a lysosomal cathepsin in intima.

CHOLESTEROL ESTER ACCUMULATION IN CULTURED AORTIC SMOOTH MUSCLE CELLS. INDUCTION OF CHOLESTEROL ESTER RETENTION BY CHLOROQUINE AND LOW DENSITY LIPOPROTEIN AND ITS REVERSION BY MIXTUTES OF HIGH DENSITY APOLIPOPROTEIN AND SPHINGOMYELIN. O. Stein, J. Vanderhoek and Y. Stein (Dept. of Experimental Med. and Cancer Res., The Hebrew Univ.-Hadassah Med. Schl., and Lipid Research Lab., Dept. of Med. "B", Hadassah Univ. Hos., Jerusalem, Israel) *Atherosclerosis* 26, 465–82 (1977). Accretion of cholesterol ester was studied in rat aortic smooth muscle cells in culture. Confluent multilayers of smooth muscle cells were exposed to human low density lipoprotein (LDL) and chloroquine and this treatment resulted in a very marked increase in cellular cholesterol ester. The degree of enrichment in cholesterol ester was related inversely to the cell density in the petri dish and was maximal in 48 hr. Removal of the accumulated cellular cholesterol ester was studied in the two cell types and it was markedly enhanced in the presence of lipoprotein-deficient serum and high density apolipoprotein-sphingomyelin mixture. The morphological findings after 24 hr. of post incubation revealed the presence of empty vacuoles, membrane whorls and cytoplasmic lipid droplets. The present results indicate that aortic smooth muscle cells in culture can serve as a good model to study the role of the lysosomal system in atherogenesis.

BUTYLATED HYDROXANISOLE (BHA) AND BUTYLATED HYDROXYTOLUENE (BHT) EFFECTS ON SERUM AND LIVER LEVELS IN *Gallus domesticus*. J.G. Surak, R.L. Bradley, Jr., A.L. Branen, A.J. Maurer and W.E. Ribelin (Depts. of Food Sci., Poultry Sci. and Vetr. Sci., Univ. of Wisconsin, Madison, Wis.) *Poult. Sci.* 56, 747–53 (1977). The food antioxidants, butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) were fed to chickens to determine their effect on lipid metabolism. BHA and BHT did not affect chicken growth, blood lipid or liver lipid levels when the birds were fed a normal ration. When a high fat, high cholesterol ration was fed, chickens developed increased levels of blood and liver lipids and experienced decreased growth rates. The addition of either antioxidant in the presence of a high fat, high cholesterol diet maintained higher serum lipid levels and caused decreases in liver lipid levels.

DEPLETION OF DOCOSAHEXAENOIC ACID IN RETINAL LIPIDS OF RATS FED A LINOLENIC ACID-DEFICIENT, LINOLEIC ACID-CONTAINING DIET. J. Tinoco, P. Miljanich and B. Medwadowski (Dept. of Nutr. Scis., Univ. of Calif. at Berkeley, Berkeley, CA) *Biochim. Biophys. Acta* 486, 575–8 (1977). Rats were raised for 2 generations on a diet in which 1.25% methyl linoleate was the only source of fat. Control rats were given 1.0% methyl linoleate plus 0.25% methyl linolenate. Lipids were extracted from retinas and their fatty acids were analyzed by gas-liquid chromatography. Docosahexaenoic acid accounted for 33.8% of total fatty acids in control retinas, for 13% of fatty acids in first-generation deficient retinas, and for 2.7% of fatty acids in second-generation deficient retinas.

HIGH DENSITY LIPOPROTEIN AND LOW DENSITY LIPOPROTEIN CATABOLISM BY HUMAN LIVER AND PARENCHYMAL AND NON-PARENCHYMAL CELLS FROM RAT LIVER. T.J. Van Berkel, J.F. Koster and W.C. Hulsmann (Dept. of Biochem. I, Faculty of Med., Erasmus Univ. Rotterdam, P.O. Box 1738, Rotterdam, The Netherlands). *Biochim. Biophys. Acta* 486, 586–9 (1977). The capacity of the homogenates from human liver, rat parenchymal cells, rat non-parenchymal cells and total rat liver for the breakdown of human and rat high density lipoprotein (HDL) and human low density lipoprotein (LDL) was determined. Human HDL was catabolized by human liver, in contrast to human LDL, the protein degradation of which was low or absent. Human and rat HDL were catabolized by both the rat parenchymal and non-parenchymal cell homogenates with, on protein base, a 10-times higher activity in the non-parenchymal liver cells. This implies that more than 50% of the total liver capacity for HDL protein degradation is localized in these cell types. Human LDL degradation in the rat could only be detected in the non-parenchymal cell homogenates. These findings are discussed in view of the function of HDL and LDL as carriers for cholesterol.

CHOLESTEROL BIOSYNTHESIS AND 3-HYDROXY-3-METHYL-GLUTARYL COENZYME A REDUCTASE IN CULTUTED GLIAL AND NEURONAL CELLS. REGULATION BY LIPOPROTEIN AND BY CERTAIN FREE STEROLS. J.J. Volpe and S.W. Hennessy (Dept. of Ped. and Neuro., Washington Univ. Schl. of Med., St. Louis, Mo.). *Biochim. Biophys. Acta* 486, 408–20 (1977). Regulation of cholesterol synthesis and, particularly 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase was studied in C-6 glial and neuroblastoma cells. Comparison of rates of incorporation of radioactivity from [^{14}C]-acetate or [^{3}H]mevalonate into digitonin-precipitable sterols indicated that HMG-CoA reductase is the major rate-limiting enzyme in cholesterol biosynthesis in both cell types. The critical regulatory component in the total lipoprotein fraction was shown to be con-

tained in the low density lipoproteins for the reductase of both cell types. Regulation of reductase by free sterols was shown in both the glial and neuronal cells. However, effects were more marked and evolved more rapidly in the glial cells. The data thus provide important insight into the regulation of cholesterol synthesis in two cell types which are considered to be good models of neurons and glia of developing brain. The occurrence of more marked and more rapid regulation in the glial than in the neuronal cells is compatible with the important role glia play in brain lipid synthesis.

