Circulating lipids and glycaemic control in insulin-dependent diabetic children.

Azad K. Parkin JM. Court S. Laker MF, Alberti KG. Arch Dis Child 1994 : 71 : 108-13.

The prevalence of dyslipidaemia in children with insulin-dependent diabetes mellitus (IDDM) and its relation to glycaemic control was studied in a group of 51 diabetic children and a control population of 132 school children. The prevalence of dyslipidaemia in the fasting state was increased in the diabetic group (39%) compared with control subjects (17%). Serum cholesterol concentration alone was raised in 25% of diabetic subjects while serum cholesterol and triglycerides were raised in 14%, compared with 16% and 0.7% respectively in control subjects. Serum total cholesterol (5.1 vs 4.5 mmol/l), low density lipoproteins cholesterol (3.2 vs 2.6 mmol/l). non-esterified fatty acids (0.91 vs 0.50 mmol/l) and triglycerides (0.94 vs 0.76 mmol/l) were higher in diabetic children. Serum total cholesterol, triglycerides and apolipoprotein (apo)B concentrations increased with worsening control, while serum high density lipoproteins cholesterol and apoA-I concentrations were unaltered. There were also positive correlations between glycated haemoglobin and total cholesterol, triglycerides and apoB in diabetic children. Thus, abnormalities in circulating lipids are common in young subjects with IDDM but largely disappear if blood glucose concentrations are reasonably controlled.

Metabolic factors in the development of retinopathy of juvenile-onset Type 1 diabetes meltitus.

Khosla PK. Sharma K. Tewari HK. Bajaj JS. Vaidya MC. Indian J Opthalmol 1994: 42 : 23-5.

Thirty-five patients of insulin-dependent diabetes mellitus (IDDM) were investigated for the effect of various metabolic factors on retinopathy. The severity of retinopathy increased with duration and age of onset of IDDM. Degree of glycaemia (fasting blood sugar. FBS) was similar in patients with or without retinopathy. All IDDM patients as a group showed severe carbohydrate intolerance with lower basal and post-glucose serum immunoreactive insulin (IRI) levels and serum C-peptide radioimmunoreactivity (CPR) as compared to controls. The insulin secretory response was similar in no retinopathy. mild retinopathy and severe retinopathy groups. Patients with retinopathy had higher incidence of hyperlipidaemia but mean serum levels of cholesterol and triglyceride were similar. This study does not suggest a direct relationship between the various metabolic factors studied and retinopathy due to IDDM.

Alpha 1-blockade for the treatment of hypertension: a megastudy of terazosin in 2214 clinical practice settings.

Itskovitz HD. Clin Ther 1994; 16 : 490-504.

The purpose of this study was to evaluate the effects of the alpha 1-blocking agent terazosin on blood pressure (BP) and blood lipids in a large variant population of patients with hypertension. A total of 16,917 patients with hypertension were evaluated at 2214 primary and community care facilities; 7808 of these patients had not been treated previously for hypertension; 3928 were switched to terazosin from another antihypertensive agent; and 5181 received terazosin in addition to an agent that had not controlled their hypertension. Terazosin produced highly significant reductions in systolic (-18.2 ± 0.2 mm Hg) and diastolic (13.2 ± 0.1 mm Hg) BP when used as monotherapy (mean dose, 3.1 mg: range 2 to 10 mg) without causing a significant increase m heart rate. Equal antihypertensive efficacy was demonstrated in men, women, blacks and whites of all ages, with particular benefit to elderly patients (≥ 65 years of age) with systolic hypertension. Comparative studies indicated that terazosin had equal antihypertensive efficacy in combination with diuretics, beta-blockers, calcium channel blockers and angiotensin-converting enzyme (ACE) inhiibitors patients who had not responded to monotherapy with one of these classes of antihypertensive drugs showed significant reductions of BP after terazosin, in the following average doses, was added to diuretics-3.1 rng; betablockers-3.4 mg; calcium channel blockers-3.3 mg; and ACE inhibitors-3.4 mg. Terazosin produced highly significant reductions in blood levels of total cholesterol (-5.0 %), triglycerides (-6.1 %) and low-density lipoprotein-cholesterol (-7.6 %) without change in high-density lipoprotein-cholesterol when used as monotherapy. Similar favorable effects on blood lipid levels were demonstrated when terazosin was used in combination with all other classes of antihypertensive drugs. The greatest reductions in blood cholesterol (-9.2%) were observed among patients with hyperlipidaemia (total cholesterol ≥ 240 mgldL). Terazosin maintained its antihypertensive efficacy and was well tolerated by patients with a variety of concomitant diseases, including congestive heart failure, peripheral vascular disease, chronic obstructive pulmonary disease, benign prostatic hyperplasia, diabetes and obesity. Adverse effects occurred in 17.9% of patients and caused 2.2% to drop out of the study. The most frequent adverse effects were dizziness (4.8%), headache (2.5%) and asthenia (2.4%). Only 0.4% suffered syncope and 0.2% impotence. These data dernonstrate the usefulness of terazosin as monotherapy or add-on therapy for treatment of hypertension.

