Abstracts

Biochemistry and nutrition

ARACHIDONIC ACID, PROSTAGLANDIN E_2 and $F_{2\alpha}$ INFLUENCE RATES OF PROTEIN TURNOVER IN SKETAL AND CARDIAC MUSCLE. H.P. Rodemann and A.L. Goldberg (Dept. of Physiology, Harvard Med. School, Boston MA 02115) *J. Biol. Chem.* 257(4):1632-1638 (1982). Experiments were undertaken to determine whether prostaglandins may be involved in the regulation of protein synthesis and degradation in various types of striated muscle. When the red soleus, white extensor digitorum longus, diaphragm, or atrial strips were incubated with arachidonic acid, rates of protein degradation increased by 20-40%. In most of these tissues, rates of protein synthesis remained unchanged by increased in the soleus. Inhibitors of prostaglandin synthesis reduced or prevented the stimulation by arachidonate of protein degradation in these muscles and the increase in protein synthesis induced in the soleus. Of all metabolites of arachidonic acid tested, only PGE_2 and $PGF_{2\alpha}$ had significant effects. PGE_2 did not alter rates of protein synthesis but increased protein degradation by about 22% ($p < 0.05$), and caused net protein balance to become more negative. $PGF_{2\alpha}$ also caused a 35% stimulation of protein synthesis ($p < 0.01$) in both muscles without affecting proteolysis. Furthermore, incubated rat muscles synthesize and release PGE_2 and $PGF_{2\alpha}$ as shown by radioimmunoassay of the medium. Addition of arachidonate to the medium caused a 5- to 6-fold increase in the release of PGE_2 and a 3-fold increase in $PGF_{2\alpha}$. Indomethacin prevented these effects. The stimulation of protein degradation by arachidonic acid and PGE could be inhibited with leupeptin or Ep475, inhibitors of lysosomal thiol proteases, and thus the prostaglandins probably activate intralysosomal proteolysis. These observations suggest a possible role of PGE_2 and $PGF_{2\alpha}$ in the acceleration of muscle protein turnover in various physiological and patholgoical states.

FATTY ACID AND GLUCOSE INCORPORATION INTO HUMAN ADIPOSE TISSUE IN NON-INSULIN-DEPENDENT DIABETES AND IN INSULINOMA. INVERSE RELATIONS WITH PLASMA TRIGLYCERIDE AND GLUCOSE CONCENTRATIONS. P. Rubba, G. Pezzella, A. Rivellese, A. Postiglione (Center for Atherosclerosis and Metabolic Diseases, Inst. of Semeiotica Medica, 2nd Faculty of Med., Univ. of Naples, Naples, Italy) *Atherosclerosis 42*:31-40 (1982). Decreased fatty acid and glucose incorporation into human adipose tissue (FIAT and GLIAT) are frequently found in primary hypertriglyceridemia (HTG) and might also contribute to the defective removal of lipoprotein triglyceride (TG) in non-insulin-dependent diabetes mellitus (NIDDM). To study this possible mechanism, FIAT and GLIAT were determined in needle biopsy specimens from 14 patients with newly diagnosed NIDDM and in 14 age-and weight-matched controls. A patient with insulinoma and hyperinsulinism was also studied. FIAT and GLIAT processes were markedly reduced in patients with NIDDM that developed at the onset of maturity. Insulinoma patients, with normal plasma TG, showed FIAT-GLIAT values in the high to normal range before operation. A direct, highly significant correlation ($P < 0.001$) was demonstrated between FIAT and GLIAT in diabetics, insulinoma and controls when considered together. Plasma TG and glucose concentrations were inversely related to FIAT and GLIAT. These relationships were independent of the degree of obesity. It is suggested that impaired FIAT and GLIAT might contribute to defective TG removal and HTG which are often demonstrated in NIDDM.