INVESTIGATION OF THE RATE-DETERMINING MICROSOMAL REACTION OF CHOLESTEROL BIOSYNTHESIS FROM LANOSTEROL IN MORRIS HEPATOMAS AND LIVER. M.T. Williams, J.L. Gaylor, and H.P. Morris (Section of Biochem., Molecular and Cell Biol., and the Div. of Nutr. Sci., Cornell Univ., Ithaca, N.Y.). *Cancer Res.* **37**, 1377–83 (1977). Previously, we reported that the properties of microsomal 4-methyl sterol demethylase isolated from liver and Morris hepatomas 5123C and 7777 are grossly similar. The individual enzymic steps of this multicomponent system have now been studied, and the rate-determining step has been determined and shown to be identical for liver and these hepatomas. Since the microsomal enzymes of liver and hepatoma appear to be catalytically similar and rate determination appears to be similar, too, the characteristic lack of response of tumor microsomes to treatments *in vivo* that alter host liver microsomal demethylation activity suggests that the insensitivity of these tumors to dietary cholesterol should not be ascribed to alterations in the catalytic proteins. Evidence in this report suggests that the postmicrosomal supernatant fraction of both liver and hepatoma contains a cytosolic protein that may participate in the regulation of the rate-determining attack of 4α-methyl sterol substrates. Thus, either qualitative or quantitative differences between the postmicrosomal supernatant fractions obtained from liver and hepatomas may account for the observed differences in rates of cholesterol biosynthesis.

COMPARATIVE INACTIVATION OF YEAST FATTY ACID SYNTHETASE COMPONENT ENZYMES BY ATMOSPHERES OF OXYGEN. F. Yein and O.R. Brown (J.M. Dalton Res. Center and Dept. of Vet. Microbio., Univ. of Missouri, Columbia, MO). *Biochim. Biophys. Acta* **486**, 421–8 (1977). Yeast fatty acid synthetase at 4°C was stable during 1- and 2-h exposures to oxygen at 100 atm, but was 48% and 90% inactivated after 20 h and 40 h, respectively, with fatty acid synthesis measured by both radioactive and optical assays. Incubation with dithiothreitol did not restore activity. Component enzyme activities were compared before and after 40 h in 100 atm of oxygen. Keotacyl reductase activity was most reduced, followed by keotacyl synthetase and then acetyl transferase while malonyl transferase, enoyl reductase and palmitoyl transferase were not significantly inactivated.

EFFECT OF DIETARY LIPIDS ON FATTY ACID COMPOSITION OF BODY LIPID IN TAINBOW TROUT *(Salmo Gairdneri)*. T.C. Yu, R.O. Sinnhuber and G.B. Putnam (Dept. of Food Sci. and Tech., Oregon State Univ., Corvallis, OR). *Lipids* **12**, 495–9 (1977). Three isocaloric diets were prepared. Diet 1 (Control) contained 22% herring oil. In diets 2 and 3, a third and a half of the herring oil was replaced, respectively, by an animal fat (lard) which contained a high percentage of saturated fatty acids. Each diet was fed to duplicate groups of rainbow trout for 14 wk. The results of the feeding trial indicated that the concentration of the saturated fatty acids in trout body lipid did not increase despite the high concentration of these fatty acids in Diets 2 and 3. Fish growth, feed efficiency, mortality and the level of fatty acid deposited in fish body lipid and phospholipids are discussed.

LIPID ACTIVATION ON UNDECAPRENYL PYROPHOSPHATE SYNTHETASE FROM *Lactobacillus plantarum*. C.M. Allen, Jr. and J.D. Muth (Dept. of Biochem., Univ. of Florida, Gainesville, Fla.). *Biochemistry* **16**, 2908–15 (1977). *Lactobacillus plantarum* undecaprenyl pyrophosphate synthetase is a soluble enzyme which has an in vitro requirement for detergent of phospholipid for activity. It is activated by the anionic detergents deoxycholate, dodecyl and cetyl sulfate, as well as Triton X series detergents. Brij 35, 56, and 96 and cetyltrimethylammonium bromide were ineffective in activating the enzyme. *L. plantarum, Escherichia coli,* and bovine cardiolipin, egg phosphatidic acid, and oleate are all good activators of the enzyme in the absence of detergent. *L. plantarum* phosphatidylglycerol and lysylphosphatidylglycerol, several lecithins, dipalmitylphosphatidic acid, phosphatidylserine, and the C_6–C_{18} saturated fatty acids (except C_{16}) are all ineffective over a wide concentration range. However, in the presence of 0.1% Triton X-100, dipalmitylphosphatidic acid, phosphatidylserine, and C_6–C_{18} saturated fatty acids exhibit a concentration-dependent stimulatory effect, with the C_{12} and C_{14} fatty acids being most effective.

EFFECT OF DIETARY FATS AND FATTY ACIDS ON THE LIVER LIPID ACCUMULATION INDUCED BY FEEDING A PROTEIN-REPLETION DIET CONTAINING GLYCEROL TO PROTEIN-DEPLETED RATS. Y. Aoyama, A. Yoshira and K. Ashida (Lab. of Nutr. Biochem., Dept. of Agr. Chem., Nagoya University, Furo-cho, Chikusa, Nagoya, Japan). *J. Nutr.* **107**, 1120–5 (1977). Lipid accumulation was not observed in the liver of rats fed the protein-repletion diet containing glucose as the sole carbohydrate source after protein-depletion. Therefore, to clarify the effect of supplementation of some compounds related to lipid synthesis on the lipid content of liver, a protein-repletion diet supplemented with glycerol, citric acid, α-glycerophosphate or malonic acid was fed. Glycerol increased the lipid content of liver although the amount of food consumed by rats fed the protein-repletion diet containing 10% glycerol was the same as that consumed by rats fed the protein-repletion diet. Citric acid and malonic acid caused a decrease in lipid content of liver. These results might be due to reduced food consumption. Without prior feeding of a protein-free, diet, dietary glycerol did not alter the lipid content of liver. Therefore, the formation of fatty liver induced by glycerol-feeding was observed during a marked increase in food consumption during the transitional state from depletion to repletion.