Augmented effect of short-term pulsatile versus continuous insulin delivery on lipid metabolism but similar effect on whole-body glucose metabolism in obese subjects.

Schmitz O. Pedersen SB. Mengel A. Porksen N, Bak J, Moller N, Richelsen B, Alberti KG, Butler F'C:, Orskov H. Metabolism 1994: 43 : 842-6.

The present study was designed to examine the effect of pulsatile versus continuous insulin delivery on glucose and lipid metabolism in insulin-resistant subjects. Six obese women (body mass index, 40.0 ± 2.8 kg/m^2) underwent a euglycaemic glucose clamp (plasma glucose, 90 mg/dl) twice. In random order, insulin was infused intravenously for 375 minutes either at a constant rate (0.4 mU/kg/min) or in a pulsatile manner (2.4 mU/kg/min for 2 minutes followed by an off interval of 10 minutes). Endogenous insulin release was suppressed by infusion of somatostatin (250 micrograms/h). Mean circulating insulin concentrations were similar during the two protocols (pulsatile vs continuous infusion, 60 ± 10 vs 56 ± 9 mU/I), but pulsatile infusion was accompanied by oscillations with an amplitude of 120 mU/l. After 6 hours of pulsatile versus continuous insulin, isotopically determined total glucose disposal (3-3H-glucose) and hepatic glucose production (HGP) were comparable (pulsatile vs continuous, 2.80 ± 0.56 vs 2.82 ± 0.51 and 0.37 ± 0.14 vs 0.32 ± 0.17 mg/kg/min). However, the rate of glucose oxidation (indirect calorimetry) was augmented ($P < .05$), whereas lipid oxidation tended to be diminished ($.10 > P > .05$) following pulsatile infusion. In addition, blood glycerol was more suppressed with pulsatile (31 ± 9 nmol/l) than with continuous infusion (36 ± 10 nmol/L, $P < .05$), whereas blood lactate, alanine and 3-hydroxybutyrate were similar in the two infusion protocols.

Fatty acid composition of erythrocytes and plasma triglyceride and cardiovascular risk in Asian diabetic patients.

Peterson DB, Fishe K, Carter RD, Mann J. Lancet 1994; 343 : 1528-30.

The excess of coronary heart disease in Indian Asians compared with Europeans is unexplained by conventional risk factors, although the high prevalence of diabetes may play a part. To explore the contribution of diet, we compared the fatty acid composition of erythrocyte membrane phospholipid and plasma triglyceride in 36 Gujarati Asians and 24 Europeans with non-insulin-dependent diabetes. Erythrocytes from Asian subjects contained higher proportions of linoleic, dihomogammalinolenic and arachidonic acids and lower proportions of oleic and n-3 series fatty acids; triglycerides contained higher linoleic and lower oleic acid levels. For example, mean percentage (SE) of oleic acid (18: 1n-9) in erythrocytes was 16.7 (0.2) in Asians and 20.5 (0.6) in Europeans ($p = 0.0001$) and total n-6:n-3 ratio was 12.8 (0.7) and 6.7 (0.7) ($p = 0.0001$) respectively. A high dietary intake of linoleic acid may not be cardioprotective unless balanced by significant intakes of oleic and n-3 series fatty acids, at least in diabetic Indian Asians. By itself, the conventional recommendation to substitute polyunsaturated for saturated fat in the diet may he inadequate to reduce thrombogenesis and the overall balance of fatty acids, including monounsaturates, should be considered.

Extracranial carotid atherosclerosis and vascular risk factors in different types of ischaemic stroke in Taiwan.

Jeng JS, Chung MY, Yip PK, Hwang BS, Chang YC. Stroke 1994; 25 1989-93.

Background and purpose: The clinical patterns of stroke and the angiographic distribution of cerebral atherosclerosis in Chinese people are different from those in Whites. Studies relating carotid atherosclerosis and vascular risk factors to various types of stroke in Chinese people are lacking.

Methods: Based on clinical information, we separated 367 stroke patients living in Taiwan into four subgroups: cortical infarction (CI), subcortical infarction (SCI), vertebrobasilar artery infarction (VBAI) and cardioembolic infarction (CEI). We assessed the extent and severity of extracranial carotid artery atherosclerosis in different types of ischaemic stroke using duplex ultrasonography. Vascular risk factors and carotid atherosclerosis were then correlated with each subgroup of ischaemic stroke.

