

Abstracts

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Biochemistry and nutrition

RELATIONSHIP OF MALIC ENZYME ACTIVITY TO FATTY ACID SYNTHESIS AND THE PATHWAYS OF GLUCOSE CATABOLISM IN DEVELOPING RAT LIVER. P. Madvig and S. Abraham (Bruce Lyon Memorial Res. Lab., Children's Hosp. Med. Center, 51st and Grove Sts., Oakland, CA 94609) *J. Nutr.* 110(1), 90-9 (1980). The rates of fatty acid synthesis and the activity of several enzymes involved in lipid and carbohydrate metabolism were determined in livers from fetal, suckling, weanling and maternal rats. An estimate of the proportion of glucose catabolized via the pentose phosphate cycle and the Embden-Meyerhoff pathway was made using ^{14}C - and ^3H -labeled glucose. The contribution of pentose phosphate cycle-generated reducing equivalents to fatty acid synthesis was assessed using glucose-3- ^3H . Developmental changes in the activity of hepatic malic enzyme were not related to developmental changes in the rate of fatty acid synthesis as might be expected if this enzyme functioned to provide NADPH for fatty acid synthesis. Malic enzyme activity did not correlate with pentose phosphate cycle activity or with utilization for fatty acid synthesis of NADPH generated via this pathway.

IN VITRO CHOLESTEROL SYNTHESIS IN FRESHLY ISOLATED MONONUCLEAR CELLS OF HUMAN BLOOD: EFFECT OF IN VIVO ADMINISTRATION OF CLOFIBRATE AND/OR CHOLESTYRAMINE. D.J. McNamara, N.O. Davidson and S. Fernandez (The Rockefeller Univ., New York, NY 10021) *J. Lipid Res.* 21(1), 65-71 (1980). The rate of incorporation of [2- ^{14}C] acetate into cholesterol has been measured in freshly isolated peripheral blood mononuclear leukocytes from patients on various hypolipidemic drugs that affect whole body cholesterol synthesis. These studies have demonstrated a significant two-fold increase in mononuclear cell cholesterol synthesis rates in patients receiving cholestyramine, a response measurable after 10 days of drug treatment. Mononuclear cell cholesterol synthesis rates were also measured in four groups of patients on the following drug regimens: 1) no medication, 2) clofibrate (2 g/day), 3) cholestyramine (16 g/day) or 4) both clofibrate and cholestyramine. The results demonstrated that the rate of acetate incorporation into cholesterol was significantly greater in the mononuclear cells from patients receiving either cholestyramine ($P < 0.005$) or clofibrate plus cholestyramine ($P < 0.001$), as compared to controls. Patients receiving clofibrate alone did not differ significantly from controls in their rates of mononuclear cell cholesterol synthesis. Factors other than plasma lipoprotein and lipid levels appeared to be responsible for the elevated sterol synthesis rates observed in all patients receiving cholestyramine.

CHARACTERISTICS OF SOFT SUBCUTANEOUS FAT IN RAM LAMBS FED CORN AND CORN-SILAGE DIETS. G.J. Miller, J.E. Kunsman, and R.A. Field (Div. of Animal Science, Univ. of Wyoming, Laramie, WY 82071) *J. Food Sci.* 45(2), 279-82 (1980). Softness of subcutaneous fat from ram lambs fed high corn silage or high corn diets varied within each dietary group, but, overall, fat from lambs fed the high corn-silage was harder. Consistent decreases in stearic acid and increases in branched-chain and odd-numbered acids accompanied increases in fat softness both within each dietary group and between dietary groups. Results of this study suggest that the synthesis of even-numbered, saturated acids is decreased as the fat becomes softer. Conversion of the high melting, even-numbered, saturated stearic acid to oleic acid, the major acid found in the subcutaneous fat, causes considerable decreases in stearic acid with consequent increase in softness. Increases in linoleic and linolenic acids in fat from the high corn dietary group were not major factors in fat softness. Low levels of elaidic acid were found in all fat samples but the presence of this *trans*-acid was not involved in fat hardness.

FATTY LIVER DUE TO DISPROPORTIONALLY ADDED METHIONINE TO A LOW SOYBEAN DIET AND LIPOTROPIC ACTION OF PHOSPHATIDES IN RATS. K. Noda and T. Okita (Faculty of Educ., Tokushima Univ., Tokushima, Japan) *J. Nutr.* 110(3), 505-12 (1980). Young female rats of the Wistar strain were

fed a 20% soybean diet (approximately 8% soybean protein) with or without the supply of 0.3% methionine. Methionine supply caused an accumulation of triglycerides in the liver. In vitro incorporation of acetate-1- ^{14}C into the liver lipid fraction and its incorporation ratios of triglyceride/phospholipid were higher in the livers from rats fed the methionine-supplemented diet (Met diet) than in those of animals fed the 20% soybean diet (basal diet). In vivo incorporation of ^{32}P into the phospholipid fraction was lower in the livers of rats fed the Met diet than in those of rats fed the basal diet. Injection of phospholipid (lecithin) through a tail vein increased the plasma level of esterified fatty acids in rats fed the Met diet only and not in those fed the basal diet. Injection of an apolipoprotein fraction produced no effect on the plasma esterified fatty acid levels. The effect of phospholipids in increasing triglyceride transport was confirmed in liver perfusion experiments. These results indicate that supplying methionine to the low soybean protein diet induced disproportionation of synthesis and transport of triglycerides by the shortage of phospholipids.

TURNOVER OF LABEL FROM [1- ^{14}C] LINOLENIC ACID IN PHOSPHOLIPIDS OF COHO SALMON, *ONCORHYNCHUS KISUTCH*. R.S. Parker, D.P. Selivonchick and R.O. Sinnhuber (Dept. of Food Sci. and Technology, Oregon State Univ., Corvallis, Oregon 97331) *Lipids* 15(2), 80-5 (1980). Juvenile coho salmon were injected intraperitoneally with [L- ^{14}C] linolenic acid, and sampled at 24, 120, and 240 hr. Liver, heart, and gill lipids were extracted, analyzed, and half-lives of individual liver glycerophospholipids and n-3 fatty acids determined from rates of loss of radioactivity. Incorporation of label into gill was much less than into either heart or liver. Total acyl half-life was shorter for the choline phospholipids than for the ethanolamine phospholipids, as were the half-lives of all individual n-3 fatty acids. Diacylglycerol analysis indicated that de novo synthesis could be responsible for the incorporation of only a small portion of the labeled long chain fatty acids found in phospholipids. The fatty acid half-lives reported here for salmon are in general agreement with those found previously in mammals.

RAPID CHANGES IN RAT HEART LIPOPROTEIN LIPASE ACTIVITY AFTER FEEDING CARBOHYDRATE. M.E. Pedersen and M.C. Schotz (Lipid Res. Lab., Res. Service, Veterans Admin. Wadsworth Med. Center, Los Angeles, CA 90073) *J. Nutr.* 110(3), 481-7 (1980). The effect of feeding various carbohydrates on the activity of lipoprotein lipase (LPL) released by heparin from perfused rat heart was investigated. Animals fasted for 8 to 12 hours were given a single 3-ml dose of 60% (w/v) glucose, sucrose or fructose solution or 3 ml water by intubation. After various time intervals, the hearts were removed and perfused with Krebs-Ringer bicarbonate buffer containing 1 unit heparin/ml. The perfusate was then assayed for LPL activity. From 35 to 80 minutes after feeding, the LPL activity released by heparin from hearts of the glucose fed animals decreased 85% compared to the LPL activity released from hearts of the control group fed water. A similar decline in lipase activity was seen in the sucrose-fed group. In contrast to the glucose and sucrose data, fructose feeding produced no change in the heparin-releasable LPL activity compared with the control animals fed water. The LPL activity remaining in the heart tissue after perfusion with heparin was not significantly different in the experimental and control groups. The capacity of the hearts to hydrolyze ^{14}C -labeled chylomicrons following glucose or sucrose feeding was also reduced by 70 to 85%.

PROTEIN-LIPID INTERACTIONS. A NUCLEAR MAGNETIC RESONANCE STUDY OF SARCOPLASMIC RETICULUM Ca^{2+} , Mg^{2+} -ATPASE, LIPOPHILIN, AND PROTEOLIPID APOPROTEIN-LECITHIN SYSTEMS AND A COMPARISON WITH THE EFFECTS OF CHOLESTEROL. D.M. Rice, M.D. Meadows, A.O. Scheinman, F.M. Goñi, J.C. Gómez-Fernández, M.A. Moscarello, D. Chapman and E. Oldfield (Dept. of Chem., Univ. of Illinois at Urbana-Champaign, Urbana, IL 61801) *Biochemistry* 18(26),

5893-903 (1979). Deuterium Fourier transform nuclear magnetic resonance (NMR) spectra at 34 MHz (corresponding to a magnetic field strength of 5.2T) have been obtained of a variety of protein-lipid systems containing specifically deuterated phospholipids. For purposes of comparison, spectra were also obtained for bilayers containing cholesterol (CHOL). The results show that proteins either disorder or have little effect on hydrocarbon chain order in membranes above the gel to liquid-crystal phase transition temperature (T_c) of the pure lipids. The results indicate that ATPase and CHOL cause small decreases in ^{31}P chemical shielding anisotropies but that in addition ATPase causes a four- to fivefold increase in ^{31}P spin-lattice and Carr-Purcell spin-spin relaxation rates, suggesting the possibility of polar group protein-lipid interaction leading to increased correlation times in the region of the lipid phosphate head group.

PROTEIN-LIPID INTERACTIONS. HIGH-FIELD DEUTERIUM AND PHOSPHORUS NUCLEAR MAGNETIC RESONANCE SPECTROSCOPIC INVESTIGATION OF THE CYTOCHROME OXIDASE-PHOSPHOLIPID INTERACTION AND THE EFFECTS OF CHOLATE. D.M. Rice, J.C. Hsung, T.E. King and E. Oldfield (Dept. of Chem., Univ. of Illinois at Urbana-Champaign, Urbana, IL 61801) *Biochemistry* 18(26), 5885-92 (1979). Deuterium quadrupole-echo Fourier transform nuclear magnetic resonance spectra (at 34 MHz) and phosphorus-31 Fourier transform nuclear magnetic resonance spectra (at 60.7 MHz) have been obtained of 1-(6,6-dideuteriopalmityl)-2-oleyl-sn-glycero-3-phosphocholine dispersions in excess water in the absence of, and complexed with, the membrane enzyme cytochrome oxidase (cytochrome $c:\text{O}_2$ oxidoreductase, EC 1.9.3.1). Thereby, we have investigated the effects of the detergent sodium cholate, and of temperature, on protein-lipid interactions in this system. Our results strongly suggest that residual detergent in these protein-lipid complexes causes a significant disordering of hydrocarbon chain and head group organization as determined by deuterium quadrupole splittings ($\Delta\nu_Q$) and phosphorus chemical shielding anisotropies ($\Delta\sigma$). There are, however, significant line-width increases, especially on approaching T_c in both deuterium and phosphorus spectra, indicating increased correlation times, in the region of the membrane surface.

LIPID BARRIER TO WATER EXCHANGE IN REPTILE EPIDERMIS. J.B. Roberts and H.B. Lillywhite (Dept. of Physiology and Cell Biology, Univ. of Kansas, Lawrence, Kansas 66045) *Science* 207(4435), 1077-9 (1980). Extraction of lipids from the shed epidermis of the terrestrial snake *Elaphe obsoleta obsoleta* increases cutaneous water loss in vitro as much as 15-fold. Partial denaturation of epidermal keratin without lipid extraction increases cutaneous water loss only twofold. Histological observations and thin-layer and gas-liquid chromatography of the lipid extracts indicate a complex mixture of polar and neutral lipids predominantly in the mesos layer of the cornified epidermis. Comparative measurements of cutaneous water loss in other species of snakes and a lizard show that permeabilities differ naturally but are essentially identical after lipid extraction. These findings establish the importance of lipids in the permeability barrier of reptilian skin and suggest that keratin or scale morphology are of nominal importance in limiting water exchange.

INFLUENCE OF DIETARY CHOLESTEROL ON MITOCHONDRIAL FUNCTION IN THE RAT. K.S. Rogers, E.S. Higgins and W.M. Grogan (Dept. of Biochem., Med. Coll. of Virginia, Virginia Commonwealth Univ., Richmond, VA 23298) *J. Nutr.* 110(2), 248-54 (1980). Rat-liver mitochondrial cholesterol ester levels were increased nine-fold and free cholesterol levels were doubled by feeding 10% lard and 2% cholesterol with Purina rabbit chow pellets to weanling male Sprague-Dawley rats for 5 weeks. This resulted in depression of State 3 (ADP-stimulated) glutamate respiration and reduced sensitivity to inhibition of phosphorylation by tetrabutylammonium bromide and oligomycin. Brain, heart, lung, spleen, kidney and testis mitochondrial functions were not responsive to changes in dietary cholesterol nor were increases noted in free cholesterol content; mitochondrial cholesterol esters in these six tissues remained at extremely low levels regardless of treatment. Inclusion of 0.01% oleyl-p-decylbenzene sulfonate (a hypocholesterolemic agent) in the 10% lard and 2% cholesterol diet prevented elevation of rat-liver cholesterol esters and restored "normal" mitochondrial functions of respiratory control. This compound has no lowering effect on the raised level of liver mitochondrial free cholesterol nor on the reduced mitochondrial sensitivity to the phosphorylation inhibitors. We concluded that cholesterol esters were associated with depression of liver mitochondrial respiratory control and that free cholesterol was related to desensitization of mitochondria to the phosphorylation inhibitors.

INTESTINAL UPTAKE OF FATTY ACIDS COMPLEXED TO PROTEINS IN THE CHICK INTESTINE. D. Sklan and S. Hurvitz (Faculty of Agri., Hebrew Univ. of Jerusalem, Rehovot, Israel) *J.*

Nutr. 110(2), 270-4 (1980). Intestinal mucosal uptake of protein complexed-fatty acids was studied in ligated duodenal loops in the chick. Increasing the concentration of an albumin oleic acid-complex resulted in a linear increase in uptake of oleic acid. Varying the albumin-to-oleic-acid ratio with constant albumin concentration resulted in depressed oleic acid uptake when the ratio was below 1:3. Uptake of oleic acid complexed to albumin was increased by some 60% on addition of taurocholic acid above its critical micellar concentration. In the absence of albumin, oleic acid uptake was some 60% high from a micellar solution. Uptake of lauric acid from aqueous solution was linear with concentration until its maximum solubility was reached, whereas uptake from albumin complexes at varying lauric acid concentrations was not linear with increasing concentration. Stearic acid exhibited lowest uptake and linoleic and linolenic acid highest uptake both when complexed to albumin or from micellar solution, although albumin-complexed fatty acids were transported at about half the rate of micellar fatty acids. We concluded that some proportion of fatty acids complexed to lipophilic proteins can be absorbed in the intestine in the absence of bile acids. When oleic acid was complexed to casein, bovine serum albumin or β -lactoglobulin at a protein:oleic acid ratio of 1:10 serosal transport was 40 to 50% of mucosal uptake.