A NEW METHOD FOR ASSAYING RAT LIVER MICROSOMAL 3-HYDROXY-3-METHYLGUTARYL-COENZYME A REDUCTASE ACTIVITY AND ITS APPLICATION IN A STUDY OF THE EFFECT OF DIETARY CHOLESTEROL ON THIS ENZYME. Y.A. Baqir and R. Booth (Dept. of Biochem., Med. Sci. Inst., Univ. of Dundee, Dundee D D1 4HN, Scotland, U.K.). *Biochem. J.* **164**, 501–8 (1977). A new method suitable for measuring rat liver 3-hydroxy-3-methylglutaryl-CoA reductase activity is described and its advantages over methods previously available are discussed. An accurate time course was measured for the inhibition of liver microsomal 3-hydroxy-3-methylglutaryl-CoA reductase activity by dietary cholesterol; this enzyme was affected 1¼ h after the rats began to consume a cholesterol-rich diet. In this experiment there was no correlation between concentrations of microsomal cholesterol ester and the activity of 3-hydroxy-3-methylglutaryl-CoA reductase.

COMPETITION FOR HOST ESSENTIAL AND NONESSENTIAL FATTY ACIDS BY EHRLICH ASCITES CARCINOMA IN MICE. N. Baker, C. Sandborg, D. Morris, and M. Ookhtens (Tumor-Lipid Lab., Res. Service, Veterans Admin. Wadsworth Hospital Center, Los Angeles, Ca.). *Cancer Res.* **37**, 2218–25 (1977). Mobilization of essential and nonessential free fatty acids (FFA) in control and Ehrlich ascites carcinoma-bearing mice was studied under varying nutritional conditions. Competition between tumor and host tissues for circulating FFA and the relationship between FFA transport rates (from blood to tumor) and FFA turnover in tumor extracellular fluid were also studied. Tracers, [9,10-^{3}H]palmitate and [1-^{14}C]-linoleate, complexed to mouse serum albumin were injected i.v. into unanesthetized animals. Plasma FFA radioactivity and pool sizes were measured. About 60 to 100% of plasma FFA was replaced per min. In no case was the mean fractional irreversible disposal rate greater in cancerous than in normal mice. Moreover, the cancer, the largest organ in the body of these mice, was unable to compete effectively with the host for plasma essential as well as nonessential FFA. Either the slow FFA transport from blood to tumor can support the net growth of the tumor and energy requirements or another source of tumor fatty acid exists.

PHOSPHOLIPID REQUIREMENT OF THE MEMBRANE-BOUND Mg^{2+}-DEPENDENT ADENOSINETRIPHOSPHATASE IN *Acholeplasma laidlawaii*. E.M. Bevers, G. T. Snoek, J.A.F. Op Den Kamp and L.L.M. Van Deenen (Lab. of Biochem., State Univ. of Utrecht, Utrecht, The Netherlands). *Biochim. Biophys. Acta.* **467**, 346–56 (1977). Treatment of membranes of *Acholeplasma laidlawii* B with phospholipase A_2 from pig pancreas and phospholipase C from *Bacillus cereus* results in complete hydrolysis of phosphatidylglycerol. Phosphatidylglycerol is not required for the activity of two membrane-bound enzymes: NADH oxidase and p-nitrophenylphosphatase. A slight increase in activity of those enzymes is observed upon complete hydrolysis of phosphatidylglycerol. The ability to restore full Mg^{2+}-

ATPase activity in membranes which contain less than 2% of their original amount of phosphatidylglycerol is lost gradually upon prolonged incubation times. This irreversible loss of Mg^{2+}-ATPase activity is not accompanied by a measurable hydrolysis of the residual phosphatidylglycerol. Reconstitution experiments show that the fatty acid composition of both the (residual) phosphatidylglycerol present in the membrane as well as the added phosphatidylglycerol, determine the activation energy of the Mg^{2+}-ATPase and the temperature at which a break in the Arrhenius plot occurs.

FATTY ACID UTILIZATION BY L1210 MURINE LEUKEMIA CELLS. C.P. Burns, S-P.L. Wei, I.R. Welshman, D.A. Wiebe, and A.A. Spector (Dept. of Med., Univ. of Iowa College of Med., Iowa City, Iowa). *Cancer Res.* 37, 1991–7 (1977). L1210 murine leukemia cells grow in an ascites plasma that contains lipids, including 0.62 ± 0.046 (S.E.) μEq free fatty acid per ml. *In vitro* incubations demonstrated that isolated L1210 cells readily utilize free fatty acid that is added to the incubation medium. When the cells were incubated with albumin-bound [1-^{14}C] Palmitate, about 12 times more radioactivity was incorporated into cell lipids than was oxidized to CO_2. Triacylglycerols contained 1.5 to 4 times more radioactivity than phospholipids, and from 48 to 69% of the phospholipid radioactivity was recovered in the choline phosphoglycerides. [1-^{14}C]Palmitate utilization increased as the fatty acid concentration of the medium was raised, the largest increase occurring in the triglycerol fraction. Palmitate utilization also was increased by the presence of carbohydrates in the medium, their effectiveness (in descending order) being glucose, mannose, galactose, fructose, and glycerol.