Results: Our data revealed that 32% of the CI subgroup, 3% of the SCI subgroup, 7% of the VBAI subgroup and 21% of the CEI subgroup possessed severe carotid stenosis (≥ or = 50% stenosis or occlusion). The extent of atherosclerosis of extracranial carotid arteries measured by plaque score was also more severe in the CI subgroup than in the other subgroups. Diabetes mellitus was more frequent in the CI subgroup. Cardiomegaly and left ventricular hypertrophy were more commonly seen in the CEI subgroup. The VBAI subgroup was younger than the other subgroups. There were no differences in hypertension, prior stroke, alcohol intake or serum levels of glucose, uric acid, hematocrit, lipids and lipoproteins among the subgroups.

Conclusions: Of the Chinese patients living in Taiwan, the extent and severity of extracranial carotid artery, atherosclerosis were more prominent in patients with CI than in patients with other types of ischaemic stroke. In Chinese patients with CI, severe carotid stenosis is not uncommon and in those with SCI, however, the frequency of carotid stenosis is quite low.

The peroxidation of human glycosylated low density lipoproteins is mediated by the superoxide radical: the protective effects of superoxide dismutase.

Napoli C, Ambrosio G, Aalumbo G, Chiariello P, Duilio C, Chiariello M. Cardiologia 1994; 39 : 345-52.

Low density lipoproteins (LDL) oxidised by oxygen radicals are a potent atherogenic stimulus. Chemically modified LDL are internalised by macrophages via a specific cell surface receptor that was termed the scavenger receptor and could induce foam cell transformation. Post-translational non-enzymatic glycosylation of low density lipoprotein (LDL) occurs in vivo in diabetic patients. Glycosylated LDL (gIc LDL) is degraded by macrophages in part by the classic LDL receptor and in part by the scavenger receptor. This latter mechanism may contribute to the formation of foam cells and acceleration of atherosclerosis in diabetes rnellitus. Oxygen free radicals (OR's) could induce LDL peroxidation and subsequent formation of foam cells. Glycosylation may alter protein conformation. A free radical is any chemical species that has an unpaired electron. This property renders it highly chemically reactive. When a radical reacts with a non-radical, another free radical is generated. This characteristic enables radicals to trigger chain reactions. Oxygen radicals are: superoxide anion ($.O^2$), hydroxyl radical (.OH) and hydrogen peroxide (H^2O^2). Thus, the aim of this study was to investigate whether glc LDL are susceptible to peroxidative modification by OR's. Glc LDL was prepared incubating LDL with 40 mM glucose in sterile phosphate-buffer-EDTA 1 mM for 10 days at 37 degrees C. Control LDL (cLDL) was similarly incubated with buffer but without glucose. After this preparation both forms of LDL were oxidised by CuSO4 (15 microM for 20 hours at 37 degrees C) or by xanthine/xanthine oxidase (X:2 mM/XO: 100 mU for 20 hours at 37 degrees C).

Effect of oral magnesium supplementation on selected cardiovascular risk factors in non-insulin-dependent diabetics.

Purvis JR, Cummings DM, Landsman P, Carroll R. Barakat H, Bray J, Whitley C, Horner RD. Arch Fam Med 1994; 3 : 503-8.

Objective: To evaluate the impact of oral magnesium supplementation on risk factors for end-organ disease in patients with non-insulin-dependent diabetes mellitus (NIDDM).

Design: A 16-week randomized, double-blind. placebo-controlled crossover trial.

Setting: Out-patient center of an academic family medicine residency program.

Patients: Twenty-eight patients (age range, 28 to 84 years; 57.1% black; 85.7% women) with NIDDM controlled by diet and/or an oral hypoglycaemic, with a serum cholesterol levels over 5.20 mmol/l (200 mg/dl).

Intervention: Following a 2-week placebo run-in period, each patient was randomised to receive either sustained-release magnesium chloride (Slo-Mag), 384 mg/d or an identical-appearing placebo for 6 weeks. After a 2-week interim washout period, each patient was then treated with the alternative regimen for an additional 6-week period.

Main outcome measures: The systolic and diastolic blood pressure and levels of serum glucose. low density and high density lipoprotein and total cholesterol. triglycerides and serum and total erythrocyte magnesium were measured at the beginning, midpoint and end of each 6-week treatment phase.

Results: Systolic blood pressure fell an average of 7.4 mm Hg ($P < .05$) with treatment. There was no significant change in diastolic blood pressure or levels of serum glucose, low density and high density lipoprotein and total cholesterol, triglycerides or serum and erythrocyte magnesium.

Conclusions: Oral magnesium supplementation in the doses and duration studied is modestly effective in reducing systolic blood pressure in patients with NIDDM but has little impact

on other important biochemical parameters related to diabetes associated end-organ disease.