LIPOPROTEINS ASSOCIATED WITH LIPOPROTEIN B IN HUMAN SERUM LOW DENSITY LIPOPROTEINS. S. Salmon, A. Van Wambeke, L. Theron, M. Ayrault-Jarrier, J. Polonovski (Lab. de Biochemie CNRS-ERA 481, CHU-Saint-Antoine, 27, rue Chaligny, 75571, Paris Cedex 12 France) *Biochim. Biophys. Acta 710*:297-305 (1982). Small amounts of lipoprotein C and lipoprotein D could be observed in low density lipoproteins (1.030-1.055 g/ml), using electroimmunomigration and polyacrylamide gel electrophoresis. Lipoprotein structures containing several apolipoproteins such as lipoprotein (B+C) or (B+D) were not detected in these low density lipoproteins. Lipoproteins C and D could not be separated from lipoprotein B by using gel filtration and affinity chromatography on heparin-Sepharose. Apolipoproteins C-III and D measured by electroimmunoassay are 3.2 ± 1.2% and 1.15 ± 0?06%, respectively, of the proteins found in the density range 1.030-1.055 g/ml, so there is, therefore, about 1 mol of apolipoprotein C-III and 0.1 mol of apolipoprotein D per mole of apolipoprotein B.

LIPID BIOSYNTHESIS IN THE BLUE-GREEN ALGA, *ANABAENA VARIABILIS*. II. FATTY ACIDS AND LIPID MOLECULAR SPECIES. N. Sato and N. Murata (Dept. of Biology, Univ. of Tokyo, Komaba, Meguro-ku, Tokyo 153 (Japan)) *Biochim. Biophys. Acta 710*(3):279-289 (1982). The biosynthesis of lipid molecular species was studied in *Anabaena variabilis* by pulse-labeling with $NaH^{14}CO_3$ and chasing. The experimental results indicate that the primary products of lipid biosynthesis are 1-stearoyl-2-palmitoyl species of monoglucosyl diacylglycerol, phosphatidylglycerol and sulfoquinovosyl diacylglycerol. In monoglucosyl diacylglycerol, stearic acid is desaturated rapidly to oleic acid and further to linoleic acid, whereas palmitic acid is hardly desaturated to palmitoleic acid. The stearoyl-palmitoyl, oleoyl-palmitoyl and linoleoyl-palmitoyl species of monoglucosyl diacylglycerol are converted to the corresponding species of monogalactosyl diacylglycerol. Desaturation of the fatty acids also takes place in monogalactosyl diacylglycerol. At 38 C the stearoyl-palmitoyl species is converted to oleoyl-palmitoyl, then to either linoleoyl-palmitoyl or oleoyl-palmitoleoyl, and finally to linoleoyl-palmitoleoyl species, and at 22 C the stearoyl-palmitoyl molecular species is sequentially converted to oleoyl-palmitoyl, linoleoyl-palmitoyl, linolenoyl-palmitoyl and linolenoyl-palmitoleoyl species. The molecular species of digalactosyl diacylglycerol are synthesized from the corresponding species of monogalactosyl diacylglycerol. Desaturation does not seem to occur in digalactosyl diacylglycerol. In phosphatidylglycerol and sulfoquinovosyl diacylglycerol, stearic acid is desaturated to oleic and to linolenic acid at 38 C, and further to linoleic acid at 22 C whereas palmitic acid is hardly desaturated.

LIPID COMPOSITION IN LIVER AND BRAIN OF GENETICALLY OBESE (*OB/OB*), HETEROZYGOTE (*OB/+*) AND NORMAL (+/+) MICE. A. Sena, G. Rebel, R. Bieth, P. Hubert, and A. Waksman (C (Centre de Neurochimie due C.N.R.S., 5, rue Blaise Pascal, 67084 Strasbourg Cedex (France)) *Biochim. Biophys. Acta 710*(3):290-296 (1982). Lipid composition was studied in liver and brain of normal (+/+), heterozygote (*ob/+*) and obese (*ob/ob*) mice. It was found that this genetic defect is expressed differently in the lipid composition of these organs. Cholesterol is increased in liver but strongly decreased in brain of obese animals. Phosphatide fatty acid composition is modified in liver and not in brain. In contrast, phospholipids and total ganglioside sialic acid are affected similarly in both organs. Although clinically normal, heterozygote (*ob/+*) mice already show an abnormal lipid composition in liver and brain. The potential importance of these results is presented.