INFLUENCE OF DIETARY FAT ON FATTY LIVERS OF CHOLINE-DEFICIENT RATS. C. Carroll and L. Williams (Home Economics Dept., Agri. Experimental Station, Univ. Arkansas, Fayetteville, AK). *J. Nutr.* 107, 1263–8 (1977). Our purpose was to evaluate the influence of type of dietary fat on nature and severity of liver lipid changes induced in male, weanling rats by low choline diets. Beef tallow, a blend of tallow and safflower oil, or safflower oil (SO) each provided 48% of total energy value of a control diet and a low choline diet. Livers from choline-deficient rats fed tallow, blend, or SO diets contained approximately 4.5,5, and 2.5 times as much lipid, respectively, as livers from corresponding control groups. Liver lipids from rats fed SO diets as compared with those from rats fed tallow diets contained lower percentages of saturated and mono-unsaturated fatty acids, and higher percentages of polyunsaturated fatty acids. Values for groups fed blend diets were intermediate, except for 18:0 and 20:4 in the control group. Choline deficiency resulted in significant increases in proportions of the predominant fatty acid(s) of the dietary fat in liver lipids (but not in fat pad lipids) at the expense of 18:0 and 20:4. Ratios of 16:0 to 18:0 in both liver and fat pad lipids were greater in choline-deficient than in corresponding control groups, probably reflecting greater fatty acid synthesis.

CHARACTERIZATION AND COMPARATIVE ASPECTS OF THE SERUM VERY LOW AND LOW DENSITY LIPOPROTEINS AND THEIR APOPROTEINS IN THE CHICKEN *(Gallus domesticus)*. M.J. Chapman, S. Goldstein, and M. Laudat (Unite 35, Unite de Recherches sur le Metabolisme des Lipides, Inst. Natl. de la Sante et de la Recherche Med, (INSERM), Hospital Henri Mondor, Creteil 94010, France). *Biochemistry* 16, 3006–15 (1977). Sera from young laying chickens, found to be hypertriglyceridemic by serum lipid and lipoprotein analyses, were fractionated by ultracentrifugation into very low ($d < 1.006$ g/mL) and low density (d 1.006–1.063 and 1.024–1.045 g/mL) lipoproteins (VLDL and LDL). The purity of these lipoprotein fractions was evaluated by electrophoretic, immunological, and electron microscopic techniques; their chemical and physical properties were subsequently determined and compared with those of the corresponding human fractions. These data indicate that the major protein component of chicken VLDL and LDL is a counterpart of human apolipoprotein B, although the lower molecular weight components of these avian lipoproteins appear to be more distinct from those of man.

THE ROLE OF DIACYLGLYCEROL-CARRYING LIPOPROTEIN I IN LIPID TRANSPORT DURING INSECT VITELLOGENESIS. H. Chino, R.G.H. Downer, and K. Takahashi (Biochem. Lab., Inst. of Low Temperature Sci., Hakkaido Univ., Sapporo, Japan). *Biochim. Biophys. Acta* 478, 508–16 (1977). A diacylglycerol-carrying lipoprotein was isolated from mature eggs of the silkworm, *Philosamia cynthia* and compared, for physiochemical properties, with the major diacylglycerol-carrying lipoprotein 1 (LP-I) of hemolymph. The two molecules are identical in electrophoretic mobility, structural configuration as revealed by electron microscopy, and amino acid composition. In addition mannose was detected in the lipid-free protein moiety, thus enabling classification of the molecules as glycoproteins. The molecules differ in lipid content with egg-LP-I containing only 3.6% of the diacylglycerol content of hemolymph LP-I and the phospholipid and cholesterol components also showing a marked reduction.

ISOLATION, MOLECULAR PROPERTIES, AND KINETIC CHARACTERIZATION OF LIPOPTOTEIN LIPASE FROM RAT HEART. J. Chung and A.M. Scanu (Dept. of Med. and Biochem., Pritzker Schl. of Med., and Franklin McLean Mem. Res. Inst., Univ. Chicago, Chicago, IL). *J. Biol. Chem.* 252, 4202–9 (1977). Lipoprotein lipase was isolated to electrophoretic and chromatographic purity from rat heart acetone/ether powder by a combination of n-butyl alcohol precipitation and heparin/Sepharose affinity column chromatography. By sedimentation equilibrium ultracentrifugation in 6 M guanidine hydrochloride, and by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, the enzyme was found to have a minimum molecular weight of about 34,000. It had a relative abundance of glutamic acid and contains 3.3% carbohydrate by weight. The composition was as follows, in moles per 34,000 g: mannose (neutral sugars), 5.1; sialic acid 0.8; and glucosamine, 2.3. When tested against a triolein glutamic acid (apo C-II); it was inactivated by 1 M NaCl and by apolipoproteins serine and alanine isolated from human serum very low density lipoprotein.

DIFFERENTIAL EFFECTS OF DIETARY METHYL ESTERS OF LONG-CHAIN SATURATED AND POLYUNSATURATED FATTY ACIDS ON RAT LIVER AND ADIPOSE TISSUE LIPOGENESIS. S.D. Clarke, D.R. Romsos and G.A. Leveille (Dept. of Food Sci. and Human Nutr., Michigan State Univ., East Lansing, Michigan). *J. Nutr.* 107, 1170–81 (1977). Four experiments were conducted to investigate what influence methyl esters of $C_{16:0}$, $C_{18:0}$, $C_{18:1}$, $C_{18:2}$, and $C_{18:3}$ fatty acids exert on rat liver and adipose tissue fatty acid synthesis and related enzymes when supplemented to a fat-free diet (FF). A randomized complete block design, in which rats were matched for body weight and food intake, was utilized. Rats previously adapted to a meal-eating regimen (access to food from 0900 to 1200 hours) were fed a FF-diet for 7 days prior to the addition of the respective dietary acids. $C_{16:0}$ had no suppressive action on liver fatty acid synthesis or related enzyme activities. Again adipose tissue lipogenesis remained unchanged by dietary fat treatment. These data clearly demonstrate the $C_{18:2}$ and $C_{18:3}$ specifically inhibit rat liver fatty acid synthesis, independent of carbohydrate intake. Under these conditions adipose tissue lipogenesis was unaffected by low levels of dietary fat regardless of the degree of unsaturation.