PROPERTIES OF LIPID-APOLIPOPROTEIN ASSOCIATION PRODUCTS. COMPLEXES OF DIMYRISTOYL PHOSPHATIDYLCHOLINE AND HUMAN APO A-1. J.B. Swaney (Depts. of Biochem. and Med., Albert Einstein College of Med., Bronx, NY 10461) *J. Biol. Chem.* 255(3), 877-81 (1980). Recombination of apo A-1 from human high density lipoprotein (HDL) with multilamellar dimyristoyl phosphatidylcholine (DMPC) liposomes over a wide range of phospholipid/protein ratios has demonstrated two discrete reconstitution products. Both the dimer and trimer complex were found to be equally stable to denaturation by guanidine hydrochloride as determined by fluorescence measurements. Under no conditions were complexes found which contained a single A-1 molecule per complex, and little tendency was observed for these components to form particles containing more than 3 A-1 molecules. These studies suggest that during the fabrication of lipoproteins *in vivo*, particles of different sizes and stoichiometries may be formed, depending upon the availability of lipid and protein components, but that the properties of the apoproteins may restrict these particles to a narrow range of sizes, such as is observed for the plasma high density lipoproteins.

ENZYMIC HYDROLYSIS OF SPHINGOMYELIN IN THE PRESENCE OF BILE SALTS. S. Yedgar and S. Gatt (Lab. of Neurochem., Dept. of Biochem., Hebrew Univ.-Hadassah Med. School, Jerusalem, Israel) *Biochem. J.* 185(3), 749-54 (1980). Sphingomyelin in mixed dispersion with bile salts was hydrolysed by the solubilized sphingomyelinase of rat brain lysosomes. In parallel studies, physical properties of these dispersions were determined. The kinetic curves that described the rate of hydrolysis as a function of increasing concentrations of bile salt were multiphasic. A region of very low activity was followed by an ascending portion, a peak, a descending portion, a trough and a second ascending portion. The positions of the initiation points, peaks and troughs were found to be a function of the respective ratios of the bile salt to sphingomyelin for the detergent sodium taurodeoxycholate, but of the absolute concentration of the detergent for sodium taurocholate. Turbidity studies suggested that hydrolysis of sphingomyelin begins at a bile salt concentration that solubilizes the lipid and incorporates it into a mixed micelle with the detergent. Ultracentrifugation studies suggested that the sizes of the mixed aggregates of detergent and lipid were a function of the ratio of taurodeoxycholate to sphingomyelin, but of the absolute concentration of the bile salt, for sodium taurocholate.

CHANGES IN PHOSPHATIDYLINOSITOL METABOLISM DURING DIFFERENTIATION OF LENS EPITHELIAL CELLS INTO LENS FIBER CELLS IN THE EMBRYONIC CHICK. P.S. Zelenka (Lab. of Vision Res., Natl. Eye Inst., Natl. Inst. of Health, Bethesda, MD 20205) *J. Biol. Chem.* 255(4), 1296-300 (1980). During the development and growth of the lens, lens epithelial cells differentiate to form lens fiber cells. The present study investigates phosphatidylinositol metabolism in these two lens cell populations in the 6-day-old embryonic chick *in vivo*, to determine whether changes in the metabolism of this phospholipid are associated with lens fiber differentiation. The time course of the specific activity of the $\gamma\text{-PO}_4$ of ATP was also determined during this time period, and was shown to be approximately equal to the specific activity of CDP-diacylglycerol, the immediate precursor of phosphatidylinositol. Thus, lens fiber formation in the 6-day-old embryonic chick is associated with increased synthesis and decreased turnover of phosphatidylinositol. This is the first report of changes in phosphatidylinositol metabolism associated with cell differentiation during embryonic development.

CURRENT STATE OF KNOWLEDGE ON THE PHYSIOLOGICAL EFFECTS OF LINOLEIC ACID-HIGH MARGARINES. R.O. Vles. *Rev. Fr. Corps Gras* 27(3), 115-20 (1980). Numerous expert committees have repeatedly formulated recommendations emphasizing the urgency of dietary preventive measures for groups of populations with a high incidence of atherosclerosis. These recommendations are aimed at reducing the consumption of foodstuffs rich in saturated fats, promoting the consumption of those poor in hidden fats and making visible fats (like margarine and oils high in linoleic acid) available. Thus, these products will contribute to a better lipid balance in the diet. Recent scientific data indicate that the proposed modifications favourably influence various risk factors of cardiovascular diseases.

FAT UTILIZATION IN RELATION TO INTESTINAL FATTY ACID BINDING PROTEIN AND BILE SALTS IN CHICKS OF DIFFERENT AGES AND DIFFERENT GENETIC SOURCES. J.B.D. Katongole and B.E. March (Dept. of Poultry Science, Univ. of British Columbia, Vancouver, British Columbia, Canada V6T 1W5) *Poult. Sci.* 59(4), 819-27 (1980). New Hampshire chicks utilized dietary fat more efficiently than did broiler-type or White Leghorn chicks. The difference was more pronounced with tallow than with corn oil. Utilization of fat by all three types of chicks increased until the chicks were about six weeks old. At hatching, the concentration of fatty acid binding protein (FABP) in the intestine of the broiler-type chicks was significantly less than in the New Hampshire and White Leghorn chicks. Concentration of FABP declined during the first 1 to 2 weeks of life and then increased. By four weeks of age the breed differences in concentration of FABP in the intestine were no longer apparent. At some time after four weeks of age, FABP reached maximum concentrations in the intestinal tissue of the chicks of different breeds and thereafter declined as a proportion of the total intestinal tissue. Broiler-type chicks, which did not utilize fat as efficiently as did New Hampshire chicks in the first weeks of life, displayed lower concentrations in the proximal third of the intestine and higher concentrations in the remainder of the intestine than was the case with the New Hampshire chicks. A high level of dietary fat or dietary supplementation with sodium taurocholate increased the concentration of FABP in the intestine.

DISSOCIATION OF THE LIPID-ENZYME COMPLEX OF HORMONE-SENSITIVE LIPASE USING HIGH DENSITY LIPOPROTEIN OR APOLIPOPROTEIN A-I. J.C. Khoo, C.A. Drevon and D. Steinberg (Div. of Met. Disease, Dept. of Med., M-013D, Univ. of Cal., San Diego, La Jolla, CA 92093) *Biochim. Biophys. Acta* 617(3), 540-4 (1980). Hormone-sensitive lipase in homogenates of adipose tissue occurs as a large, lipid-rich complex including several acylhydrolase activities that emerge quantitatively in the void volume on gel filtration chromatography (2% agarose). Incubation with intact human plasma high density lipoprotein or with lipid-free apolipoprotein A-I, however, disrupted the lipid-rich complex almost completely and most of the enzyme activity eluted from a 2% agarose column at about $V_e = 2.3 \times V_0$. This use of the detergent-like properties of apolipoprotein A-I may be of value for dissociation of other lipid-associated or membrane-bound enzymes.

EFFECT OF DIETARY TAURINE ON BILE ACID METABOLISM IN GUINEA PIGS. A. Kibe, C. Wake, T. Kuramoto, and T. Hoshita (Inst. of Pharmaceutical Scis., Hiroshima Univ., Schl. of Med., Kasumi 1-2-3, Hiroshima, Japan) *Lipids* 15(4), 224-9 (1980). The effect of oral administration of taurine (200-300 mg daily) on the metabolism of bile acids was studied in male guinea pigs which have predominantly glycine conjugated bile acids. The results were summarized as follows: (a) oral administration of taurine for 10 days increased taurine-conjugated bile acids and the ratio of glycine to taurine-conjugated bile acids (G:T ratio) shifted from 3.95 to 0.19; (b) in taurine fed guinea pigs, the half-life of chenodeoxycholic acid (CDC) was about 40% shorter than that in controls and the fractional turnover rate increased by 70%; (c) the synthetic rate (mg/day/500 g body weight) of bile acids increased from 4.28 to 7.27 by taurine feeding; (d) hepatic cholesterol 7 α -hydroxylase activity was increased 2.4-fold by taurine feeding; (e) the total pool size of bile acids did not change significantly but the amount of lithocholic acid in the caecum and large intestine increased by about 40%; (f) neither free cholesterol nor cholesterol ester levels in liver and serum changed significantly. Results of this study suggest that changing the G:T ratio in the bile acid conjugation pattern may influence the rate of hepatic bile acid synthesis.

ACTIVATION OF CALCIUM AND PHOSPHOLIPID-DEPENDENT PROTEIN KINASE BY DIACYLGLYCEROL, ITS POSSIBLE RELATION TO PHOSPHATIDYLINOSITOL TURNOVER. A. Kishimoto, Y. Takai, T. Mori, U. Kikkawa, and Y. Nishizuka (Dept. of Biochem. Kobe Univ. School of Med., Kobe 650 Japan) *J. Biol. Chem.* 255(6) 2273-6 (1980). Ca^{2+} -activated, phospholipid-dependent protein kinase from various mammalian tissues was greatly

stimulated by the addition of diacylglycerol at less than 5% (w/w) the concentration of phospholipid. This stimulation was due to an increase in the apparent affinity of enzyme for phospholipid and to a concomitant decrease in the K_a value for Ca^{2+} from about 1×10^{-4} M to the micromolar range. Diacylglycerol alone showed little or no effect on enzymatic activity over a wide range of Ca^{2+} concentrations. This effect was greatest for diacylglycerol which contained unsaturated fatty acid at least at position 2. In contrast, diacylglycerols containing saturated fatty acids such as dipalmitin and distearin were far less effective. Cholesterol and free fatty acids were also ineffective. Based on these observations, a possible coupling is proposed between the protein kinase activation and phosphatidylinositol turnover which can be provoked by various extracellular messengers.

A LIPID MOBILIZING FACTOR IN SERUM OF TUMOR-BEARING MICE. S. Kitada, E.F. Hays and J.F. Mead (Lab. of Nuclear Med. and Radiation Bio., 900 Veteran Ave., Univ. of California, Los Angeles, CA 90024 and Dept. of Bio. Chem., UCLA Schl. of Med. and Dept. of Med., UCLA Schl. of Med., Los Angeles, CA 90024) *Lipids* 15(3), 168-74 (1980). There is considerable evidence that the growing tumor requires a source of unsaturated fatty acids, but the nature of this source and the mechanism of mobilizing the fatty acids from it are obscure. These experiments make use of AKR mice with implanted adipose tissue labeled with $1-^{14}C$ linoleic acid. With this experimental animal, it has been found that: (a) in the normal, fed mouse, fat is mobilized slowly and appears largely as respiratory CO_2 , following oxidation, (b) in the normal, fasted mouse, fat is mobilized rapidly and appears largely as respiratory CO_2 ; (c) in the tumor-bearing, fed mouse, fat is mobilized rapidly and appears largely in the tumor; and (d) the serum from tumor-bearing mice, when injected into normal mice, produces an immediate massive fat mobilization that does not respond to feeding, whereas the serum from normal, fed mice does not. It is concluded that a mobilizing factor of unknown nature is present in the serum of tumor-bearing AKR mice.

SODIUM n-BUTYRATE INDUCES PROSTAGLANDIN SYNTHETASE ACTIVITY IN MASTOCYTOMA P-815 CELLS. Y. Koshihara, T. Senshu, M. Kawamura and S.-I. Murota (Dept. of Pharmacology, and Dept. of Biochem., Tokyo Metropolitan Institute of Gerontology, Itabashi-ku, Tokyo 173, Japan) *Biochim. Biophys. Acta* 617(3), 526-9 (1980). Cultured mouse mastocytoma P-815 cells were treated with 1 mM sodium n-butyrate for 40 h. The treated cell homogenate showed high activities in synthesizing prostaglandin D_2 , E_2 , and $F_2\alpha$. Such activities were virtually absent in untreated cell homogenate. Direct addition of sodium n-butyrate to the homogenate showed no effects. Pre-exposure of cells to acetylsalicylic acid did not diminish the effect of the subsequent treatment with sodium n-butyrate. These data suggest that sodium n-butyrate induces fatty acid cyclooxygenase in P-815 cells.

LIPOPROTEIN MODIFICATIONS WITH CHANGING DIETARY PROTEINS IN RABBITS ON A HIGH FAT DIET. C. Lacombe, M. Nibelink (Univ. Paul Sabatier, Inst. de Physiologie ERA 412, CNRS, rue F. Magendie, F-31400 Toulouse France) *Artery (Leontidas, Mich.)* 6(4), 280-9 (1980). Rabbits received a high-fat diet containing either casein or soya protein. Casein, in contrast to soya, enhanced the effect of the high-fat diet on the rise in plasma and liver cholesterol. The very low density lipoprotein (VLDL) and low density lipoprotein (LDL) of animals receiving casein showed an enrichment in cholesterol esters which coincided with a decrease in the triglyceride content. These cholesterol-rich β lipoproteins may contribute to the potential atherogenicity of casein.

EVIDENCE OF ACCUMULATION OF CERAMIDES CONTAINING ^{14}C NERVONIC ACID IN THE RAT LUNG FOLLOWING INJECTION OF ^{14}C ERUCIC ACID. J. Lecerf (Laboratoire de Physiologie Animale et de la Nutrition, Faculte des Sciences Mirande, B.P. 138-21004 Dijon Cedex, France) *Biochim. Biophys. Acta* 617(3), 398-409 (1980). A mixture of albumin-bound ^{14}C erucate and 3H oleate was injected into rats fed a stock pellet diet containing 4% by weight of lipid. Chylomicrons containing the same labelled fatty acids were also injected into rats fed diets containing 15% by weight of rapeseed oil (48% of erucic acid), canbra oil (<5% of erucic acid) or ground nut oil (no erucic acid). Lung lipids were analyzed at various times after injection. Ceramides containing ^{14}C nervonic acid disappeared from the lung with time and their incorporation with time into sphingomyelin was also observed. The absence of accumulation of 3H and ^{14}C (18:1) in ceramides showed that oleic acid was not incorporated into sphingomyelin in the same way as nervonic acid. In the rapeseed oil diet group, there was no accumulation of ^{14}C radioactivity in ceramides and conversion of erucic acid into nervonic acid was less, and into oleic acid more, than in other diet groups indicating a possible enzyme adaptation.