STABILIZATION OF LIPOPROTEIN LIPASE BY ENDOTHELIAL CELLS. K. Shimada, J.J. Lanzillo, W.H.J. Douglas, and B.L. Fanburg (Dept. of Med., New England Med. Center Hosp., Boston, MA and Dept. of Anatomy and Cellular Biol., Tufts Univ. Schl. of Med., Boston, MA 02111) *Biochimica et Biophysica Acta 710*(2):117-121 (1982). Lipoprotein lipase, purified from bovine milk, lost 90% of its activity when incubated in Hanks' balanced salt solution for 5 min at 37 C. Bovine pulmonary artery endothelial cells, maintained in culture, markedly stabilized this enzyme. The stabilizing factor of endothelial cells was non-dialyzable, resistant to heating at 100 C and to changes in pH, and unaffected by treatments of cells with proteolytic enzymes or with heparinase (*Flavobacterium heparinum* enzyme). However, the stabilizing effect on lipoprotein lipase was reduced by 60-70% by the extraction of cells with chloroform/methanol (2:1). The lipid extract of the cells stabilized the enzyme, suggesting that lipid component(s) of the endothelial cells account for their stabilizing effect. Since the endothelial cell is thought to be the site of action of lipoprotein lipase, stabilization of the enzyme by this cell may play a role in its preservation and function in vivo.

ABSENCE OF EFFECT OF PROSTAGLANDINS ON CHOLESTERYL ESTER METABOLISM OF 3T3 MOUSE FIBROBLASTS GROWN IN TISSUE CULTURE. S.P. Singh, F.A. Shamgar, A.J. Day (Dept. of Physiology, Univ. of Melbourne, Parkville, Vic. 3052, Australia) *Atherosclerosis 42*:109-119 (1982). This study examines the effect of prostaglandin E_2 and 6-keto $F_{1\alpha}$ on the cholesteryl ester metabolism of cells grown in tissue culture. When 3T3 mouse fibroblasts were incubated with cationized low density lipoprotein (LDL) and ^3H-labelled oleic and ^{14}C-labelled linoleic acids a marked increase in cholesteryl ester content of cells was observed. Oleic acid was the preferred substrate for cholesterol esterification. However, the presence of prostaglandin E_2 of 6-keto $F_{1\alpha}$ (up to 10 μg/ml) did not affect the cholesteryl ester content or the uptake of labelled fatty acids into cellular lipids. Following preincubation with cationized LDL and labelled fatty acids the cells were reincubated in normal medium with or without prostaglandins. The presence of PGE_2 or $6KPGF_{1\alpha}$ (up to 10 μg/ml) did not appreciably change the rate of removal of cholesteryl ester or labelled lipids. This indicated that

these prostaglandins even when present in relatively large doses in the incubation medium do not affect lipid metabolism of cells grown in tissue culture.

BIOLOGICAL ACTIVITY OF 1,24(R)-DIHYDROXYVITAMIN D_3 AND 1,24(s)-DIHYDROXYVITAMIN D_3 IN THE RAT. C.M. Smith, Y. Tanaka, H.F. DeLuca (Dept. of Biochem., Coll. of Agr. and Life Sci., Univ. of Wisconsin-Madison, Madison, WI 53706) *Proc. Soc. Exp. Biol. Med. 170*(1):53-58 (1982). The activities of 1,24(R)-dihydroxyvitamin D_3 and 1,24(s)-dihydroxyvitamin D_3 have been compared with that of 1,25-dihydroxyvitamin D_3 in the stimulation of intestinal calcium transport, mobilization of bone calcium, elevation of serum inorganic phosphorus concentration, and in healing rickets in vitamin D-deficient rats. The 1α-hydroxyvitamin D_3 was also compared with the 1,24-dihydroxyvitamin D_3 compounds in antirachitic activity. In all parameters 1,25-dihydroxyvitamin D_3 is about 10 times more active than either 1,24(R)-dihydroxyvitamin D_3 and 1,24(S)-dihydroxyvitamin D_3. In antirachitic activity 1,25-dihydroxyvitamin D_3 is about two times more active than 1α-hydroxyvitamin D_3 which in turn is two times more active than 1,24(R)-dihydroxyvitamin D_3. The 1,24(R)-dihydroxyvitamin D_3 and 1,24(s)-dihydroxyvitamin D_3 compounds are equally active except in the healing of rickets where the 1,24(S)-dihydroxyvitamin D_3 elicits weak biological activity.