INFLUENCE OF DIETARY FATTY ACIDS ON LIVER AND ADIPOSE TISSUE LIPOGENESIS AND ON LIVER METABOLITES IN MEAL-FED RATS. S.D. Clarke, D.R. Romsos, and G.A. Leveille (Dept. of Food Sci. and Human Nutr., Michigan State Univ., East Lansing, Mi.). *J. Nutr.* 107, 1277–87 (1977). Rats were trained to eat a fat-free high carbohydrate diet from 800 to 1100 hours each day. After adaptation to meal-eating, the fat-free diet was supplemented with 8% methyl stearate ($C_{18:0}$) or 3% methyl linoleate ($C_{18:2}$) for 7 days. Relative to the fat-free group, hepatic utilization of acetate unit equivalents (C_2 units) for fatty acid synthesis per mg soluble protein by the $C_{18:0}$ group was not significantly altered, whereas $C_{18:2}$ supplementation significantly depressed hepatic fatty acid synthesis. Quantitation of long chain acyl CoA esters in freeze-clamped liver tissue of rats fed fat-free or fat-free plus 3% $C_{18:2}$ or $C_{18:3}$ diets revealed no concentration differences between treatments either before or after a meal. Similarly, lactate and pyruvate concentrations as well as the lactate:pyruvate ratios were not significantly changed by dietary $C_{18:2}$ or $C_{18:3}$. The inhibitory effects of $C_{18:2}$ or $C_{18:3}$ appear not be be mediated through changes in total plasma free fatty acid levels, in total hepatic long chain acyl CoA concentration or in hepatic cytosolic redox state.

MECHANISM OF CARBON ISOTOPE FRACTIONATION ASSOCIATED WITH LIPID SYNTHESIS. M.J. DeNiro and S. Epstein (Div. of Geol. and Planetary Sci., Cal. Inst. of Tech., Pasadena, CA). *Science* 197, 261–3 (1977). The low carbon-13/carbon-12 ratio of lipids is shown to result from isotopic fractionation during the oxidation of pyruvate to acetyl coenzyme A. In vitro analysis of the kinetic isotope effects of this reaction indicates that there will be a large, temperature-dependent difference in the carbon-13/carbon-12 ratio between the methyl and carbonyl carbon atoms of acetyl coenzyme A and between those carbon

atoms of lipid components which derive from them.

ALTERATIONS IN GLYCOSPHINGOLIPIDS OF PLASMA MEMBRANES FROM MORRIS HEPATOMA 5123TC. A.M. Dnistrian, V.P. Skipski, M. Barclay, and C.C. Stock (Memorial Sloan-Kettering Cancer Center, New York, N.Y.) *Cancer Res.* 37, 2182–7 (1977). Neutral glycosphingolipids and gangliosides were quantified in lipid extracts from normal rat liver and Morris hepatoma 5123TC and their isolated plasma membranes to determine differences in these components in the cell surface membranes of malignant cells. Glycosphingolipids present in rat liver and hepatoma were concentrated in plasma membranes, and glycosphingolipid patterns in plasma membranes reflected those of their respective whole cells. Neutral glycosphingolipids of plasma membranes from normal liver and from hepatoma consisted of ceramide mono- and dihexosides, together accounting for 83 to 86% of the total neutral glycosphingolipids and some ceramide tri- and tetrahexosides. These data are compatible with a concept of incomplete synthesis of trisialogangliosides in hepatoma and an accumulation of precursor gangliosides.

CHANGES IN BODY FAT AND LIPOGENIC ENZYME ACTIVITIES IN RATS AFTER TERMINATION OF EXERCISE TRAINING. G.L. Dohm, Barakat, E.B. Tapscott and G.R. Beecher (Biochem. Dept., Schl. of Med., East Carolina Univ., Greenville, N.C.). *Proc. Soc. Exp. Biol. Med.* 155, 157–9 (1977). During a recent investigation, we observed that trained rats gained weight at a remarkable rate after termination of training. Since training resulted in the loss of body fat, it was of interest to determine whether lipid deposition was enhanced after the termination of training (detraining). Thus, the present study was conducted to investigate alterations in body fat content during a 2-week detraining period. The activities of several lipogenic enzymes have also been measured to determine whether these enzymes play a role in the deposition of fat after termination of training.

ADIPOSE TISSUE REGENERATION FOLLOWING LIPECTOMY. I.M. Faust, P. Johnson and J. Hirsch (Rockefeller Univ., New York). *Science* 197, 391–3 (1977). Surgical removal of subcutaneous fat deposits in weaning leads to a regenerative response. If the rats are fed a diet high in fat, adipose mass and adiposcyte number are precisely restored within seven months of surgery. Thus, under appropriate experimental circumstances, compensatory hyperplasia will occur in adipose tissues of the rat.

SURGICAL REMOVAL OF ADIPOSE TISSUE ALTERS FEEDING BEHAVIOR AND THE DEVELOPMENT OF OBESITY IN RATS. I.M. Faust, P.R. Johnson and J. Hirsch (Rockefeller Univ., New York). *Science* 197, 393–6 (1977). Lipectomized and sham-operated rats were fed a high-fat diet to induce hyperphagia and rapid fat accumulation. Lipectomized rats with 25% fewer adipocytes were less hyperhagic and accumulated less fat, but their adipocytes remained equal in size to adipocytes of controls. A role for adipocyte size in fat storage regulation and food intake control is postulated.

EFFECT OF DIETARY LINOLEATE ON SYNTHESIS AND DEGRADATION OF FATTY ACID SYNTHETASE FROM RAT LIVER. P.K. Flick, J. Chen, and P.R. Vagelos (Merck Sharp & Dohme Res. Labs., Rahway, N.J.). *J. Biol. Chem.* 252, 4242–9 (1977). The induction of fatty acid synthetase activity in rat liver is markedly reduced by feeding a diet containing a source of linoleate. Within 48 h after changing from fat-free, high carbohydrate diet to one containing 15% by weight of safflower oil, the specific activity of rat liver fatty acid synthetase is approximately 2-fold lower than that from rats fed a fat-free diet throughout. In contrast, feeding a diet containing 15% hydrogenated coconut oil, a source of saturated fatty acids, or 5% methyl oleate for the same length of time has little effect on the activity of the enzyme. The rate of synthesis of the enzyme is reduced by safflower oil feeding from the fat-free (control) level and after 48 h is approximately one-half that of the control. The rate of degradation of fatty acid synthetase is markedly increased in the safflower oil-fed animals over the control; the half-lives are 1.8 days and 3.8 days, respectively. It is suggested that polyunsaturated fatty acids, or a product derived from them, may directly or indirectly regulate the transcription or translation (or both) of fatty acid synthetase messenger RNA.