SODIUM ION DIFFUSION THROUGH LIPOSOME MEMBRANES

CONTAINING CEREBROSIDE. B. Liljenfors and H. Lofgren (Dept. of Structural Chem., Faculty of Med., Univ. of Goteborg, P.O. Box 3303S-400 33 Goteborg, Sweden) *Chem. Phys. Lipids* 26(2), 111-20 (1980). Na⁺ efflux from liposomes (small unilamellar vesicles, SUV) of various compositions was studied, using ²²Na⁺ and ³H-labelled stachyose in simultaneous dual isotope measurements, stachyose being used as a measure of liposome disintegration. Dialysis was utilised to separate liposomes from extra-liposomal activity. Liposomes were made from egg lecithin and sphingomyelin and from mixtures of egg lecithin, sphingomyelin cerebroside, sulphatide and cholesterol. All mixtures produced more leaky and less stable SUV's than pure lecithin and pure sphingomyelin. The incorporation of cerebroside is significantly smaller than that of the phospholipids including sphingomyelin. It was found that membranes containing cerebroside had a significantly higher Na⁺ permeability than membranes without cerebroside.

A COMPARISON OF THE TURNOVER AND METABOLISM OF CHOLESTEROL IN NORMAL AND ATHEROSCLEROTIC MONKEY AORTAS. D.S. Lin, W.E. Connor, R.W. Wissler, D. Vesselinovitch and R. Hughes (Dept. of Med. and the Clinical Res. Center, Univ. of Oregon Health Sciences Center, Portland, OR 97201) *J. Lipid Res.* 21(2), 192-201 (1980). Rhesus monkeys were fed high cholesterol and cholesterol-free diets for 21-24 months. The animals were then given isotopic cholesterol intravenously and autopsied from 1 to 51 weeks later. The plasma and aortic cholesterol contents were 633 ± 130 mg/dl and 35.6 ± 11.4 mg/g dried tissue (4.5% in ester form) for atherosclerotic monkeys and 135 ± 25 mg/dl and 9.9 ± 3.6 mg/g (15.0% in ester form) for control monkeys, respectively. The minimal influx rate of cholesterol from plasma into the aorta was much greater for atherosclerotic animals, 0.470 ± 0.20 mg/g per day versus 0.088 ± 0.031 for control monkeys. There was a rapid turnover of both free and esterified cholesterol in the atherosclerotic aortas, greater than for normal aortas. These studies of cholesterol ester metabolism indicated a likely origin of aortic cholesteryl ester from the plasma cholesteryl esters. Our data indicated a dynamic cholesterol metabolism and turnover in the aorta during atherogenesis.

THE ANTI-HEPARIN PROPERTIES OF HUMAN LOW-DENSITY LIPOPROTEIN. I.R. MacGregor, D.A. Lane and V.V. Kakkar (Thrombosis Res. Units, King's College Hospital Med. School, Denmark Hill, London SE5 8RX, U.K.) *Biochim. Biophys. Acta* 617(3), 472-9 (1980). High-density (HDL), low-density (LDL) and very low-density lipoproteins (VLDL) have been purified from normal human plasma by combination of ultracentrifugation in high-density salt and agarose gel filtration. The ability of these lipoproteins to inhibit different molecular weight heparin fractions has been compared, using incubation mixtures comprised of anti-thrombin III and factor Xa. Residual factor Xa activity was measured using the chromogenic peptide substrate Bz-Ile-Glu-Gly-Arg-pNA. LDL inhibited the high molecular weight (but not low molecular weight) heparin accelerated neutralisation of factor Xa by anti-thrombin III. VLDL showed a similar, though much reduced anti-heparin activity, while the addition of HDL to the factor Xa incubation mixture produced no measurable anti-heparin activity. These observations suggest that certain plasma lipoproteins may selectively modulate the inhibitory action of heparin against factor Xa.

ISOLATION AND CHEMICAL CHARACTERIZATION OF NEUTRAL GLYCOSPHINGOLIPIDS OF HUMAN NEUTROPHILS. B.A. Macher and J.C. Klock (Dept. of Medicine, Div. of Hematology-Oncology, Cancer Res. Inst., Univ. of Calif., San Francisco, CA 94143) *J. Biol. Chem.* 255(5), 2092-6 (1980). Six neutral glycosphingolipids were isolated from purified preparations of human neutrophils. The chemical structure of each compound was characterized by degradation with exoglycosidases, methylation analysis, and electron impact/desorption mass spectrometry. Neutral glycosphingolipids containing N-acetylgalactosamine were not detected in human neutrophils. The major neutral glycosphingolipids were lactosylceramide and lactoneotetraosylceramide. Although lactoneotetraosylceramide accounts for only 10% of the neutral glycosphingolipid fraction, neutrophils are the most readily available source of this compound. We may conclude that human neutrophils, in contrast to human erythrocytes and platelets, contain as their major neutral glycosphingolipids lactoneo-type structures and smaller amounts of gala-type structures. These findings are discussed in terms of blood group antigens and glycosphingolipid changes due to malignancy.

FACTORS INFLUENCING THE IN VITRO ACTIVITY OF DIACYLGLYCEROL ACYLTRANSFERASE FROM BOVINE MAMMARY GLAND AND LIVER TOWARDS BUTYRYL-CoA AND PALMITOYL-CoA. M.O. Marshall and J. Knudsen (Biokemisk Institut, Odense Universitet, Campusvej 55, 5230 Odense M, Denmark) *Biochim. Biophys. Acta* 617(3), 393-7 (1980). Factors affect-

ing the incorporation of butyrate relative to palmitate into the sn-3 position of triacylglycerol by the diacylglycerol acyltransferase from bovine mammary gland and liver was studied in vitro. Butyrate incorporation from butyryl-CoA in the presence of palmitoyl-CoA was favoured by a high concentration of butyryl-CoA and by the presence of a long-chain acyl-CoA binding protein such as bovine serum albumin. The relative activity of the enzyme from both tissues towards butyryl-CoA and palmitoyl-CoA was independent of the concentration of membrane-bound 1,2-dipalmitoylglycerol. The significance of these results in relation to the unique presence of short-chain acids in ruminant milk triacylglycerols is discussed.

STUDIES ON DRUG-INDUCED LIPIDOSIS: SUBCELLULAR LOCALIZATION OF PHOSPHOLIPID AND CHOLESTEROL IN THE LIVER OF RATS TREATED WITH CHLOROQUINE OR 4,4'-BIS (DIETHYLAMINOETHOXY) α,β -DIETHYLDIPHENYLETHANE. Y. Matsuzawa and K.Y. Hostetler (Dept. of Med., Veterans Admin. Med. Center and the Univ. of California, San Diego, CA 92161) *J. Lipid Res.* 21(2), 202-14 (1980). Administration of chloroquine or 4,4'-bis (diethylaminoethoxy) α,β -diethyldiphenylethane (DH) to rats in oral doses of 100 mg/kg for 7 days causes phospholipid and cholesteryl ester accumulation in liver. To further characterize this drug-induced lipodosis, we have isolated and characterized the lipids of subcellular fractions from control rats and rats treated with chloroquine, DH, and Triton WR-1339. Analysis of the phospholipid content of the respective control and drug-treated liver fractions shows that the entire excess phospholipid content of chloroquine- or DH-treated liver can be accounted for by the drug-induced multilamellar bodies. The multilamellar bodies are the principal intracellular site of accumulation of chloroquine and DH, respectively. Increased delivery of phospholipid to lysosomes and decreased lysosomal catabolism of phospholipid are the factors which are thought to cause this experimental lipodosis. High levels of phosphatidylinositol in the multilamellar body may be in part responsible for the increased content of bis(monoacylglycerol) phosphate since it has been identified as an acyl donor in bis(monoacylglycerol) phosphate synthesis.

CHOLESTEROL, PHYTOSTEROLS, AND POLYUNSATURATED/SATURATED FATTY ACID RATIOS DURING THE FIRST 12 MONTHS OF LACTATION. M.J. Mellies, K. Burton, R. Larsen, D. Fixler, and C.J. Glueck (Lipid Res. and General Clin. Res. Centers, Depts. of Med. and Pediatrics, Univ. of Cincinnati Med. Center, Cincinnati, OH 45267) *Am. J. Clin. Nutr.* 32(12), 2383-9 (1979). Maternal diet, plasma, and breast milk, and infant plasma cholesterol, phytosterols, and polyunsaturated/saturated fatty acid (P/S) ratios were studied cross-sectionally in 33 normal women and in one woman homozygous for familial hypercholesterolemia during the 1st year of lactation. In the normal women, breast milk cholesterol levels varied from 2.2 to 13.3 mg cholesterol per gram milk fat; a 30% variation in breast milk cholesterol within the same subject from month to month was not unusual. Mean (\pm SE) maternal milk cholesterol levels for all normal subjects were $5.7 \pm .3$ mg/g milk fat for both the first 6 months of lactation and $6.0 \pm .4$ for months 7 to 12. In the first 7 months lactation, the homozygous familial hypercholesterolemic's breast milk had a 16-fold enrichment with cholesterol, with levels ranging from 93 to 319 mg/100 ml of milk. Maternal milk cholesterol did not correlate with infant plasma cholesterol, nor did milk phytosterol correlate with infant plasma phytosterol levels. Maternal dietary polyunsaturated to saturated fatty acid ratios inversely related to maternal plasma cholesterol. Maternal plasma phytosterol and P/S levels both were positively associated with breast milk phytosterol and P/S levels. Alteration of maternal diet can thus ultimately lead to alteration of breast milk phytosterol (but not cholesterol content), and to alteration of P/S ratios.

MITOCHONDRIAL METABOLISM OF (D,L)-THREO-9, 10-DIBROMO PALMITIC ACID. H.G. Mohamed, T.L. Andreone and R.L. Dryer (Dept. of Pharmacology, College of Pharmacy, Univ. of Alexandria, Alexandria, U.A.R. and Dept. of Biochem., College of Med., Univ. of Iowa, Iowa City, IA 52242) *Lipids* 15(4), 255-62 (1980). Bromination of palmitoleic or palmitelaic acid proceeds by *trans* addition and yields brominated products which cannot undergo β -oxidation when incubated with mitochondria isolated from hamster brown adipose tissue. These mitochondria were selected because they have a high capacity for oxidation of C₁₆ fatty acids and because they are readily uncoupled by an excess of free fatty acids of this chain length. The only metabolites which could be recovered from the incubation mixtures were dibromopalmitoylcarnitine and dibromopalmitoyl CoA. Free fatty acid was also recovered. Addition of synthetic carnitine or CoA esters of brominated fatty acids did not interfere with subsequent oxidation of palmitoylcarnitine. Addition of the free brominated fatty acids did significantly increase the rate of oxidation of subsequent additions of palmitoylcarnitine, as did other known synthetic uncouplers.

These results are consistent with observations by others that feeding brominated oils leads to brominated fatty acid incorporation into tissue lipids, and indicate why this is so. They also provide a possible explanation for the hepatic damage noted in feeding experiments.

EFFECT OF ETHANOL ADMINISTRATION ON FATTY ACID DESATURATION. A.M. Nervi, R.O. Peluffo, R.R. Brenner and A.I. Leikin (Cátedra de Bioquímica, Instituto de Fisiología, Facultad de Ciencias Médicas, Universidad Nacional de La Plata, Calle 60 y 120, 1900-La Plata, Argentina) *Lipids* 15(4), 263-8 (1980). The effect of ethanol on the fatty acid desaturation by rat liver has been studied using liquid diets of different composition. Acute ethanol administration increased triacylglycerols of total liver lipids, but did not modify significantly the lipid composition of microsomes. The $\Delta 6$ and $\Delta 5$ desaturases were inhibited by ethanol whereas the $\Delta 9$ desaturase and fatty acid synthetase were apparently modified only by diet composition. NADH-cytochrome (cyt.) c reductase was partially inhibited, whereas NADH-cyt._b₅ reductase remained practically unaltered and NADPH-cyt. c reductase activity was enhanced. Decreased electrons supplied by the microsomal cyt._b₅ electron transport chain would not be the reason for the inhibition of $\Delta 6$ and $\Delta 5$ desaturases by ethanol.

CHARACTERIZATION OF HUMAN HIGH DENSITY LIPOPROTEINS BY ZONAL ULTRACENTRIFUGATION. W. Patsch, G. Schonfeld, A.M. Gotto, Jr., and J.R. Patsch (Lipid Res. Center, Depts. of Preventive Medicine and Medicine, Washington Univ., St. Louis, MO 63110) *J. Biol. Chem.* 255(7), 3178-85 (1980). The two major subspecies of high density lipoproteins (HDL), HDL₂ and HDL₃, were obtained from the plasma of normolipidemic male and female human subjects of a single zonal ultracentrifugation step. These two species were evaluated for homogeneity by compositional, physical, and quantitative immunochemical criteria. Three subfractions of HDL₂ and five subfractions of HDL₃ were obtained by recentrifugation and analyzed. The data indicate that HDL in man contain density subclasses whose relative plasma concentrations can vary: a rather homogeneous HDL₂ with an average density of 1.096 g/ml, and a heterogeneous HDL₃ consisting primarily of particles with an average density of 1.140 g/ml, and in lesser abundance, particles with an average density of 1.160 g/ml. Both of these populations are flanked by closely related particles in lower amounts, suggesting the existence of two distinct subclasses. The data, however, do not rule out that these subclasses are the most prominent representatives of a continuum of gradually differing particles composing HDL₃.

THE UPTAKE OF HIGH DENSITY LIPOPROTEIN CHOLESTERYL ESTER IN THE PERFUSED RAT LIVER. S. Quarfordt, J. Hanks, R. Scott Jones, and F. Shelburne (The Cooperative Lipid Laboratory, Durham Veterans Administration Med. Center, and The Dept. of Med. and Surgery, Duke Univ. Med. Center, Durham, NC 27705) *J. Biol. Chem.* 255(7), 2934-7 (1980). The hepatic uptake of high density lipoprotein cholesteryl ester was determined in a nonrecycling isolated rat liver perfusion. High density lipoprotein rich in the E apoprotein (apoE) showed about 10 times more uptake of the ester on a single pass than the bulk of the high density lipoproteins rich in the A-I protein. The apoprotein recoveries in the liver paralleled the ester for both lipoproteins. The uptake appeared to occur primarily in the hepatic parenchymal cell. Addition of human C-III-1 apoprotein to the rat apoE-rich high density lipoprotein inhibited the hepatic uptake of its constituents.