SECRETION OF CHOLESTEROL, TRIGLYCERIDE AND APOLIPOPROTEIN A-I BY ISOLATED PERFUSED LIVER FROM RATS FED SOYBEAN PROTEIN AND CASEIN OR THEIR AMINO ACID MIXTURES. M. Sugano, K. Tanaka, T. Ide (Lab. of Nutr. Chem., Kyushu Univ. Schl. of Agr., Fukuoka 812, Japan) *J. Nutr. 112*(5):855-863 (1982). Isolated livers from rats fed soybean protein isolate and casein or amino acid mixtures simulating these proteins were perfused for 4 hours with Krebs-Henseleit buffer containing 0.15% glucose and 25% human red blood cells. Feeding soybean protein as compared with casein resulted in a significant reduction of the secretion of cholesterol triglyceride and apo A-I. The results agreed well with the responses of serum counterparts reported previously. When amino acid mixture diets were fed, however, no such difference could be demonstrated, though the soy-type amino acid mixture had also been shown to decrease serum cholesterol and apoA-I. The production rate of total ketone bodies was the same, but the ratio of β-hydroxybutyrate:acetoacetate was significantly higher in rats fed plant protein. The perfusate glucose tended to be higher on soybean protein. These differences were less clear on feeding amino acid mixtures. Neither the rate of bile flow nor the concentration of biliary bile acids and cholesterol were influenced by the type of dietary protein. These observations led us to conclude that soybean protein exerts the cholesterol-lowering action primarily through the regulation of hepatic contribution. The data also suggested that the protein-dependent difference in the concentration of serum cholesterol and apo A-I might not be explained throughly by the difference in the amino acid profile alone.

THE EFFECT OF SEMIPURIFIED DIETS CONTAINING DIFFERENT PROPORTIONS OF EITHER CASEIN OR SOYBEAN PROTEIN ON THE CONCENTRATION OF CHOLESTEROL IN WHOLE SERUM, SERUM LIPOPROTEINS AND LIVER IN MALE AND FEMALE RATS. A.H.M. Terpstra, G. Van Tintelen, C.E. West (Dept. of Human Nutr., Agr. Univ., De Dreijen 12, 6703 BC Wageningen, Netherlands) *Atherosclerosis 42*:85-95 (1982). Male and female lean Zucker strain rats were fed cholesterol-enriched semipurified diets containing 2 levels (20% and 50%, w/w) of either casein or soybean protein for a period of 14 weeks. In the female rats, the feeding of casein diets resulted in significantly higher levels of serum cholesterol than when diets containing soybean protein were fed. In addition, the hypercholesterolemic effect of dietary casein could be enhanced by increasing the proportion of this protein in the diet. Modulations in the proportion of dietary soybean protein did not significantly affect the serum cholesterol levels. In the male rats, however, no such differential effects were observed, indicating a difference between male and female rats in susceptibility to the induction of changed in serum cholesterol levels by dietary means. Upon feeding casein diets, both the male and female rats exhibited a shift of cholesterol from the high density lipoproteins to the lipoproteins with a lower density. This effect was more pronounced in the female than in the male rats. Liver cholesterol concentrations were markedly affected by modulations both in the type and proportion of dietary protein in both sexes. The concentration of cholesterol in th liver of the rats was highest in those fed the 50% casein diet and progressively lower in the animals on diets containing 20% casein, 20% soybean protein and 50% soybean protein.

VITAMIN A AND VITAMIN E CONCENTRATION OF THE MILK FROM MOTHERS OF PRE-TERM INFANTS AND MILK OF MOTHERS OF FULL TERM INFANTS. M.R. Thomas, M.H. Pearsons, M. Demkowica, I.M. Chan and C.G. Lewis. (College of Health, Univ. of Utah, Salt Lake City, UT 84112) *Acta Vitaminol. Enzymol. 3*(3):135-144, (1981). The vitamin E, vitamin A and beta carotene concentrations of milk from eight mothers delivering premature infants and ten mothers delivering full term infants were determined and compared. Milk samples were collected three times per day on days 3, 9, 15, 21, 27, and 33 postpartum. Dietary records were kept on days 2-3, 14-15, and 32-33. There was no significant difference in vitamin E, vitamin A and beta carotene levels between the two groups. The mean retinol concentration was higher in the milk of mothers of premature infants on all days except day three. The highest mean carotene and retinol concentrations in the milk of mothers of full term infants were on day three;but the peak occurred in the preterm group on day nine and did not drop as rapidly as the milk retinol of the full term group. The milk of mothers of premature infants reflected no significant changes in vitamin E concentration between days. In the milk of mothers of fullterm infants, day 3 vitamin E concentration was significantly higher than days 15, 21, 27, and 33 postpartum. There were no significant differences in the dietary intake of the full term and preterm groups. The amount of vitamin E in the milk was not affected by dietary vitamin E intake of the subjects regardless of gestational age of the infant. More research is needed to determine the exact quantity of vitamin A and E ingested by the premature infants if breastfed by their respective mothers.