REGULATION OF LIPID SYNTHESIS BY LOW DENSITY LIPOPROTEINS IN CULTURED SKIN FIBROBLASTS IN HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA. C.H. Fung, A.K. Khachadurian, C. Wang and I.F. Durr (Dept. of Med. and Biochem., Rutgers Med. Schl., College of Med. and Dentistry of New Jersey, Piscataway, NJ). *Biochim. Biophys. Acta* 487, 445–57 (1977). The regulation of cholesterol and fatty acid syntheses by low density lipoproteins (LDL) was studied in cultured skin fibroblasts from a normal subject with homozygous familial hypercholesterolemia the fibroblasts of which had no LDL binding to specific cell surface receptors (receptor negative) and no cholesterol esterifying activity. Assays were done in cells preincubated in media containing lipoprotein-deficient serum (serum A) or serum A delipidated with ether-ethanol (serum B). Our data indicate that in homozygous familial hypercholesteroilemia there is a derangement in the regulation of fatty acid synthesis. It is, however, less marked than the derangement of sterol synthesis. The inhibitory action of LDL both on sterol and fatty acid synthesis in cells that do not show any LDL binding activity by the presently available technique is in contrast to the findings of Goldstein et al. ((1975) Proc. Natl. Acad. Sci. U.S. 72, 1092-1096) which indicate that LDL has no inhibitory effect in receptor negative cell lines.

ROLE OF ω OXIDATION OF FATTY ACIDS IN FORMATION OF THE ACETYL UNIT FOR ACETYLATION. E. Hemmelgarn, K. Kumaran, and B.R. Landau (Dept. of Med., Case Western Reserve Univ. Schl. of Med., Cleveland, Ohio). *J. Biol. Chem.* 252, 4379–83 (1977). Specifically ^{14}C-labeled fatty acids and 2-amino-4-phenylbutyric acid were administered to fed and starved normal and nonketotic and ketotic diabetic rats. The acetylated amino acid was isolated from their urines, hydrolyzed, and the resulting acetates degraded. The percentage of distribution of [^{14}C] in the acetate from [2-^{14}C] stearate and [2-^{14}C] palmitate formed by the nonketotic diabetic rats was about carbon 1 = 5% and carbon 2 = 95%. For terminally labeled laurate, palmitate, and stearate it was about carbon 1 = 30% and carbon 2 = 70%. Similar distributions were found in the acetates formed by the normal and ketotic diabetic rats, although incorporation into carbon 1 from [16-^{14}C] palmitate was less. These distributions mean that a significant portion of the acetyl carbons arose by other than β oxidation of the fatty acids.

AGE-INFLUENCED VARIATIONS IN THE LEVELS OF CHOLESTEROL AND ATPASE ACTIVITY IN THE TESTS OF PREPUBERAL CHICKS. F.I. Ikewuonu and T.A. Aire (Dept. of Vet. Anatomy, Univ. of Ibaden, Ibaden, Nigeria). *Poultry Sci.* 56, 1158–60 (1977). Changes in the levels of total, free and esterified cholesterol and ATPase activity were measured in male prepuberal Nigerian fowl. Results showed that in all cases, the testicular levels of the parameters increased to peak levels and decreased thereafter. Total and free cholesterol levels were maximal at 12 weeks while the esterification of cholesterol was maintained from 14 weeks through to the 16th week. The results of ATPase activity corroborated these findings. The data suggest that peak androgen formation occurred in these chicks between 14th–16th weeks of age. As evidenced by the higher percentages of esterified cholesterol at all the ages studies, it is suggested that the Nigerian male fowl is an early-maturing specie.

PHOSPHATIDYLCHOLINE EXCHANGE BETWEEN THE BOUNDARY LIPID AND BILAYER DOMAINS IN CYTOCHROME OXIDASE CONTAINING MEMBRANES. P.C. Jost, K.K. Nadakavukaren, and O.H. Griffith (Inst. of Molecular Biol., Univ. of Oregon, Eugene Or.). *Biochemistry* 16, 3110–4 (1977). A phospholipid spin label, 16-doxylphosphatidylcholine, is employed in a study of lipid-protein interactions in cytochrome oxidase containing membranes. Two methods are used to label the membranous cytochrome oxidase: dispersion in cholate with subsequent detergent removal, and fusion with vesicles of the pure phospholipid label in the absence of detergent. A fraction of the label is immobilized, which is calculated to fall in the range of 0.17–0.21 mg of phospholipid/mg of protein (0.15–0.19 after correction for lipids not extracted by chloroform-methanol). These observations are evidence that boundary lipid, as reflected by the partitioning of the phosphatidylcholine label, is in equilibrium with adjacent bilayer regions and that it consists of a relatively constant amount of phospholipid associated with the hydrophobic portion of the protein.

DIETARY FIBER AND OTHER DIETARY FACTORS IN HYPERCHOLESTEREMIA. D. Kritchevsky (Wistar Inst. of Anatomy and Biol., 36th St. at Spruce, Philadelphia, Pa.). *Am. J. Clin. Nutr.* 30, 979–84 (1977). The current interest in the role of fiber in human disease can be attributed largely to the observations of Burkitt and Trowell who found that certain diseases which are common in western countries are virtually unknown in the developing countries of Africa. They concluded that the differences in disease spectra could be related to the decreased consumption by the developed countries. Their finding must be viewed as correlative associations and they do not prove cause

and effect. For example, colon cancer is considered by Burkitt to be one of the conditions related to low fiber intake. A high fiber diet, it is argued, by decreasing intestinal transit time, reduces the colonic residence time of potential carcinogenic agents. Hill on the other hand, presents a good case for considering the differences in disease spectra to be related to the action of different intestinal microflora (due to diet?) with their specific metabolic effects.