REGULATION OF LIPID METABOLISM IN CHICKEN LIVER BY DIETARY CEREALS. A.A. Qureshi, W.C. Burger, N. Prentice, H.R. Bird and M.L. Sunde (USDA, SEA, Barley and Malt Lab., 501 N. Walnut St., Madison, WI 53705) *J. Nutr.* 110(3), 388-93 (1980). The activities of acetyl-CoA carboxylase (EC 6.4.1.2), fatty acid synthetase (FAS) and β -hydroxy- β -methylglutaryl-CoA (HMG-CoA) reductase (ED 1.1.1.88) were determined in subcellular fractions of livers from chicks fed different cereal-based diets. With a barley-based diet as compared to corn, the following was observed: body and liver weights decreased 31%; HMG-CoA reductase activity of liver decreased 79%; acetyl-CoA carboxylase activity increased 3-fold; fatty acid synthesis increased 5-fold, and plasma and liver cholesterol decreased 45% and 35%, respectively. The suppression and induction of activities of the two divergent pathways (cholesterol and fatty acid biosynthesis) persisted for at least 21 days. Wheat, oats and rye showed a similar but less pronounced effect. The pronounced decrease in plasma cholesterol level and HMG-CoA reductase activity have implications for human nutrition and possible control of the cardiovascular diseases in which cholesterol plays a key role.

THE FECAL MICROFLORA AND BILE ACIDS IN CHILDREN WITH CYSTIC FIBROSIS. C.C. Roy, G. Delage, A. Fontaine, L. Robitaille, L. Chartrand, A. Weber, C.L. Morin (Dept. of Pediatrics, Hôpital Ste-Justine, 3175 Ste-Catherine Road, Montreal H3T 1C5,

Quebec, Canada) *Am. J. Clin. Nutr.* 32(12), 2404-9 (1979). Fecal fat, bile acids, and the rectal microflora were studied in seven control children and in three groups of patients with cystic fibrosis (CF), seven were off antibiotics, ten on oral cloxacillin, and six on i.v. triple therapy (cloxacillin, gentamycin, and carbenicillin) for at least 2 weeks. Controls had lower concentrations (milligrams per gram dry stool) of both fat ($P < 0.005$) and bile acids ($P < 0.025$) than CF children off antibiotics. Antibiotics had little or no effect on fat but led to a striking decrease ($P < 0.01$) of bile acids in the triple therapy group. Concomitantly, there was reduced deconjugation of bile acids ($P < 0.01$) and formation of secondary bile acids ($P < 0.005$). This was associated with a 5-fold increase in the percentage of bile acids found in the aqueous phase of stools and with a marked reduction ($P < 0.001$) of the anaerobic flora (log counts per gram wet stool) in children on triple therapy (4.3 ± 1.9) when compared to controls (9.8 ± 0.1), CF off antibiotics (9.1 ± 0.1) and CF on colxacillin (9.6 ± 0.2). The close relationship between the anaerobic flora, the extent of bile acid microbial transformation, and fecal bile acid concentrations suggest that reduction of the anaerobic flora decreases adsorption of bile acids to dietary residues and microbes, favors bile acid absorption, and leads to a decreased fecal loss of bile acids in CF.

SERUM LIPOPROTEINS AND ATHEROSCLEROSIS IN HYPERTENSIVE BROAD BREASTED WHITE TURKEYS. A. Pagnan, G. Thiene, A.C. Pessina, and C. Dal Palù (Clinica medica II-Anatomia Patologica Univ. di Padova 35100 Padova (Italia)) *Artery (Leonidas, Mich.)* 6(4), 320-7 (1980). The serum lipid and lipoprotein profiles as well as the degree of atherosclerotic involvement in the aorta were studied in hypertensive strain of male broad-breasted white turkeys (BBWT). Serum phospholipid concentrations were found to be high while those of cholesterol and triglycerides were low. The alpha lipoprotein fraction, separated by agarose gel electrophoresis, represented the major lipoprotein fraction. Despite these facts, severe atherosclerosis was found in the abdominal aortas, suggesting the importance in this model of hypertension, functioning independently of the serum lipoprotein pattern. The cystic necrosis observed in the thoracic aorta represents a degenerative lesion possibly a result of the mechanical stress of hypertension. Structural differences of the aorta at the two different levels, thoracic and abdominal, may explain the different pathological findings. Neither platelet aggregates nor fibrin deposition were seen in the arterial wall.

HIGH FAT RATIONS FOR DAIRY COWS. TALLOW AND HYDROLYZED BLENDED FAT AT TWO INTAKES. D.L. Palmquist and H.R. Conrad (Dept. of Dairy Sci., Ohio Agr. Res. and Dev. Center, Wooster, OH 44691) *J. Dairy Sci.* 63(3), 391-5 (1980). Tallow and blended animal-vegetable fat were mixed as 10% of diet concentrate and compared with a concentrate containing no added fat. Concentrate containing fat was fed at two percents of diet dry matter, 50% (supraenergetic) and 33% (isoenergetic). The dry matter of the control diet was 50% concentrate. Isoenergetic high fat diets contained more fiber than control or supraenergetic high fat diets. Change of body weight and intake of feed dry matter were not different among feed groups. Milk and 4% fat-corrected milk production were less when high tallow was fed. Milk fat percent was lowest on the high concentrate diet, intermediate with high grain-high fat feeding, and normal with high fat isoenergetic rations. Multiple regression analysis of digestibility data showed that fat did not influence diet digestibility negatively and that calcium positively influenced digestibility of all diet components.

CLOFIBRATE ENHANCEMENT OF MITOCHONDRIAL CARNITINE TRANSPORT SYSTEM OF RAT LIVER AND AUGMENTATION OF LIVER CARNITINE AND γ -BUTYROBETAINE HYDROXYLASE ACTIVITY BY THYROXINE. S.V. Pande and R. Parvin (Lab. of Intermediary Metabolism, Clinical Res. Inst. of Montreal, Montreal, H2W 1R7, Canada) *Biochim. Biophys. Acta* 617(3), 363-70 (1980). The possibilities that the hypotriglyceridemic effect of clofibrate involves activation of carnitine-dependent oxidation of fatty acids in liver and that this may be partially mediated through thyroxine have been examined. 0.25% clofibrate in diet for 10-15 days, was found to increase carnitine 3-fold in livers of male as well as female rats. Liver carnitine was nearly doubled by L-thyroxine, 6 mg/kg of diet fed for 10 days, and so was the activity of γ -butyrobetaine hydroxylase. Clofibrate decreased carnitine in heart and urine; thyroxine did not affect these parameters but increased serum carnitine by 26%. Clofibrate feeding doubled the concentration of hepatic long-chain acyl(-)carnitine, mitochondrial carnitine translocase reaction, and enhanced acetoacetate production in liver homogenates as well as mitochondrial oxidation of palmitoylcarnitine in the presence of malonate. The ratio of esterified to free carnitine in urine and serum was also increased by clofibrate. These results suggest that clofibrate and thyroxine may exert their hypo-

triglyceridemic effect, in part, through the activation of carnitine-mediated transport of fatty acids in liver mitochondria.

EFFECT OF PURIFIED CELLULOSE, PECTIN, AND A LOW-RESIDUE DIET ON FECAL VOLATILE FATTY ACIDS, TRANSIT TIME, AND FECAL WEIGHT IN HUMANS. G.A. Spiller, M.C. Chernoff, R.A. Hill, J.E. Gates, J.J. Nassar and E.A. Shipley (Dept. of Nutritional Science, Syntex Res., Palo Alto, CA 94304) *Am. J. Clin. Nutr.* 33(4), 754-9 (1980). Some relationships have been proposed between fecal volatile fatty acids, transit time, fecal weight, and dietary fiber intake. In this study, the effect of purified cellulose, purified pectin, and a natural low-residue diet on fecal acetic, propionic, butyric, isobutyric, valeric and isovaleric acids, transit time, and fecal weight was investigated. Forty-two healthy male and female adults were fed low-residue diets for 2 weeks, followed by 3 weeks on the same diet plus either 14 g/day cellulose or 6 g/day pectin or a sucrose placebo. Feces were collected for 7 days during weeks 2 and 5. Volatile fatty acid changes with placebo and cellulose paralleled changes in fecal weight, thus fecal volatile fatty acid concentration did not change. Conversely, volatile fatty acid increase of the pectin group was not paralleled by fecal weight increase, signifying an increase in volatile fatty acid concentration ($P < 0.05$) of possible physiological significance. Some volatile fatty acids are probably absorbed, a fact worthy of further investigation. This study confirms: 1) that generalization of the effects of dietary fiber on volatile fatty acids, fecal weight and transit time should be avoided, 2) the mild antidiarrheal effect of pectin and, 3) the bulking properties of cellulose.

INHIBITION OF MITOCHONDRIAL FATTY ACID ELONGATION BY ANTIBODIES TO 3-KETOACYL-COA-THIOLASE. H. Staack, B. Davidson, and H. Schulz (Dept. of Chem., City College of the City Univ. of New York, New York, NY 10031) *Lipids* 15(3), 175-8 (1980). Antibodies to pig heart 3-ketoacyl-CoA thiolase inhibited almost completely and in a parallel fashion thiolase and the acetyl-CoA-dependent fatty acid elongation system present in an acetone powder extract of pig heart mitochondria. This finding leads to the conclusion that mitochondrial fatty acid elongation occurs by reversal of fatty acid oxidation. Several lines of evidence point to the thiolase-catalyzed condensation reaction as the rate-limiting step in the formation of elongated products. However, the accumulation of hydroxy acids suggests the enoyl-CoA reductase activity is limiting in the synthesis of saturated fatty acids.

THE EFFECT OF D-THYROXINE ON LIPOPROTEIN LIPIDS AND APOLIPOPROTEINS IN PRIMARY TYPE IIA HYPERLIPOPROTEINEMIA. P. Schwandt and P. Weisweiler (2nd Med. Clinic, Klinikum Grosshadern, Univ. of Munich, Marchioninstr. 15, D-8000 Munich 70 (F.R.G.)) *Atherosclerosis* 35(3), 301-6 (1980). The effect of 3 months' treatment with D-thyroxine on the lipoprotein lipids and apolipoproteins AI and B was investigated in 12 patients with type IIA hyperlipoproteinemia. VLDL, LDL and HDL were separated by preparative ultracentrifugation. Both apolipoproteins were measured in serum by electroimmunoassay procedures with monospecific antisera. There was a significant decrease of cholesterol, phospholipids and apolipoprotein B in serum and of all lipids in the LDL class. VLDL and HDL lipids and apolipoprotein AI showed no significant alterations. The atherogenic ratios LDL/HDL lipids and apolipoprotein B/apolipoprotein AI were lowered with the most pronounced effect on the ratio between the two apolipoproteins. It is concluded that there is an effective reduction of LDL particles by D-thyroxine. Further investigations are necessary to evaluate whether lipoprotein lipids or apolipoproteins are a better discriminator of the influence on atherosclerotic risk in type IIA hyperlipoproteinemia.

LIPOPROTEIN LIPID AND PROTEIN SYNTHESIS IN EXPERIMENTAL NEPHROSIS AND PLASMAPHERESIS. I: STUDIES IN RAT IN VIVO. E. Shafir and T. Brenner (Dept. of Biochem., Hebrew Univ., - Hadassah Med. Sch. and Hadassah Univ. Hosp., Jerusalem, Israel) *Lipids* 14(8), 695-702 (1979). Of the citrate carbons incorporated into serum and liver lipids, the proportion in cholesterol was higher in nephrotic rats when compared to normal rats. These results point out that while leucine is not an efficient in vivo precursor of lipoprotein lipids in nephrosis, de novo lipogenesis proceeds from other precursors. Similar trend of changes, though of smaller magnitude, was elicited in rats after double plasmapheresis, 18 hr apart, when measured 3 hr after the second plasma withdrawal. This indicates that the loss of circulating proteins either by direct removal or through kidney lesion stimulates the compensatory hepatic response involving excessive lipoprotein synthesis. Time-course studies showed that peak incorporation of leucine and citrate into the protein and lipid components of lipoproteins, respectively, as well as into serum albumin, occurred coincidentally 3 hr after the second plasmapheresis, suggesting an interdependence of the enhanced protein and lipid synthesis.

A DEFICIENCY OF MIXED FUNCTION OXIDASE ACTIVITIES IN THE CHOLESTEROL BIOSYNTHETIC PATHWAY OF HUMAN GRANULOCYTES. I. Shechter, A.M. Fogelman, and G. Popják (Dept. of Biol. Chem. and Div. of Cardiology, Dept. of Med., UCLA Schl. of Med., Los Angeles, CA 90024) *J. Lipid Res.* 21(3), 277-83 (1980). Highly purified human granulocytes synthesize [14 C]farnesol and [14 C]squalene but not [14 C]sterols from [14 C]mevalonic acid. Dimethylsulfoxide was found to be an excellent vehicle for carrying [3 H]squalene-2, 3-oxide into the intact cells. The granulocytes synthesized [3 H]lanosterol from this substrate, but were unable to further process the newly synthesized lanosterol along the cholesterol biosynthetic pathway. In contrast, intact lymphocytes and monocytes were able to synthesize radioactive cholesterol from either [14 C]mevalonic acid or [3 H]squalene-2,3-oxide. These results indicate that normal human granulocytes have retained squalene-2,3-oxide-lanosterol cyclase activity but have lost squalene epoxidase activity and at least one other mixed function oxidase activity that is required to transform lanosterol into cholesterol. These results may provide an explanation for the accumulation of farnesol and squalene that has been previously observed in populations of mixed leukocytes (Fogelman, A.M., Edmond, J., Seager, J., and Popják, G. (1975) *J. Biol. Chem.* 250 2045-55 (1); Burns, C.P., Welshman, I.R., Edmond, J., and Spector, A.A. (1979) *Biochim. Biophys. Acta* 572:345-51) (12).