MULTIPLE REGRESSION AND RESPONSE SURFACE ANALYSES OF THE EFFECTS OF DIETARY PROTEIN, FAT AND CARBOHYDRATE ON THE BODY PROTEIN AND FAT GAINS IN GROWING CHICKS. M. Toyomizu, Y. Akiba, M. Horiguchi, and T. Matsumoto (Dept. of Animal Sci., Faculty of Agric. Tohoku Univ., Sendai, 980, Japan) *J. Nutr. 112*(5):886-896 (1982). Multiple regression analysis of biological response as a function of three factors having a common denominator, on a triangular graph, was investigated for qualitative and quantitative evaluation of nutritional phenomena. As an example of its application, 33 groups of White Leghorn male chicks were isocalorically force-fed purified diets and prediction equations for the body weight gain, protein gain and fat gain were formulated by multiple regression techniques. Perspective views, contour maps and cross-sectional views of the response surfaces constructed from the equations revealed 1) that both body weight gain and protein gain increased with an increase in the metabolizable energy of dietary protein, and were not much affected by the calorie ratio of dietary carbohydrate to fat; 2) that fat gain decreased and appeared to become more dependent on the calorie ratio of dietary carbohydrate to fat with an increase in the metabolizable energy of dietary protein; and 3) that dietary protein, fat and carbohydrate were replaceable with one another with respect to body weight gain and protein gain, while replaceability of fat and carbohydrate with each other seemed to decrease with an increase in protein metabolizable energy with respect to fat gain. These results demonstrated that the proposed mechod is a valuable tool in nutrition studies.

THE EFFECT OF MALONYL-CoA ON FATTY ACID OXIDATION IN RAT MUSCLE AND LIVER MITOCHONDRIA. J.H. Veerkamp and H.T.B. Van Moerkerk (Dept. of Biochem., Univ. of Nijmegen, P.O. Box 9101, 6500 HB Nijmegen (The Netherlands)) *Biochimica et Biophysica Acta 710*(2):252-255 (1982). The effect of malonyl-CoA on palmitate oxidation was compared for skeletal muscle and liver mitochondria from fed rats and rats starved for 18 and 42 h. The nutritional state did not influence the palmitate oxidaion rate by both types of mitochondria. Muscle mitochondria are more sensitive to malonyl-CoA inhibition of palmitate oxidation than are liver mitochondria. Their response is not influenced by the nutritional state, in contrast to that of liver mitochondria. The extent of inhibition was not dependent on the carnitine concentration (above 0.5 mM), but higher at lower palmitate:albumin ratio or palmitate concentration.

CELLULAR AND ENZYMIC SYNTHESIS OF SPHINGOMYELIN. D. Voelker, E. Kennedy (Dept. of Biol. Chem., Harvard Med. Schl., MA 02115) *Biochem. 21*(11)2753-2759 (1982). The synthesis of sphingomyelin was studied in baby hamster kidney cells and in subcellular fractions derived from rat liver. During pulse-chase experiments with [^{3}H] choline in tissue culture cells, the specific radioactivity of sphingomyelin continued to increase after the specific activities of phosphocholine and cytidine 5′-diphosphate choline (CDP-choline) had declined by a factor of 10. The addition of [^{3}H] methionine to cells that were grown in 1 mM dimethylethanolamine efficiently radiolabeled phosphatidylcholine (by methylation of phos-