CHOLESTEROL VEHICLE IN EXPERIMENTAL ATHEROSCLEROSIS. PART 15: RANDOMIZED BUTTER AND RANDOMIZED LARD. D. Kritchevsky and S.A. Tepper (The Wister Inst. of Anatomy and Biol., Philadelphia, PA). *Atherosclerosis* 27, 339–45 (1977). Randomized lard and butter oil were compared with native lard and butter oil for their effects on cholesterol-induced atherosclerosis in rabbits. In each experiment there was also a group fed corn oil. The diets contained 2% cholesterol and 6% fat and were fed for eight weeks. Randomization of either butter or lard had virtually no effect as regards their atherogenic potential when fed as part of a diet containing 2% cholesterol. The corn oil-containing diet was less atherogenic than any of the other fats.

EFFECTS OF A PROLONGED VITAMIN E DEFICIENCY IN THE RAT. L.J. Machlin, R. Filipski, J. Nelson, L.R. Horn and M. Brin (Dept. of Biochem. Nutr., Roche Res. Cntr., Hoffmann-LaRoche, Inc., Nutley, New Jersey). *J. Nutr.* 107, 1200–8 (1977). Rats fed a vitamin E-deficient diet containing 10% "stripped" corn oil had reduced growth rate and elevated platelet count by 12 weeks of age, and a normocytic anemia with elevated reticulocytes by 16 weeks of age. After 5 months, rats became emaciated and developed kyphoscoliosis. Some rats developed skin ulcers and termors, and mortality was high. Neuromuscular lesions included a chronic necrotizing myopathy and localized axonal dystrophy. There was also a selective activation of lysosomes in the central nervous system microcirculation. Liver ascorbic acid of deficient rats was the same as in those receiving vitamin E. Urinary excretion of p-hydroxyphenylpyruvate after a tyrosine load was also the same in deficient and control rats. It was concluded that neither vitamin C synthesis or utilization was effected in the E-deficient rats.

EFFECT OF PLANT STEROL ESTERS ON THE ABSORPTION OF DIETARY CHOLESTEROL. F.H. Mattson, R.A. Volpenhein, and B.A. Erickson (The Procter & Gamble Co., Miami Valley Labs., P.O. Box 39175, Cincinnati, Ohio). *J. Nutr.* 107, 1139–46 (1977). Cholesterol absorption decreases when either free or esterified plant sterols are added to the dietary fat. The effectiveness of various plant sterols, which were added to the dietary fat at the same molar concentration, in causing this decrease was determined in thoracic duct-cannulated rats. The oleate ester of β-sitosterol, campesterol, and stigmasterol, individually or in a mixture, were all similar in their ability to decrease the absorption of cholesterol from a diet that contained otherwise sterol-free triolein as the only fat. Their effectiveness was equal to that of free β-sitosterol or stigmasterol. β-Sitosterol esterol esters of short (acetate), medium (decanoate), or long (oleate) chain fatty acids *did not* differ in their ability to lower cholesterol absorption. The extensive solubility of the phytosterol esters in fat, in contrast to the limited solubility of their unesterified forms, provides a means for administering effective amounts of these hypocholesterolemic agents.

METABOLISM OF GLYCEROPHOSPHOLIPIDS OF MYELIN AND MICROSOMES IN RAT BRAIN. S.L. Miller, J.A. Benjamins and P. Morell (Biol. Sci. Res. Ctr. and Dept. of Biochem. and Nutr., Univ. of NC at Chapel Hill, Chapel Hill, NC). *J. Biol. Chem.* 252, 4025–37 (1977). The metabolic turnover of phospholipids of rat brain myelin and microsomes was investigated after 17-day old animals received intracranial injections of [2-^{3}H] glycerol and either [1,3-^{14}C] glycerol, [1,2-^{14}C] choline, [1-^{14}C] acetate, [1,2-^{14}C] ethanolamine, [*methyl*-^{14}C] choline, D-[U-^{14}C] glucose or [^{32}P] orthophosphate. The turnover rate, with respect to the ^{3}H at the C-2 position of the glycerol moiety of individual lipids, was calculated for the first 15 days after injection (rapid phase) and for the time period between 15 and 80 days following injection (slow phase). The results for the half-life of phosphatidylcholine and phosphatidylethanolamine in microsomes were similar (3 to 4 days in the fast phase and 13 to 14 days in the slow phase, respectively). In myelin, the corresponding values were 6 to 10 days in the fast phase and 25 days in the slow phase.

CHARACTERIZATION OF SERUM LIPOPROTEINS OF THE SHARK CENTROPHORUS SQUAMOUS. G.L. Mills, C.E. Taylaur, M.J. Chapman and G.R. Forster (Courtauld Inst. of Biochem. Middlesex Hosp. Med. Schl., London, U.K.) *Biochem. J.* 163, 455–65 (1977). Blood serum form the shark *Centrophorus squamosus* (Bonnaterre) was shown to contain VLD (very-low-density), LD (low-density) and HD (high-density) lipoproteins. In shape, size and general physical properties, these lipoproteins were very similar to those described for other animals. The VLD lipoproteins were the major components of the mixture, and HD lipoproteins were present at the lowest amount. In addition to the usual lipid components, the shark lipoproteins also contain substantial amounts of hydrocarbon, probably mainly squalene, and monoalklyldiaclglycerols. Only trace amounts of wax ester were detected. The protein moiety of the VLD and LD lipoproteins contained a component which, in its solubility and electrophoretic properties, molecular weight and amino acid composition, resembled the B apolioprotein of man and other mammals. This accounted for a large part of the total shark apolioprotein. There were also present smaller amounts of proteins which were soluble in 8 m-urea. In their electrophoretic mobility on basic polyacrylamide gel, some of these were like the A and C apoproteins of man. The electrophoretic distribution of the soluble proteins from the VLD and LD lipoproteins resembled that in higher mammals, but in the HD lipoproteins the similarity was less.