SOME FACTORS INFLUENCING SERUM LIPID LEVELS IN A WORKING POPULATION. R.J. Shephard, M. Cox and C. West (Dept. of Preventive Medicine and Biostatistics, Univ. of Toronto Faculty of Medicine, Toronto, Ontario M5S 1A8, Canada) *Atherosclerosis* 35(3), 287-300 (1980). Life-style variables (perceived fitness, excess body mass, percent fat, lean mass, predicted maximum oxygen intake, cigarette consumption, alcohol consumption, use of contraceptive medication) have been related to the lipid profile (serum triglycerides, total cholesterol, HDL and LDL cholesterol) in a sizeable volunteer population of Toronto office-workers. Multivariate analysis demonstrates an independent positive association of age with total cholesterol, HDL and LDL cholesterol, and (in women only) a weak negative association with triglycerides. Much of the fitness effect is related to body fat, which is positively correlated with triglycerides and (in the men only) with total and LDL cholesterol, but is negatively related to HDL cholesterol. While multivariate analysis allows for the inter-relationship of smoking habits, alcohol consumption, and the various fitness measurements, it cannot prove cause and effect. Nevertheless, the potential improvement of lipid profile associated with (i) abstinence from cigarettes, (ii) a 4% reduction of body fat, and (iii) avoidance of contraceptive medication is sufficient to warrant experimental trial of such a change in lifestyle.

EFFECT OF VITAMIN E SUPPLEMENTATION ON LEUKOCYTE FUNCTION. J. Siva Prasad (National Inst. of Nutrition, Indian Council of Med. Res., Jamai-Osmania P.O., Hyderabad, 500007, A.P., India) *Am. J. Clin. Nutr.* 33(3), 606-8 (1980). The effect of megadoses of vitamin E was studied in 13 adult males and five young boys. Three hundred milligrams of vitamin E as *dl*- α -tocopheryl acetate, given daily for a period of 3 weeks produced a significant depression in the bactericidal activity of the leukocyte and the mitogen induced lymphocyte transformation. The delayed hypersensitivity of the skin to phytohemagglutinin was, however, not affected by the supplementation. The implication of the study and the discrepancy between the in vitro and the in vivo results of the cell-mediated immunity are discussed.

THE EFFECT OF DIETARY CORN OIL AND CHOLESTEROL LEVEL ON THE NEUTRAL STEROID COMPOSITION IN THE LARGE INTESTINAL CONTENTS OF THE RAT. L.B. Smith, D.E. Pratt and A.J. Clark (Dept. of Foods and Nutr., Purdue Univ., West Lafayette, IN 47907) *J. Nutr.* 109(10), 1730-8 (1979). The influence of dietary cholesterol and fat on the composition of neutral steroids within the large intestinal contents of rats was investigated. Concentrations and total amounts of cholesterol and its metabolites, coprostanol and coprostanone, were determined in the cecum and colon, initially and after being fed experimental diets for 3, 6 and 9 months. Eight week old rats were fed one of four semi-purified diets. The effect of dietary fat levels was complicated by interaction with cholesterol feeding. Without cholesterol feeding a greater concentration of neutral steroids was present in the large intestine of rats fed the higher level of fat. With cholesterol feeding a greater amount of neutral steroid was found in the large intestine of rats fed the 5% fat diet. Fraction of cholesterol degradation was greatest when the 5% fat diet without supplemental cholesterol was fed. Increasing dietary fat to 20% decreased fraction of cholesterol degradation and feeding cholesterol decreased it more. The fraction of cholesterol degradation value was the same regardless of dietary fat level when cholesterol was fed.

MECHANISM OF CHAIN LENGTH DETERMINATION IN BIOSYNTHESIS OF MILK FATTY ACIDS. S. Smith (Bruce Lyon Memorial Res. Lab., Children's Hospital Med. Center, 51st and Grove Sts., Oakland, CA 94609) *J. Dairy Sci.* 63(2), 337-52 (1980). Fatty acid synthetases isolated from all mammalian tissues synthesize predominantly palmitic acid. However, in vivo the mammary gland fatty acid synthetases of some species are responsible for the synthesis of medium chain fatty acids. The objective of this presentation is to outline the mechanism which regulates the product specificity of fatty acid synthetases in general and to illustrate how this control is modified in the mammary gland. By studying separately the kinetics of chain elongation by the core of the trypsinized complex and of chain termination by the isolated thioesterase I component, it has been possible to establish that the specificities of the elongation and termination reactions account for the synthesis of predominantly the carbon-16 fatty acid by purified fatty acid synthetases. At all stages of development of rat mammary gland, the amount of thioesterase II present correlates well with the proportion of medium chain fatty acids synthesized by the gland. This mammary gland-specific thioesterase appears responsible for the ability of this tissue to synthesize medium chain fatty acids characteristic of milk fat.

CHARACTERIZATION OF THE HIGH-DENSITY LIPOPROTEIN AND ITS MAJOR APOPROTEIN FROM HUMAN, CANINE, BOVINE AND CHICKEN PLASMA. J.B. Swaney (Depts. of Biochem. and Medicine of the Albert Einstein College of Medicine, Bronx, NY 10461) *Biochim. Biophys. Acta* 617(3), 489-502 (1980). The high-density lipoproteins (HDL) from canine, bovine, and chicken plasma have been shown to contain almost exclusively the apolipoprotein A-I, while human HDL contains a second major component, the apolipoprotein A-II. Chemical cross-linking demonstrated that dog and chicken HDL contain three apolipoprotein A-I molecules per particle, while bovine HDL contain approximately six apolipoprotein A-I molecules per particle. Comparison of the apolipoprotein A-I from various animal species indicated that the canine and human apolipoprotein A-I proteins were the most similar by fluorescence, self-association properties, and immunoreactivity. Cross-linking of chicken and bovine apolipoprotein A-I yielded patterns distinctly different from that obtained with the human or canine counterpart. It is concluded that the quaternary structure of the various species of HDL is not directly correlated with the degree of self-association found for the protein constituents.

SERUM CHOLESTEROL AND DISEASES IN NIGERIANS. G.O. Taylor, and A.E. Bamgboye (Depts. of Chem. Pathology and Preventive and Social Med., Univ. of Ibadan, Ibadan, Nigeria) *Am. J. Clin. Nutr.* 32(12), 2540-5 (1979). A study of 3451 cholesterol determinations in different diseases was carried out. The mean cholesterol levels for male and female adults and children with different diseases were compared with values for their healthy counterparts. Sickle cell anemia, leukemia, liver cirrhosis, hepatosplenomegaly, tuberculosis, and diabetic, nutritional, ataxic, and tropical neuropathies in male and female adults were associated with reduced cholesterol level while in children malnutrition and anemia were the main causes of low cholesterol levels. Obesity and hypertension caused an elevated level but the mean values were within the range for adult Nigerians in the high income group. Only nephrotic syndrome in both adult and children was associated with a markedly increased cholesterol level in Nigerians of low income status.

EFFECTS OF DIETARY SAPONINS ON FECAL BILE ACIDS AND NEUTRAL STEROLS, PLASMA LIPIDS, AND LIPOPROTEIN TURNOVER IN THE PIG. D.L. Topping, G.B. Storer, G.D. Calvert, R.J. Illman, D.G. Oakenfull and R.A. Weller (Div. of Human Nutr., CSIRO, Adelaide, S.A. 5000, Australia) *Am. J. Clin. Nutr.* 33(4), 783-6 (1980). Four young mature male pigs, 110 to 120 kg of body weight, were maintained on a low (0.01%) cholesterol diet. A double changeover design was used so that at any time two pigs received additionally 20 g/day of saponins as a 0.33% solution in drinking water. Saponins raised concentrations of fecal bile acids and neutral sterols and increased the contribution of primary acids to excretion. Neither the concentration of total plasma cholesterol nor low-density and high-density lipoprotein cholesterol were affected by saponins. There was also no change in either absolute or fractional catabolic rate of low-density or high-density lipoprotein apoproteins. The data are discussed in relation to the effects of cholestyramine on plasma cholesterol and bile acid excretion in the pig and to the possible role of saponin-containing foods in the control of plasma cholesterol in man.

ACTIVATION OF THE PHOSPHOLIPASE A₁ ACTIVITY OF LIPOPROTEIN LIPASE BY APOPROTEIN C-II. J. Stocks and D.J. Galton (Lipid Res. Lab., St. Bartholomew's Hosp., West Smithfield, London, EC1A 7BE, England) *Lipids* 15(3), 186-90 (1980). The effect of apo very low density lipoprotein (apo VLDL) and apoprotein C-II on the phospholipase A₁ activity associated with lipo-

protein lipase (E.C.3.1.1.3) was studied using purified bovine milk lipoprotein lipase. The enzyme degraded ¹⁴C phosphatidylcholine (PC) to ¹⁴C 2-acyl lysophosphatidylcholine at a rate of 0.28 ± 0.01 nmol/min/ml and triolein at a rate of 20.3 ± 0.4 nmol/min/ml in mixed emulsions of PC and triolein. The phospholipase activity and triacylglycerol lipase activity were both increased by the addition of apo VLDL and apoprotein C-II. After maximal activation, the rate of PC degradation was 1.19 ± 0.02 nmol/min/ml and triolein degradation 64.4 ± 0.4 nmol/min/ml. Activation of phospholipase A₁ activity and triacylglycerol lipase activity occurred in parallel.

VITAMIN A INDUCED HYPERTRIGLYCERIDEMIA IN CHOLESTEROL-FED RATS. L.W. Solomon and J.W. Erdman, Jr. (567 Bevier Hall, Dept. of Food Sci., Univ. of Illinois, Urbana, IL 61801) *Lipids* 15(3), 157-62 (1980). The effects of level and feeding frequency of retinoic acid (OIC) or retinyl acetate (YL) on the accumulation of lipids in the serum and liver of rats were investigated. Male Sprague-Dawley rats were fed ad libitum 1% cholesterol diets with or without supplemental OIC or YL. Vitamin A-fed groups included (per g of dry diet): 105 µg of OIC or 113 µg YL daily for 28 days, 735 µg OIC or 791 µg YL once each week for 28 days; and 735 or 105 µg of OIC on day 1 or 105 µg OIC daily for the week experiment. Daily feeding of OIC or YL increased serum triglyceride concentrations as compared to controls. Several days after removal of OIC or 1 week after removal of supplemental YL from the rat diets, serum triglyceride concentrations returned to basal levels. Cholesterol feeding elevated serum cholesterol as well as hepatic cholesterol, total lipids and vitamin A concentrations. Daily OIC feeding depressed serum and hepatic cholesterol concentrations. These results show that daily supplement of vitamin A increased serum triglycerides and reduced serum and hepatic cholesterol concentrations. Serum and liver alterations were dependent on continued feeding.

EFFECT OF DIETARY FAT SATURATION ON ACYLCOENZYME A: CHOLESTEROL ACYLTRANSFERASE ACTIVITY OF RAT LIVER MICROSOMES. A.A. Spector, T.L. Kaduce, and R.W. Dane (Depts. of Biochem. and Med., Univ. of Iowa, Iowa City, IA 52242) *J. Lipid Res.* 21(2), 169-79 (1980). The saturation of the fat contained in the diet has been observed to affect the acylcoenzyme A: cholesterol acyltransferase (ACAT) activity of rat liver microsomes. ACAT activity in microsomes (M₀) prepared from livers of rats fed a polyunsaturated fat-enriched diet containing 14% sunflower seed oil was 70-90% higher than in microsomes (M_S) prepared from livers of rats fed a saturated fat-enriched diet containing 14% coconut oil. This difference was observed within 20 days after the diets were begun, the earliest time tested, and persisted throughout the 70-day experimental period. There were no differences in the phospholipid or cholesterol content, phospholipid head group composition, or protein composition of the two microsomal preparations. The possibility is discussed that the changes in ACAT activity result from the differences in fatty acid composition of the microsomes. Other microsomal enzymes exhibited varying responses to these dietary fatty acid modifications. Therefore, dietary fat modifications do not produce a uniform effect on the activity of microsomal enzymes.

PRONOUNCED LIPOPROTEIN LIPID REDUCTION OBTAINED BY COMBINED LIPID-LOWERING TREATMENT IN PATIENTS WITH ATHEROSCLEROTIC DISEASE. B. Vessby, H. Lithell, I.B. Gustafsson and J. Boberg (Dept. of Geriatrics, Univ. of Uppsala, Uppsala Sweden) *Atherosclerosis* 33(4), 457-77 (1979). The feasibility of reducing serum lipoprotein levels in patients with atherosclerotic disease by combining diet, clofibrate and nicotinic acid (niceritrol) has been investigated. An additive lipid-lowering effect of diet and the two drugs was demonstrated. Clofibrate and niceritrol differed with regard to the effect on serum lipoprotein concentrations as well as on other metabolic parameters. The two drugs differed also with regard to the effects on serum uric acid concentration and the liver function tests. The plasma fibrinogen levels and the erythrocyte sedimentation rates were reduced during treatment with both niceritrol and colfibrate. The present study demonstrates that it is possible to obtain substantial reductions of serum lipoprotein concentrations by combining lipid-lowering diet, colfibrate and niceritrol treatment. There was an additive lipid-lowering effect of this treatment and the combination of the two drugs seemed beneficial in regard to certain possible side effects. The impact of a lipid reduction within this range on cardiovascular morbidity and mortality remains to be evaluated.

EFFECT OF STARVATION AND REFEEDING A HIGH-PROTEIN OR HIGH-CARBOHYDRATE DIET ON LIPID COMPOSITION AND GLYCOGEN CONTENT OF RAT LIVERS IN RELATION TO AGE. W. Weigand, E. Hannappel and K. Brand (Institut of Physiological Chem., Univ. of Erlangen-Nuremberg, FRG, Fahrstr. 17, 8520 Erlangen, West Germany) *J. Nutr.* 110(4), 669-74 (1980). Rats of two different ages (72 and 490 days) were

subjected to a 3-day fast and then refed for the same period a high-protein (89%) or high-carbohydrate (99%) diet. This experimental model served to study whether alterations occur in the content of the main lipid components, triacylglycerol, phospholipids and cholesterol in liver. It also examined whether the aging process itself has any effect on the lipid pattern. With the high-protein diet the content of all lipids returned to or nearly to the control level regardless of age. Refeeding the 72-day-old rats the high-carbohydrate diet led to a 2.4-fold overshoot in the triacylglycerol content, while the phospholipids and the cholesterol remained far below their control levels. In the 490-day-old rats the total lipids, phospholipids and cholesterol remained at the starvation level. With aging, the total cholesterol content showed a marked increase of about four-fold when corrected for growth.