phatidyldimethylethanolamine) and sphingomyelin but not phosphocholine or CDP-choline. Thus, the proximal donor of the phosphocholine moiety of sphingomyelin was not CDP-choline but probably phosphatidylcholine. These in vivo results prompted investigation of the enzymic synthesis using phosphatidyl[^{3}H]choline or [^{3}H]ceramide as substrates. With both, the subcellular fraction with the highest specific enzyme activity was the plasma membrane. When phosphatidyl-[^{3}H]choline was used, phospholipid exchange proteins were included in the reaction to effect the transfer of the labeled phospholipid from liposomes into the membrane bilayer in which the enzyme resided. The synthesis of sphingomyelin was almost completely dependent upon the addition of phospholipid exchange proteins. When [^{3}H]ceramide was used, the addition of detergents was necessary for sphingomyelin synthesis. The use of phospholipid exchange proteins to introduce lipid substrates to membrane-bound enzymes may have much broader applicability.

UPTAKE AND TISSUE CONTENT OF FATTY ACIDS IN DOG MYOCARDIUM UNDER NORMOXIC AND ISCHEMIC CONDITIONS. G.J. van der Vusse, Th. H.M. Roemen, F.W. Prizen, W.A. Coumans, and R.S. Reneman (Dept. of Physiol. Biomedical Center, Univ. of Limburg, Maastricht, The Netherlands) *Circ Res 50*(4): 538-546 (1982). The effect of ischemia on the myocardial content of nonesterified fatty acids (NEFA), triacylglycerol, cholesteryl esters, and phospholipids assayed with gas-liquid chromatography was studied in an open-chest dog preparation. Ischemia was induced by partial occlusion of the left interventricular coronary artery during 120 minutes. Tissue content of the lipid classes was assessed in biopsies taken from ischemic and normoxic areas of the left ventricular free wall. Local venous blood from the concomitant vein of the left interventricular coronary artery was collected to determine myocardial extraction of lipids. In eight other dogs, no ischemia was induced (control group). Under normoxic conditions, NEFA appeared to be present in trace amounts. Durning ischemia, NEFA increased in the affected area. This accumulation was most pronounced in the least perfused layer: the subendocardium. Blood flow, estimated with radioactively labeled microspheres fell in this particular layer. The uptake of NEFA by the ischemic myocardium was decreased, indicating that enhanced lipolysis of endogenous lipids or reduced combustion may be held responsible for the accumulation of NEFA in ischemica tissue. Since arachidonic and linoleic acids showed the highest relative increase, lipolysis of endogenous phospholipids, rich in these fatty acids, seems to be reasonable. Ischemia had no significant effect on the content of triacylglycerol and cholesteryl esters. Phospholipids tended to decrease in the affected subendocardial layers.

EFFECTS OF PLATELET-DERIVED AND ENDOTHELIAL CELL-DERIVED GROWTH FACTORS ON THE LOW DENSITY LIPOPROTEIN RECEPTOR PATHWAY IN CULTURED HUMAN FIBROBLASTS. L.D. Witte, J.A. Cornicelli, R.W. Miller, and D.S. Goodman (Arteriosclerosis Res. Center and Dept. of Med., Columbia Univ. Col. of Physicians and Surgeons, New York, NY 10032) *J. Biol. Chem. 257*(10):5392-5401 (1982). Human platelet-derived growth factor (PDGF) has been previously shown to stimulate low density lipoprotein (LDL) receptor activity in cultured cells. Studies were conducted to delineate in detail the effects of PDGF on the LDL receptor pathway in normal human fibroblasts and to explore relationships between the effects of PDGF on LDL metabolism, on cholesterol metabolism, and on DNA synthesis. The results indicate tht PDGF-stimulated cells metabolize receptor-bound LDL in a manner that is identical with that seen with quiescent cells. A single study with highly purified PDGF demonstrated that it was PDGF itself that was responsible for the observed effects. Studies were conducted on the effects of PDGF on hydroxymethylglutaryl CoA reductase activity on cholesterol esterification, and on down-regulation by LDL of the LDL receptor. These studies indicated that LDL cholesterol appeared to become available normally and to have metabolic effects within the cell similar to those seen in quiescent cells. Fibroblasts from subjects with familial hypercholesterolemia showed a normal mitogenic response to PDGF, despite the absence or near absence of an effect on the LDL receptor pathway. Studies were also conducted with endothelial cell-conditioned medium (ECCM). ECCM was similar to PDGF in stimulating LDL binding, but differed strikingly from PDGF in that the degradation of internalized LDL was inhibited. ECCM-treated cells did not effectively increase cholesterol esterification or suppress hydroxymethylglutaryl CoA reductase activity when LDL was present. These findings with substance produced by endothelial cells may have important implications for atherogenesis.