REGULATION BY LIPIDS OF COFACTOR BINDING TO A PERIPHERAL MEMBRANE ENZYME: BINDING OF THIAMINE PYROPHOSPHATE TO PYRUVATE OXIDASE. T.A. O'Brien, R. Blake II, and R. B. Gennis (Depts. of Chem. and Biochem., Univ. of Illinois, Urbana, Il.). *Biochemistry* 16, 3105–9 (1977). Pyruvate oxidase is a peripheral membrane flavoenzyme isolated from *Escherichia coli*. Lipids have been shown to influence dramatically the kinetics of the enzymatic reaction; the V_{max} is enhanced by about 25-fold, and the K_m for both the substrate, pyruvate, and the cofactor, thiamin pyrophosphate, are altered in the presence of lipids. In addition, the Hill coefficient for thiamin pyrophosphate determined using steady-state kinetics is influenced by lipids. The observed effects are different for the different lipids and detergents used in this study. The results clearly illustrate one manner in which lipids can affect the behavior of a membrane enzyme, by modulating the interaction between the enzyme and those ligands involved in catalysis.

STUDIES ON VITAMIN D (CALCIFEROL) AND ITS ANALOGUES. 12. STRUCTURAL AND SYNTHETIC STUDIES OF 5,6-*trans*-VITAMIN D_3 AND THE STEREOISOMERS OF 10,19-DIHYDROVITAMIN D_3 INCLUDING DIHYDROTACHYSTEROL$_3$[1,2]. W.H. Okamura, M.L. Hammond, A. Rego, A.W. Norman, and R.M. Wing (Depts. of Chem. and Biochem., Univ. of California, Riverside, Ca.). *J. Org. Chem.* 42, 2284–91 (1977). Catalytic hydrogenation of 5,6-*trans*-vitamin D_3 (3a,5*E*-D_3) afforded the previously unknown C_{10} epimer of dihydrotachysterol$_3$ (2a,DHT$_3$ or 10*S*-b), 10*R*,19-dihydro-5*E*-vitamin D_3 (10*R*-b). Reaction of 3a with 9-borabicyclo 3.3.1 nonane (9-BBN) produced the 9-BBN/3a adduct, which upon treatment with acetic acid produced low yields of equal amounts of 2a and its C_{10} epimer 10*R*-b. When the 9-BBN/3a adduct was oxidized with basic hydrogen peroxide, good yields of the 19-hydroxy counterparts of 10*S*-b and 10*R*-b, 7a and 7b, respectively, were produced. The 9-BBN/2a adduct, produced similarly by treating vitamin D_3 (1a) with 9-BBN, reacted with acetic acid to afford 10*S*,19-(10*S*-a) and 10*R*,19=dihydrovitamin D_3 (10*R*-a), which differ from 10*S*-b and 10*R*-b, respectively, in their 5-double bond configurations. The stereochemistries and conformations of the A ring of the five analogues (5*E*-D_3, 10*S*-a, 10*R*-a, 10*S*-b, and 10*R*-b) have been studied by two ^{1}H NMR methods: correlation of the observed coupling constants with the limiting values for the two conformers (coupling constant method) and computer analysis of the 300-Mhz tris(dipivalomethanato)europium(III) [Eu(dpm)$_3$] shifted spectra (the lanthanide induced shift or LIS method).

EFFECT OF BM 15.075 ON LIPOPROTEIN CONCENTRATIONS IN DIFFERENT TYPES OF HYPERLIPOPROTEINAEMIA. A.G. Olsson, S. Rossner, G. Walldius, L.A. Carlson and P.D. Lang (King Gustav V Res. Inst. and Dept. of Med., Karolinska Hosp., Stockholm, Sweden). *Atherosclerosis* 27, 279-87 (1977). The four-week lipoprotein lowering effect of 0.2 g t.i.d. of BM 15.075 and of 0.5 g t.i.d. of clofibrate was studied in 29 subjects with different types of hyperlipoproteinaemia in a single blind crossover fashion. BM 15.075 decreased very low density lipoproteins (VLDL), triglycerides (TG) and cholesterol concentration in all types of hyperlipoproteinaemia the effect being dependent on initial lipoprotein concentrations. BM 15.075 decreased VLDL triglyceride concentrations on average 20% more than did clofibrate. BM 15.075 decreased low density lipoproteins (LDL) cholesterol concentrations in Type IIA and IIB but did

not significantly affect this lipoprotein lipid in type IV hyperlipoproteinaemia. Regression analysis showed that the drug tended to decrease LDL cholesterol if initial concentrations were above 157 mg/100 ml and to increase initially lower levels. No significant differences between BM 15.075 and clofibrate was found in the effect of LDL cholesterol. High density lipoproteins (HDL) cholesterol concentrations were not influenced by BM 15.075. No subjective side effects were noted on BM 15.075. S-ASAT increased and alcaline phosphatases decreased on both treatments.

EFFECTS OF PROSTAGLANDINS E_1 AND E_2 ON THE DE NOVO SYNTHESIS OF LIPIDS IN HUMAN PLATELETS & WHOLE BLOOD. K.C. Srivastava and S.C. Rastogi (Inst. of Hygiene & Social Medicine, Odense University, DK-5000 Odense, Denmark) and J. Clausen. *Indian J. Biochem. Biophys.* 14(1), 98–9 (1977). The effect of prostaglandins E_1 and E_2 on the *de novo* synthesis of lipids in human platelets and whole blood has been studied. While the *de novo* synthesis of most of the lipid components remained unaffected both in the platelets and whole blood, there seemed to be 3-fold increase in radioactivity incorporation into triglyceride fraction of blood in the presence of PGE_1. Similarly, in blood, the radioactivity incorporation into phosphatidylserine plus phosphatidylinositol (PS + PI) fraction increased more than twice in the presence of PGE_1. In the platelets, increased radioactivity incorporation in the PS + PI fraction was observed in the presence of PGE_2.

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