THE EFFECT OF FEEDING DI-(2-ETHYLHEXYL) PHTHALATE (DEHP) ON THE LIPID METABOLISM OF LAYING HENS. D.L. Wood and J. Bitman (Milk Secretion and Mastitis Lab., Animal Science Institute, SEA-AR, USDA, Beltsville, MD 20705) *Lipids* 15(3), 151-6 (1980). Di-(2-ethylhexyl) phthalate (DEHP), a commonly used plasticizer, is now seen as an environmental pollutant. DEHP has been found to inhibit lipid and sterol synthesis in rats and mice. The effects of DEHP on various aspects of lipid metabolism were examined in chickens. White Leghorn laying hens were fed either a standard laying mash control diet (C) or the control diet containing 1% DEHP (DEHP) or 1% DEHP and 5% tallow (DEHP-T) for 28 days. DEHP and DEHP-T lowered feed consumption 10% but did not significantly affect body weight. After 3 weeks on the diets, egg production was 15-20% less in DEHP-T than in C and DEHP hens. Total liver lipid and cholesterol increased 19% and 26% in DEHP hens and 54% and 79% in DEHP-T hens when compared to controls. In contrast, the fat content of pectoralis major muscle decreased significantly in DEHP and DEHP-T hens. These results, in showing that DEHP alters plasma and tissue cholesterol but not yolk cholesterol, demonstrate again that egg cholesterol is remarkably resistant to alteration by dietary means.

EFFECT OF METHYL 2-HEXADECYNOATE ON HEPATIC FATTY ACID METABOLISM. R. Wood, T. Lee and H. Gershon (Dept. of Biochem. and Biophysics, Texas Agricultural Exp. Station, Texas A & M Univ. System, College Station, TX 77843) *Lipids* 15(3), 141-50 (1980). Normal and hepatoma bearing rats were fed a low level of methyl 2-hexadecynoate in a low fat diet for one month. The effect of the acetylenic acid on lipid metabolism as derived from mass analysis of lipid classes, fatty acids and positional monoene isomers isolated from the major lipid classes of liver and hepatoma has been assessed. Methyl 2-hexadecynoate caused a 25% decrease in body weight and the appearance of essential fatty acid deficiency symptoms within one week. Non-tumor-bearing animals contained a seven-fold increase in all neutral lipid classes, except cholesterol, while host animals did not contain fatty livers. The apparent protective effect of the host animal by the hepatoma also resulted in only marginal changes in the fatty acid and positional monoene isomers from host liver and hepatoma lipids. All of the data strongly suggest that long-chain 2-ynoic acids inhibit elongation of saturated and monoene fatty acids.

THE EFFECTS OF DIETARY TRANS, TRANS METHYL OCTADECADIENOATE ACID ON COMPOSITION AND FATTY ACIDS OF RAT HEART. P.H. Yu, J. Mai, and J.E. Kinsella (Inst. of Food Sci., Cornell Univ., Ithaca, NY 14853) *Am. J. Clin. Nutr.* 33(3), 598-605 (1980). *Trans, trans* linoleate (18:2) as the sole source of dietary fat (10% of calories) for 12 weeks induced the typical symptoms of essential fatty acid deficiency in rats and markedly altered the gross and lipid composition of hearts. The cardiac protein and phospholipids were decreased compared to rats receiving adequate *cis, cis* linoleate, i.e., 180.0 and 18.5 versus 214.4 and 23.8 mg/g heart, respectively, while DNA levels were 1.4 and 1.2 mg/g heart tissue, respectively. The hearts from rats on *trans, trans* 18:2 contained less phosphatidylcholine than hearts from rats on an essential fatty acid deficient diet of hydrogenated coconut fat or rats fed an essential fatty acid sufficient diet. The fatty acid composition of the various cardiac lipid classes were markedly affected by dietary fatty acids. The levels of *cis, cis* 18:2n6 and 20:4n6 were depressed in lipids from hearts of rats on *trans, trans* 18:2 or hydrogenated coconut fat diets while 18:1n9 and 20:3n9 were increased compared to rats receiving *cis, cis* 18:2. However, the amount of 20:3n9 was much lower in the *trans, trans* 18:2 group compared to the hydrogenated coconut fat group indicating that the dietary *trans* 18:2 depressed the elongation and further desaturation of 18:1n9 which, with 16:1 and *trans, trans* 18:2, accumulated in the cardiac lipids of the rats fed *trans* 18:2. There was a marked increase in 22:5n6 in phosphatidylcholine of rats receiving *cis, cis* C18:2 as sole source of fat.

PHOSPHOLIPID ACTIVATION OF COBRA VENOM PHOSPHOLIPASE A₂. 2. CHARACTERIZATION OF THE PHOSPHOLIPID-

ENZYME INTERACTION. M. Adamich, M.F. Roberts, and E.A. Dennis (Dept. of Chem., Univ. of Calif. at San Diego, La Jolla, CA) *Biochemistry* 18(15), 3308-14 (1979). Activation of cobra venom phospholipase A₂ toward phosphatidylethanolamine by phosphatidylcholine in mixed micelles has been suggested to be caused by a direct phosphatidylcholine-enzyme interaction. Comparable activation of phospholipase A₂ toward phosphatidylethanolamine also occurs with nonsubstrates sphingomyelin and lysophosphatidylcholine.

USE OF A SIMPLE ENZYMATIC ASSAY FOR CHOLESTEROL ANALYSIS IN HUMAN BILE. H. Fromm, P. Amin, H. Klein, and I. Kupke (Gastrointestinal and Nutr. Unit, Montefiore Hospital, Dept. of Medicine, Univ. of Pittsburgh School of Medicine, Pittsburgh, PA 15213) *J. Lipid Res.* 21(2), 259-61 (1980). An enzymatic technique for cholesterol analysis in serum was applied to human bile. The analytical yield was very satisfactory in experiments in which known amounts of cholesterol were added to untreated, as well as Millipore-filtered, samples of human bile. The analytical results of the enzymatic test agreed closely with those of a method utilizing the Liebermann-Burchard reaction. The enzymatic assay of cholesterol in bile proved to be sensitive and precise. In comparison to other methods of biliary cholesterol determination, it has the advantage of being rapid and simple.

CONTROL OF ENDOGENOUS TRIGLYCERIDE BREAKDOWN IN THE MOUSE DIAPHRAGM. N.A. Abumrad, H.M. Tepperman, and J. Tepperman (Dept. of Pharmacology, State Univ., of New York, Upstate Med. Center, Syracuse, NY 13210) *J. Lipid Res.* 21(2), 149-55 (1980). The control of endogenous triglyceride breakdown was studied in vitro, in the incubated intact mouse diaphragm. Isoproterenol (2 µg/ml) produced parallel increases in glycerol and free fatty acid release, and in tissue cyclic AMP levels, suggesting that cyclic AMP mediates the action of the catecholamine on triglyceride mobilization. In addition to cyclic AMP, calcium seems to be involved in the action of isoproterenol because preincubation of hemidiaphragms in the presence of the calcium ionophore A23187 decreased the lipolytic effect of the drug. Insulin (12.5 mU/ml) antagonized the action of isoproterenol on triglyceride breakdown (it decreased glycerol and free fatty acid release) without altering its stimulatory effect on cyclic AMP production, suggesting that the antilipolytic action of insulin is not mediated by a decrease in cyclic AMP levels. On the other hand, no detectable effect on lipolysis was observed with carbachol in control and denervated hemidiaphragms, although the latter possess acetylcholine receptors over the entire surface area of the muscle. It was concluded that catecholamines control triglyceride breakdown in the muscle while the cholinergic system does not seem to be involved. Cyclic AMP, calcium, and insulin all affect lipolysis in muscle and the interrelationships remain to be elucidated.

LIPOLYSIS AND CYCLIC AMP RESPONSE TO ISOPROTERENOL IN DIAPHRAGMS FROM CONTROL AND DYSTROPHIC MICE. N.A. Abumrad, H.M. Tepperman, and J. Tepperman (Dept. of Pharmacology, State Univ. of New York, Upstate Med. Center, Syracuse, NY 13210) *J. Lipid Res.* 21(2), 156-61 (1980). A comparison was made of the sensitivity of lipolysis (glycerol and free fatty acid release) and of cyclic AMP production to the action of isoproterenol in diaphragms from control and dystrophic Bar Harbor mice at 7 weeks of age. An increased lipolytic response was observed in diaphragms from dystrophic mice that was more apparent in the males, and was demonstrable when cyclic AMP was used instead of isoproterenol. The increased glycerol and free fatty acid release in response to isoproterenol and cyclic AMP cannot be explained by a higher triglyceride content of diaphragms from dystrophic mice, because it was found to be similar to that of controls when it was estimated by biochemical and light microscopic techniques. The increased lipolytic response was not paralleled by changes in cyclic AMP levels, which were found to be similar in diaphragms from control and dystrophic mice, whether in the basal or the stimulated state. It was concluded that the lipolytic apparatus in muscles from dystrophic mice shows an increased sensitivity to isoproterenol that seems to be related to events more intracellular than the cAMP production step.

ABSOLUTE RATES OF CHOLESTEROL SYNTHESIS IN EXTRA-HEPATIC TISSUES MEASURED WITH ³H-LABELED WATER AND ¹⁴C-LABELED SUBSTRATES. J.M. Andersen and J.M. Dietschy (Depts. of Pediatrics and Internal Medicine, Univ. of Texas Health Science Center at Dallas, Dallas, TX 75235) *J. Lipid Research* 20(6), 740-52 (1979). This study was undertaken to develop techniques for measuring absolute rates of sterol synthesis in extra-hepatic tissues in vitro and to estimate the magnitude of the errors inherent in the use of various ¹⁴C-labeled substrates for such measurements. In a second set of experiments, the H/C incorporation ratio in cholesterol was determined in the liver by measuring the absolute rates of hydrogen and acetyl CoA flux into sterols. In a

third set of studies, rates of incorporation of [^3H] water or [^{14}C] labeled acetate, octanoate, and glucose into digitonin-precipitable sterols were simultaneously measured in nine different extrahepatic tissues. Assuming that the H/C ratio measured in the liver also applied to these tissues, the [^3H] water incorporation rates were multiplied by the reciprocal of the H/C ratio to give the absolute rates of sterol synthesis in each tissue. When these were compared to the incorporation rates determined with the [^{14}C] labeled substrates the magnitude of the errors in the rates of sterol synthesis obtained with these substrates in each tissue could be assessed. These studies document the large and highly variable errors inherent in estimating rates of sterol synthesis in extrahepatic tissues using [^{14}C] labeled substrates under in vitro conditions.

EFFECTS OF MEDIUM- AND LONG-CHAIN TRIGLYCERIDE DIETS IN THE GENETICALLY OBESE ZUCKER RAT. A. Bach, H. Schirardin, F. Chanussot, M. Bauer and A. Weryha (Laboratoire de la Clinique Medicale A, Hopital Civil, 67091 Strasbourg Cedex, France) *J. Nutr.* 110(4), 686-96 (1980). To test whether the property of medium-chain fatty acids (which have 6-12 carbon atoms) being incorporated only in small amounts into the various tissues of a living organism could be exploited to treat obesity, genetically obese Zucker rats and their lean littermates were fed a diet containing 20% medium-chain triacylglycerols (MCT) or long-chain triacylglycerols (LCT) for 10 weeks. MCT, as compared with LCT, had the following effects: 1) MCT did not diminish weight gain in either the nonobese or the obese rats; 2) they increased ketogenesis more in the former than in the latter; 3) they increased the concentration of triacylglycerols in the liver of the obese rats but not of the lean ones; 4) they decreased the concentration of cholesterol in the liver of the lean but not of the obese rats, and 5) they did not particularly affect the concentration of proteins, glucose and insulin in the blood. We therefore conclude that the influence of the genotype is much more important in the establishment of the biochemical characteristics of rats than is the nature of the fatty acids ingested. Replacing LCT in the diet with MCT did not correct any of the major metabolic disorders in obese rats and therefore cannot unaided constitute a solution to the problem of genetic obesity.

KINETIC STUDIES OF THE TRANSFER OF ESTERIFIED CHOLESTEROL BETWEEN HUMAN PLASMA LOW AND HIGH DENSITY LIPOPROTEINS. P.J. Barter and M.E. Jones (Units of Clinical Biochem. and Human Morphology, School of Med., The Flinders Univ. of South Australia, Bedford Park, 5042, South Australia, Australia) *J. Lipid Res.* 21(2), 238-49 (1980). In vitro incubations (6 hr at 37 degrees C) of human low density lipoproteins (LDL), high density lipoproteins (HDL), and lipoprotein-free plasma revealed no significant net mass transfers of esterified cholesterol from either lipoprotein fraction to the other. Transfers of esterified [^3H] cholesterol from LDL to HDL must therefore have represented a process of molecular exchange between the two fractions. In molar terms, the exchange increased with increasing incubation concentrations of LDL, regardless of whether the HDL was increased in parallel, decreased, or kept constant. In direct contrast, with LDL kept constant, an increase in the concentration of HDL resulted in a decrease in the molar rate of exchange of esterified cholesterol between LDL and HDL. The data were then fitted to a mathematical model describing a physical model in which an esterified cholesterol transfer protein circulates in the plasma, interacting with lipoprotein particles into which it deposits and from which it picks up esterified cholesterol molecules. According to this model, to which the experimental data fit extremely well, the transfer protein had a much greater affinity for HDL than for LDL in a transfer process that was readily saturable by HDL but not by LDL.

EFFECTS OF THREE DIETARY FATS ON PLASMA LIPIDS AND LIPOPROTEINS IN FASTING AND POST-PRANDIAL HUMANS AFTER A SHORT-TERM DIET. M.F. Baudet, O. Esteve, B. Delaplanque, N. Winchenne and B. Jacotot (Unité de Recherches sur l'Atherosclérose, INSERM U 32, Henri-Mondor, F 94010 Créteil, France) *Lipids* 15(4), 216-23 (1980). The effects of 3 dietary fats (olive oil, canbra oil, and butter) on the fatty acids of blood lipids and on serum lipoproteins were compared in 6 healthy adult outpatients, after a 6-day normocaloric diet including 35% of the studied fat. Important, although incomplete, changes appeared in the fatty acid composition of the various serum lipids and in the composition and distribution of serum lipoproteins. These changes probably result from the degree of saturation of the fat ingested. Moreover, differences were observed among individual subjects. Genetic differences, which are important in clinical practice, are stressed in connection with risks of vascular diseases and hyperlipidemia and affect intestinal fat absorption and lipoprotein metabolism.