MYOCARDIAL-ISCHEMIC RATS (MIR). CORONARY VASCULAR ALTERATION INDUCED BY A LIPID-RICH DIET. Y. Yamori M. Kihara, Y. Nara, and R. Horie (Dept. of Pathology, Shimane Med. Univ., Izumo 693 (Japan)) *Atherosclerosis 42*(1):15-20 (1982). A new strain of rats in which there is a high incidence of heart failure (myocardial-ischemic rats: MIR) has been inbred in our laboratory from a substrain of stroke-prone spontaneously hypertensive rats (SPSHR). The clinicopathological manifestations of MIR on a high-fat-cholesterol diet (HFCD) were found to be similar to those seen in ischemic heart disease (IHD) in man, in terms of vectorcardiographical (VCGcal) alterations, coronary fat deposition, thrombosis and resultant myocardial fibrosis. MIR should serve as a good experimental model of IHD.

ABNORMAL APOPROTEIN A-I ISOPROTEIN COMPOSITION IN PATIENTS WITH TANGIER DISEASE. V. Zannis, A. Lees, R. Lees, J. Breslow (Children's Hosp. Med. Center and Harvard Med. Schl., Boston MA 02115) *J. Biol. Chem. 257*(9):4978-4986 (1982). Recently we described differences between plasma apolipoprotein A-I (apo-A-I) isoproteins and those synthetized by human intestine or liver in organ culture. The plasma apo-A-I isoproteins and their relative concentrations are: isoproteins 2 and 3 (<2%); isoprotein 4 (79±7%); isoproteins 5 and 6 (19±6%). The intestinal or hepatic isoproteins which are secreted into the organ culture medium and their relative concentrations are: isoprotein 2 (78±5%); isoprotein 3(21±5%); isoproteins 4 and 5 (usually <1%). Three Tangier disease patients had apo-A-I isoprotein profile which differed from those found in 100 normal control subjects. The apo-A-I isoproteins of the patients' plasma and their relative concentrations are: sioprotein 2 (49±7%); isoprotein 3 (<5%); isoproteins 4 and 5 (46±7%). Intestinal organ culture synthetized and secreted apo-A-I isoproteins 2 and 3 in normal amounts which comigrated on two-dimensional gel electrophoresis with normal intestinal apo-A-I isoproteins 2 and 3. These findings show a plasma apo-A-I isoprotein abnormality in patients with Tangier disease. The basis for these observations could be a defect in converting the major intestinal of hepatic apo-A-I isoprotein (isoprotein 2) to the major plasma apo-A-I isoprotein (isoprotein 4). Further studies are required to determine whether defective apo-A-I conversion in Tangier disease is the result of an altered post-translational apo-A-I modifying system or a structural defect in apo-A-I that either precludes normal conversion or results in a very unstable conversion product.

STEROL EFFLUX FROM MAMMALIAN CELLS INDUCED BY HUMAN SERUM ALBUMIN-PHOSPHOLIPID COMPLEXES. L.C. Bartholow and R.P. Geyer (Dept. of Nutr., Harvard Schl. of Public Health, Boston, MA 02115) *J. Biol. Chem. 257*(6):3126-3130 (1982). Human serum albumin and phospholipids can interact to cause a synergistic sterol release from mammalian cells in tissue culture. In the presence of the complexes formed between albumin and saturated phosphatidylcholine, release was twice as great as that which occurred with the unsaturated phospholipid complexes. Within the saturated series, sterol release increased with chain length until the number of carbon atoms in the acyl group was 18, after which sterol release decreased. In the unsaturated series, sterol release decreased as the number of double bonds increased. Branching of the acyl chain, or analogues with the polar group in the *sn*-2 position reduced sterol efflux. In the presence of human serum albumin, maximal sterol efflux occurred with phospholipids having two adjacent acyl chains and zero net charge; sterol release decreased as net charge increased.