THE EFFECT OF DIETARY FAT ON THE FATTY ACID COMPOSITION OF LIPIDS SECRETED IN RATS' MILK. N.P. Bran-

dorff (Dept. of Biochem., Royal Danish Schl. of Pharmacy, Universitetsparken 2, DK-2100 Copenhagen ϕ , Denmark) *Lipids* 15(4), 276-8 (1980). During pregnancy and lactation, female rats were fed diets containing either 28% partially hydrogenated marine oil (28MO), 2% arachis oil (2AO), or no fat (FF). Milk lipid composition was examined by gas chromatographic analysis of the gastric content of 10-day old suckling pups. An increase to 45% in the milk content of long chain monoenoic acids, 18:1, 20:1 and 22:1, reflects the fatty acid composition of the marine oil. Milk fatty acids of medium chain length comprised 6%, 31% and 24% of total fatty acids in the (28MO), (2AO) and (FF) groups, respectively, suggesting that a high-fat diet (28MO) inhibits the lipid synthetic activity of mammary glands. The amount of dienoic C $_{18}$ -acids (6%) in the group fed (28MO) containing no essential fatty acids (EFA) was similar to the amount of 18:2 in the group receiving a low-fat, EFA-rich diet (2AO). However, only half the dienoic acid from the milk of the (28MO)-fed animals was linoleic acid, which was most likely mobilized from fat depots.

DISTRIBUTION AND MOBILITY OF ω 3 FATTY ACIDS IN RAINBOW TROUT FED VARYING LEVELS AND TYPES OF DIETARY LIPID. A.J. Castledine and J.T. Buckley (Dept. of Biochem. and Microbio., Univ. of Victoria, Victoria, B.C., Canada V8W 2Y2) *J. Nutr.* 110(4), 675-85 (1980). The availability of essential fatty acids in fish neutral lipid to tissue phospholipids was determined under conditions of adequate and inadequate essential fatty acid intake as well as during fasting. Juvenile rainbow trout were fed a semi-purified diet containing varying levels of cod liver oil, with or without supplementary olein. Fatty acid analysis indicated that in all treatments the neutral lipid pool was not turned over during feeding but was enhanced by exogenous or endogenously synthesized fatty acids. Fish that received diets devoid of essential fatty acids maintained virtually all of the docosahexenoic acid originally present in each lipid pool. Fish fed diets containing essential fatty acids deposited them in proportion to the dietary levels. After a 4-week fast, no change was noted in the relative levels of fatty acids in neutral lipid indicating that all fatty acids in neutral lipid were catabolized equally - including essential fatty acids. During fasting there was a selective retention of docosahexenoic and linoleic acids in the phospholipid pool.

VERY LOW DENSITY LIPOPROTEIN SECRETION BY CULTURED RAT HEPATOCYTES. INHIBITION BY ALBUMIN AND OTHER MACROMOLECULES. R.A. Davis, S.C. Engelhorn, D.B. Weinstein and D. Steinberg (Dept. of Medicine, Div. of Metabolic Disease, Univ. of Calif., San Diego, La Jolla, CA 92093) *J. Biol. Chem.* 255(5), 2039-45 (1980). Adult rat hepatocytes maintained in cell culture were used to study the role of serum albumin and other macromolecules in regulating the rate of very low density lipoprotein secretion. The incorporation of [^3H] glycerol, [^{14}C] acetate, and [^3H] amino-acids into cellular lipids and protein and into very low density lipoprotein secreted into a serum-free culture medium was determined with and without the addition of fatty acid-free bovine serum albumin, ovalbumin, γ -globulin, or dextrans of different molecular weights. At concentrations of macromolecules equal to that of albumin in rat serum, the incorporation of labeled precursors into the apoprotein B and into the triglycerides of very low density lipoprotein was inhibited by 50 to 93%, as was the net secretion of all very low density lipoprotein components. The results support the concept that serum albumin contributes to the regulation of hepatic very low density lipoprotein secretion but suggest that the underlying mechanism involves more than an osmotic effect.

CELLULARITY OF ADIPOSE TISSUE IN FETAL PIG. F. Desnoyers, G. Pascal, M. Etienne, and N. Vodovar (Station de Recherches de Nutrition, Institut National de la Recherche Agronomique, Centre National de Recherches Zootechniques, 78350 JOUY-en-JOSAS, France) *J. Lipid Res.* 21(3), 301-8 (1980). Adipose tissue cellularity was studied in the 85-day old Large-White pig fetus. The aim of this work was to count the adipose cells of forming tissue in an animal species which could be a possible model for studying adipose tissue in humans. Using a morphometric method with electron microscopy, mean triglyceride volume per cell was determined independently of mean cell volume. This method is suitable for counting adipose cells in the early stage of differentiation whatever their size and lipid inclusion volume. Site-by-site dissection of adipose tissue was not feasible in the 85-day old fetus and adipose cell number was computed by dividing total carcass triglyceride volume by mean triglyceride volume per cell. The carcass triglyceride seemed to originate only from adipose cells. The mean total carcass triglyceride volume per fetus (1.84 g) was low but, owing to the low mean triglyceride volume per cell (180.28 μm^3), the adipose cell number (11.15×10^9) was relatively important, as it represented about 27% of the extramuscular adipose cell number in the Large-White adult pig (41×10^9).

METABOLIZABLE ENERGY VALUES OF FATS MEASURED BY SEVERAL PROCEDURES. H.D. Halloran, and I.R. Sibbald (Halleran Res. Farm, Inc., Modesto, CA 95351) *Poult. Sci.* 58(5), 1299-307 (1979). Six experiments were conducted to measure the available energy values of 11 feed fats by several procedures. Only 45% of the variation in TME values was associated with the variation in the corresponding AME values. This may be explained in part by the use of birds of differing species, sexes and ages in the AME assays. Both AME and TME values tended to increase with the iodine values and linoleic acid levels of the fats, but such relationships can be misleading.

INCORPORATION OF [1-¹⁴C] OCTADECANOL INTO THE LIPIDS OF *LEISHMANIA DONOVANI*. H. Herrmann and G. Gercken (Dept. of Organic Chem. and Biochem., Univ. of Hamburg, Hamburg, Germany) *Lipids* 15(3), 179-85 (1980). After incubation of stationary phase *Leishmania donovani* with [1-¹⁴C] octadecanol, about 70% of the precursor was taken up within 3 hr. Wax esters and acyl moieties of glycerolipids contained most of the ¹⁴C-activity from 3 to 6 hr, because octadecanol was partly oxidized to stearate. Ether moieties were only weakly labeled. After 40 hr, 1-0-alkyl and 1-0-alk-1'-enyl diacylglycerols as well as 1-0-alkyl and 1-0-alk-1'-enyl-2-acyl-*sn*-glycero-3-phosphoethanolamines contained nearly all of the radioactivity. Most of the label in the neutral ether lipids was located in the alkyl ether side chain, whereas, in the phosphatidylethanolamine fraction, most of the label was found in the alkenyl ether side chain. Administration of 1-0-[1-¹⁴C] hexadecyl glycerol resulted in rapid labelling of the vinyl ether side chain of phosphatidylethanolamine plasmalogen (1 hr) increasing further at 2.5 hr. Most of the radioactivity in the alkoxy diacylglycerols was found in the 1-0-alkyl moiety.

SUPPRESSION OF CHOLESTEROL SYNTHESIS IN CULTURED FIBROBLASTS FROM A PATIENT WITH HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA BY HER OWN LOW DENSITY LIPOPROTEIN DENSITY FRACTION. A POSSIBLE ROLE OF APOLIPOPROTEIN. E.L. Havekes, B.J. Vermeer, E. De Wit, J.J. Emeis, H. Vaandrager, C.M. Van Gent and J.F. Koster (Gaubius Inst., Health Res. Organization TNO, Herenstraat 5d, 2313 AD Leiden, The Netherlands) *Biochim. Biophys. Acta* 617(3), 529-35 (1980). The suppression of cellular cholesterol synthesis by low density lipoprotein (LDL) from a normal and from a homozygous familial hypercholesterolemic subject was measured on normal fibroblasts and on fibroblasts derived from the same homozygous familial hypercholesterolemic patient. On normal fibroblasts both LDL preparations (density 1.019 to 1.063 g/ml) exerted a similar suppression of cellular cholesterol synthesis. With the homozygous familial hypercholesterolemic fibroblasts homozygous hypercholesterolemic LDL suppressed the cholesterol synthesis to a much greater extent than did LDL from a normal subject. Analysis of lipid and protein composition of both LDL preparations showed that homozygous hypercholesterolemic LDL differs from normal LDL. It is suggested that the presence of apolipoprotein E in the LDL density fraction from plasma from this homozygous familial hypercholesterolemic patient could offer an additional means for suppression of cellular cholesterol synthesis of this patient.

ESSENTIAL FATTY ACID RESTRICTION INHIBITS VITAMIN D DEPENDENT CALCIUM ABSORPTION. A.W.M. Hay, A.G. Haslam, M.A. Crawford, P.A. Stevens, E.B. Mawer and F. Sutherland Jones (Dept. of Chemical Pathology, Univ. of Leeds, Leeds, U.K. LS2 9NL) *Lipids* 15(4), 251-4 (1980). Essential fatty acid (EFA) restriction has been found to inhibit the action of vitamin D on the active transport of calcium in the intestine. This inhibition suggests EFAs are involved in facilitating the active transport of calcium across the mucosal membrane.

HEPATOCARCINOGENICITY OF GLANDLESS COTTONSEEDS AND COTTONSEED OIL TO RAINBOW TROUT (*SALMO GAIARDNERII*). J.D. Hendricks, R.O. Sinnhuber, P.M. Loveland, N.E. Pawlowski and J.E. Nixon (Dept. of Food Science and Tech., Oregon State Univ., Corvallis, OR 97331) *Science* 208(4441), 309-11 (1980). Glandless cottonseed kernels are available for purchase and consumption by the general public. These kernels contain no gossypol but still have a full complement of naturally occurring cyclopropenoid fatty acids, which in rainbow trout are active as synergists with aflatoxins and primary liver carcinogens. Diets containing glandless cottonseed kernels or a lightly processed cottonseed oil produced significant numbers of hepatocellular carcinomas in rainbow trout after 1 year. The much greater incidence of cancer induced by the kernel than by the oil indicates that synergists or other carcinogens may be present in the kernel in addition to the cyclopropenoid fatty acids.

DIACYL, ALKENYL, AND ALKYL ETHER PHOSPHOLIPIDS IN EJACULATED, IN UTERO-, AND IN VITRO-INCUBATED

PORCINE SPERMATOZOA. R.W. Evans, D.E. Weaver and E.D. Clegg (Dept. of Animal Sciences, Purdue Univ., West Lafayette, IN 47907) *J. Lipid Res.* 21(2), 223-8 (1980). The phospholipids of porcine spermatozoa were analyzed by a hydrolytic procedure directly after ejaculation, and after incubation for 120 min in vitro or in ligated uterine segments of females with induced estrus. Total phospholipid content of ejaculated sperm was 65.7 μ g lipid P per 10⁹ sperm, of which 41% was alkyl ether and 23% was alkenyl ether glycerophospholipid. All of the ether phospholipids were choline and ethanolamine glycerophospholipids. Phosphorus-containing sphingolipid separated into two components during thin-layer chromatography. Sphingosine was the only long-chain base identified in either band. Choline was the only water-soluble base present in the lower R_f sphingomyelin while ethanolamine was prevalent in the higher R_f component. Incubation of washed spermatozoa in Ca²⁺-free Ringer-fructose at 37°C for 2 hr produced no significant change in the level of any of the phospholipids. Incubation of washed sperm in the uterus for 2 hr, in the presence of oviductal secretions, produced an increase in phosphatidylcholine from 7.2 to 10.2 μ g lipid P per 10⁹ sperm.

VERY LOW DENSITY LIPOPROTEIN. REMOVAL OF APOLIPOPROTEINS C-II AND C-III-1 DURING LIPOLYSIS IN VITRO. S. Eisenberg, J.R. Patsch, J.T. Sparrow, A.M. Gotto, and T. Olivecrona. (Dept. of Med., Baylor College of Med., Houston, TX and Dept. of Clin. Chem., Univ. of Umea, Umea, Sweden) *J. Biol. Chem.* 254(24), 12603-8 (1979). In this study we have investigated the effects of very low density lipoprotein (VLDL) lipolysis on the removal of radiolabeled apolipoprotein C-II and apolipoprotein C-III-1 from *in vitro* lipolyzed lipoproteins. Lipolysis was carried out *in vitro* using lipoprotein lipase purified from bovine milk, and mixtures with or without plasma. Lipoproteins were isolated by ultracentrifugation and by gel filtration. The transfer was proportional to the extent of triglyceride hydrolysis, and similar for the two apoproteins. Gel filtration of incubation mixtures, on 6% agarose, revealed that the removal of labeled apo-C molecules from VLDL is not a consequence of either centrifugation or high salt concentration. These results suggest that there is no preferential removal of apo-C-II or apo-C-III-1 from lipolyzed VLDL particles. They further indicate that the ratio of apo-C-II to apo-C-III-1 does not regulate the extent of lipolysis if different VLDL particles, at least in VLDL isolated from nonlipidemic humans.

DISSOCIATION OF APOLIPOPROTEIN A-I FROM PORCINE AND BOVINE HIGH DENSITY LIPOPROTEINS BY GUANIDINE HYDROCHLORIDE. T.M. Forte, R.W. Nordhausen, A.V. Nichols, G. Endemann, P. Miljanich and J.J. Bell-Quint (Donner Lab., Lawrence Berkeley Lab., Univ. of Calif., Berkeley, CA 94720) *Biochim. Biophys. Acta* 573(3), 451-63 (1979). Dissociation of apolipoprotein A-I from pig and steer high density lipoproteins (HDL) deficient in apoA-II was determined by exposing native HDL fractions to 6 M guanidine hydrochloride (Gdn-HCl) at 37°C for periods from 5 min to 18 h. Bovine high density lipoprotein (HDL-B) was isolated at *d* 1.063 - 1.100 g/ml while porcine high density lipoprotein (HDL-P) was isolated at *d* 1.125 - 1.21 g/ml. The difference in behavior of HDL-B and HDL-P to Gdn-HCl exposure is discussed in terms of differences in apolipoprotein A-I amino acid composition, interaction of apolipoprotein A-I with phospholipids and the possible involvement of the cholesteryl ester core.

ENERGETIC EFFICIENCY OF CORN OIL AND POULTRY FAT AT DIFFERENT LEVELS IN BROILER DIETS. H.L. Fuller and M. Rendon (Dept. of Poultry Science, Univ. of Georgia, Athens, GA 30602) *Poult. Sci.* 58(5), 1234-8 (1979). The energetic efficiency of broiler finishing diets containing poultry fat or corn oil at levels of 5, 10, 15, and 20% was determined. Diets were formulated so that energy and nutrient density increased at each increment of added fat and calorie-nutrient ratios remained constant for all diets. Body weight gains were significantly greater for all diets containing added fats with no significant difference between fat sources. Feed efficiency adjusted to the same metabolizable energy (ME) and nutrient density was similar for all diets. Calorie efficiency (energy gain/energy absorbed) was slightly greater in the diets containing added fat than in the low fat control diet. Heat increment (HI) plus heat of activity (HA) corrected for intake (GE intake) was significantly less for the diets containing poultry fat at all levels than for the control diet. In the case of corn oil only the 10% level significantly reduced HI plus HA/GE intake. Values for the poultry fat were slightly lower than for the corn oil. Level or source of fat had no effect on its ME value as determined by the total excreta collection method.

INTERACTION OF HUMAN PLASMA HIGH-DENSITY LIPOPROTEIN HDL_{2b} WITH DISCOIDAL COMPLEXES OF DIMYRISTOYLPHOSPHATIDYLCHOLINE AND APOLIPOPROTEIN A-I. A.V. Nichols, E.L. Gong, P.J. Blanche and T.M. Forte (Donner Lab., Lawrence Berkeley Lab., Univ. of Calif., Berkeley,

CA 94720) *Biochim. Biophys. Acta* 617(3), 480-8 (1980). The interaction of HDL_{2b}, a major subclass ($d = 1.063-1.100$ g/ml) of human plasma high-density lipoproteins, with discoidal complexes composed of dimyristoylphosphatidylcholine (DMPC) and apolipoprotein A-I (weight ratio, DMPC/apolipoprotein A-I (2.1-2.5:1); dimensions, 10.0 X 4.4 nm) was investigated. Incubation at 37°C for 4.5 h of HDL_{2b} with discoidal complexes resulted in a transfer of DMPC from the discoidal complexes to the HDL_{2b}, a release of lipid-free apolipoprotein A-I from the discoidal complexes during such transfer, and a dissociation of some apolipoprotein A-I from the HDL_{2b} surface. The number of discoidal complexes degraded during interaction with HDL_{2b} depended on the initial molar ratio of HDL_{2b} discoidal complexes. Approximately one molecule of HDL_{2b} was required for the degradation of one discoidal complex particle, and the degradation process appeared limited by the capacity of the HDL_{2b} for uptake of DMPC. Degradation of discoidal complexes was also observed when human plasma LDL ($d = 1.006-1.063$ g/ml) was substituted for HDL_{2b} in the interaction mixture.

REGULATION OF PHOSPHATIDYLCHOLINE METABOLISM BY CYCLIC AMP IN A MODEL ALVEOLAR TYPE 2 CELL LINE. R.M. Niles and J.S. Makarski (Div. of Surgery and Dept. of Biochemistry, Boston Univ. School of Med., Boston, MA 02118) *J. Biol. Chem.* 254(11), 4324-6 (1979). The influence of cyclic AMP on the metabolism of phosphatidylcholine, the major component of pulmonary surfactant was examined in a cell line (A549) with type 2 pneumocyte characteristics. It was found that cyclic AMP increased both the total amount of phosphatidylcholine and disaturated phosphatidylcholine as well as the incorporation of [³H] choline into these fractions. The effect was specific for cyclic AMP since 5'-AMP, adenosine, and cyclic GMP did not alter phosphatidylcholine or disaturated phosphatidylcholine levels. Since the ability of various cyclic AMP analogs to increase phosphatidylcholine levels was correlated with their ability to activate protein kinase, it seems likely that a protein phosphorylation mechanism is involved in controlling phosphatidylcholine metabolism.

DECREASED CHEMOTACTIC AND RANDOM MIGRATION OF LEUKOCYTES DURING INTRALIPID INFUSION. J. Nordenstrom, C. Jarstrand, A. Wiernik (Dept. of Clin. Bacteriology, Serafimerlasarettet, Box 12700, S-112 21 Stockholm, Sweden) *Am. J. Clin. Nutr.* 32(12), 2416-22 (1979). The soybean oil emulsion Intralipid was given intravenously to 12 healthy subjects for 2 hr. During the infusion an impairment of the chemotactic and random migration of leukocytes was noted. It was correlated to the dose given and to the degree of hypertriglyceridemia induced. Migration was fully restituted 22 hr after the infusion. Also when added in vitro Intralipid caused an impairment of leukocyte motility that followed a dose response pattern.

EFFECTS OF DIETARY PROTEINS FROM A VARIETY OF SOURCES ON PLASMA LIPIDS AND LIPOPROTEINS OF RATS. L.B. Neves, C.K. Clifford, G.O. Kohler, D. De Fremery, B.E. Knuckles, C. Cheowtirakul, M.W. Miller, W.C. Weir and A.J. Clifford (Depts. of Nutr., and Food Science and Tech., Univ. of Calif., Davis, CA 95616) *J. Nutr.* 110(4), 732-42 (1980). Five experiments were conducted to study the effect of various protein sources on fasting blood lipids and lipoproteins in the rat. Plasma levels of total cholesterol, high density lipoprotein (HDL)-cholesterol and total triglyceride, as well as weight gain, food intake, protein efficiency ratio and net protein utilization were measured over 28-day test periods with male Sprague-Dawley rats. The purified proteins studied included casein, egg albumin, lactalbumin, soy and alfalfa. Crude proteins studied included yeast, fish meal and blood meal. Plasma HDL-cholesterol accounted for approximately 70% of the plasma total cholesterol. Plasma HDL-cholesterol concentrations correlated positively ($R = 0.72$) with plasma total cholesterol and negatively ($R = -0.34$) with plasma triglyceride levels. These results clearly show that the pure and crude plant proteins did not have a hypocholesterolemic effect compared with pure and crude animal proteins in rats. Plasma HDL-cholesterol levels were the same in rats fed plant and animal proteins.

ERUCIC ACID-INDUCED ALTERATION OF CARDIAC TRIGLYCERIDE HYDROLYSIS. H. Stam, T. Geelhoed-Mieras and W.C. Hülsman (Dept. of Biochem. I, Med. Faculty, Erasmus Univ. Rotterdam, P.O. Box 1738, 3000-DR Rotterdam, The Netherlands) *Lipids* 15(4), 242-50 (1980). Male Wistar rats were fed for 3 or 10 days with high erucic acid rapeseed oil (HEAR) or trierucate (TE). These diets produced increased myocardial triglyceride (TG) levels. Cardiac lipid accumulation was related to basal- and hormone- (glucagon, norepinephrine) stimulated lipolysis, determined as glycerol release, which proved to be enhanced in isolated, perfused hearts from HEAR- and TE-fed rats. Endogenous TG levels in isolated hearts from rats fed the stock and the sunflowerseed oil (SSO) diet

were low and probably rate-limiting for tissue lipolytic activities. HEAR feeding of rats did not modify the rate of erucic acid (22:1) oxidation in heart. Prolonged HEAR and TE feeding led to a decrease in the endogenous TG level, a process in which the increased rate of TG hydrolysis might play an important role. Fatty acids seemed to be an important regulator of tissue lipase activity: palmitate inhibited glucagon-stimulated lipolysis, which suggests the tissue lipase is subject to product inhibition by fatty acids.

EFFECT OF PREGNANCY, LACTATION AND A HIGH-FAT DIET ON ADIPOSE TISSUE IN OSBORNE-MENDEL RATS. L. Steingrimsdottir, M.R.C. Greenwood and J.A. Brasel (Columbia Univ., Inst. of Human Nutr. and Dept. of Pediatrics, College of Physicians and Surgeons, 630 W. 168th St., New York, NY 10032) *J. Nutr.* 110(4), 600-9 (1980). Adult Osborne-Mendel female rats were fed either standard laboratory or high-fat diets during the course of pregnancy and lactation. Animals were killed on day 20 of pregnancy and 20 days post-partum after nursing either 0, 4, 8 or 14 pups. High-fat feeding increased total carcass fat, adipose depot weights and fat cell size by two to three-fold. Pregnancy also increased carcass fat but the distribution was not uniform; in both dietary groups the parametrial depot was unchanged. The subscapular and retroperitoneal depots increased in pregnant standard-fed rats while the subscapular and omental depots increased in pregnant high-fat-fed rats. Increased fat cell size accounted for almost all pregnancy-related fat deposition. High-fat-feeding, which promoted fat deposition in nonpregnant animals and further exaggerated the fat accretion during pregnancy, did not prevent the extensive fat mobilization accompanying normal lactation. It is hypothesized that during lactation hormonally induced metabolic changes in adipose tissue may favor fat mobilization and hence promote weight loss even when a diet which normally induces triglyceride storage is fed.

A NOVEL USE OF CHITOSAN AS A HYPOCHOLESTEROLEMIC AGENT IN RATS. M. Sugano, T. Fujikawa, Y. Hiratsuji, K. Nakashima, N. Fukuda, and Y. Hasegawa (Lab. of Nutr. Chem., Kyushu Univ. School of Agric., Fukuoka 812, Japan) *Am. J. Clin. Nutr.* 33(4), 787-93 (1980). A series of experiments with male rats clearly demonstrated the hypocholesterolemic activity of dietary chitosan. On feeding a high cholesterol diet for 20 days, addition of 2 to 5% chitosan resulted in a significant reduction, by 25 to 30%, of plasma cholesterol without influencing food intake and growth. The concentration of liver cholesterol and triglyceride also decreased significantly. Plasma, but not liver cholesterol-lowering effect, was roughly comparable with that of cholestyramine. Chitosan at the 10% level further reduced plasma cholesterol, but depressed growth. Also, finer chitosan particles tended to restrain growth even at the 2% level. In rats fed a cholesterol-free diet containing 0.5% chitosan for 81 days, the concentration of serum cholesterol was the same with that of the corresponding control, but relatively more cholesterol existed as high-density lipoproteins and less as very low-density lipoproteins. Dietary chitosan increased fecal excretion of cholesterol, both exogenous and endogenous, while that of bile acids remained unchanged. There was no constipation or diarrhea. A proper supplementation of chitosan to the diet seemed to be effective in lowering plasma cholesterol.

THROMBIN-INDUCED HYDROLYSIS OF PHOSPHATIDYLINOSITOL IN HUMAN PLATELETS. R.L. Bell and P.W. Majerus (Div. of Hematology-Oncology, Depts. of Internal Medicine and Biological Chem., Washington Univ. School of Medicine, St. Louis, MO 63110) *J. Biol. Chem.* 255(5), 1790-2 (1980). Arachidonate is released from phosphatidylinositol when platelets are stimulated by either thrombin or calcium ionophore A23187. The initial step in arachidonate liberation involves hydrolysis of phosphatidylinositol to form 1,2-diacylglycerol. We have measured platelet phosphatidylinositol at various times after stimulation of intact human platelets with these agonists. Maximal depletion of phosphatidylinositol occurs at concentrations of 0.03 μ g of thrombin/ml (0.1 NIH unit). The loss of membrane phosphatidylinositol is paralleled by a corresponding rise in free inositol in platelets. The only species of phosphatidylinositol hydrolyzed to a significant extent is monophosphatidylinositol; levels of diphosphatidylinositol and triphosphatidylinositol are relatively unchanged. The time course and magnitude of the hydrolysis of phosphatidylinositol parallels that of arachidonate release in platelets and is therefore consistent with our theory that this phospholipid provides the arachidonate for prostaglandin synthesis and for the lipoxygenase pathway in platelets.

INFLUENCE OF DIETARY FATS ON THE FLUIDITY OF THE LIPID DOMAINS OF RABBIT PLASMA LIPOPROTEINS. E. Berlin and C. Young, Jr. (Lipid Nutr. Lab., Nutr. Inst., Human Nutr. Center, United States Dept. of Agric., Beltsville, MD 20705) *Atherosclerosis* 35(3), 229-41 (1980). The effects of dietary stearic and other saturated fatty acids on the fluidity of the plasma lipoproteins were assessed with fluorescence polarization techniques. Rabbits were maintained on diets containing either cocoa butter, milkfat,

coconut oil, or corn oil as the only source of fat. Microviscosities, η , of the lipid regions of plasma very low density lipoproteins (VLDL), low density lipoproteins (LDL), and high density lipoproteins (HDL) were determined by measuring the anisotropy of fluorescence from the probe 1,6-diphenyl-1,3,5-hexatriene. The microviscosity values followed the sequence $\eta_{HDL} > \eta_{LDL} > \eta_{VLDL}$ when the lipoproteins were isolated from the plasma of rabbits fed cocoa butter, milkfat, or corn oil. HDL and LDL consist of an invariant phase in the temperature range 0-50° C regardless of diet. VLDL from rabbits fed milkfat, corn oil, or cocoa butter displayed monophasic behavior in the same range, while VLDL from rabbits fed coconut oil showed a phase transition at $31.9 \pm 3.7^\circ$ C. Lipoproteins were less fluid in fasted than in non-fasted rabbits and VLDL and LDL from fasted milkfat-fed rabbits showed phase transitions. Despite the fatty acid compositions of the dietary fats, VLDL and LDL were more fluid from rabbits fed cocoa butter than from rabbits fed corn oil; apparently metabolism influences microviscosity.

INTERACTION OF ZINC AND VITAMIN E IN THE CHICK. W.J. Bettger, P.G. Reeves, J.E. Savage and B.L. O'Dell (Dept. of Biochem., Univ. of Missouri, Columbia, MO 65211) *Proc. Soc. Exp. Biol. Med.* 163(3), 432-6 (1980). Chicks fed a low zinc diet (5 ppm) based on soybean protein, cornstarch, and corn oil developed severe skin lesions on the toes and foot pads as well as gross joint abnormalities that severely impaired locomotion. Incubation of foot skin

in a peroxidative buffer containing 5 ppm Cu resulted in the release of malondialdehyde or other thiobarbituric acid reactive substances. The rate of release from skin or zinc deficient chicks was 4-5 times as great as from skin of controls fed adequate zinc. Supplementation of the zinc deficient diet with fat soluble antioxidants, particularly vitamin E, decreased the severity of the skin and joint pathology. High levels of dietary vitamin E also decreased the rate of release of peroxidative products from zinc-deficient skin but had no effect on control skin. The results show a significant physiological interaction between dietary vitamin E and zinc. It appears that cells from zinc-deficient chicks can benefit from incorporating higher than normal levels of vitamin E into their membrane structure. It is postulated that zinc protects against peroxidative damage and promotes membrane integrity.

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