Impact of lisinopril and atenolol on kidney function in hypertensive NIDDM subjects with diabetic nephropathy.

Nielsen FS, Rossing P, Gall MA, Skott P, Smidt UM, Parving HH. Diabetes 1994; 43: 1108-13.

Diabetic nephropathy is characterised by hypertension and a relentless decline in kidney function. Angiotensin-converting enzyme inhibitors have been claimed to preserve kidney function better than an equal blood pressure (BP) reduction with conventional antihypertensive treatment (reno-protection). We compared the effect on kidney function of lisinopril (10-20 mg/day) and atenolol (50-100 mg/day) in hypertensive NIDDM patients (mean age 60 ± 8 years) with diabetic nephropathy. Forty-three (21 lisinopril and 22 atenolol) patients were enrolled in a 1-year randomised double-blind parallel study. Eight patients dropped out and the results for the remaining 35 patients (16 lisinopril and 19 atenolol) are presented. Diuretics were required in 10 of 16 lisinopnl patients and 12 of 19 atenolol patients. The following variables were measured: 24-hour ambulatory BP (Takeda TM2420), albuminuria (enzyme-linked immunosorbent assay), fractional albumin clearance and glomerular filtration rate (GFR) ([51 Cr]EDTA technique). The average reduction in mean arterial BP during the 12 months was identical in the two groups 12 ± 2 vs, 11 ± 1 mmHg in the lisinopril and atenolol group respectively. Albuminuria was on average reduced 45% in the lisinopril group vs. 12% in the atenolol group ($P < 0.01$) and fractional albumin clearance was on average reduced 49% in the lisinopril group vs. 1% in the atenolol group ($P < 0.05$). GFR declined identically in the two groups 11.7 ± 2.3 vs. 11 .6 ± 2.3 $ml.min^{-1}.year^{-1}$ in the lisinopril and atenolol groups respectively.

Simvastatin in non-insulin-dependent diabetes mellitus: effect on serum lipids. lipoproteins and haemostatic measures

Farrer M Winocour PH. Evans K, Neil HA. Laker MF, Kesteven P, Alberti KG. Diabetes Res Clin Pract 1994: 23: 11f-9.

The clinical efficacy of the 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitor simvastatin in the treatment of hypercholesterolaemia in non-insulin-dependent diabetes (NIDDM) was examined in a double-blind placebo-controlled study of 6 months in 70 patients with NIDDM (age 25-70 years), of whom 57 were randomised to placebo (29 patients) or simvastatin for 6 months., following a 3-month run-in on diet. Patients were hypercholesterolaemic [7.8 (7.6-8.0) (mean (95% confidence intervals)) mmol/l simvastatin vs. 8.0 (7.7-8.5) mmol/l placebo] and mildly hypertriglyceridaemic [2.6 (2.2-3.0) simvastatin vs. 2.9 (2.3-3.5) placebo], Other lipid measures and estimates of glycaemic control and haemostasis were similar in both groups. There were no significant changes in lipids, haemostatic factors or measures of glycaemic control in the placebo treatment group. Conversely, by the end of 24 weeks, simvastatin produced a 28% reduction in cholesterol [to 5.6 (5.0-6.2) mmol/l ($P < 0.001$)], a 38% reduction in LDL cholesterol [from 5.5 (5.4-5.6) mmol/l to 3.4 (2.8-4.0) mmol/l, $P < 0.001$, a 15% reduction in triglyceride [to 2.2 (1.8-2.6) mmol/l, $P < 0.05$ and a 9% rise in HDL (from 1.16 (1.07-1.25) to 1.23 (1.14-1.32) mmol/l, $P < 0.05$]. Improvements in apolipoprotein B (apo B) (28% $P < 0.001$), the LDL-cholesterol to apo B ratio (-20%, $P < 0.001$) and apo A^1 (+15%, $P < 0.001$) were recorded. There were no effects upon fibrinogen, factor VII activity, factor VIII activity or measures of glycaemic control (fasting glucose, insulin, C-peptide or HbA^1).

Platelets, vascular disease and diabetes mellitus.

Winocour PD. Can J Physiol Pharmacol 1994; 72: 295-303.

Diabetes is associated with increased risk for atherosclerosis and its thromboembolic complications. Theories about mechanisms of atherosclerosis in diabetes are similar to those in the non-diabetic population. Platelets contribute to atherosclerosis through effects on vessels by materials released from the platelets. which interact with injured or altered vessels. In diabetes, platelets could contribute to enhanced atherosclerosis through hypersensitivity to agonists at sites of vessel injury and increased release of materials from adherent platelets. Diabetic platelets are hypersensitive to agonists in vitro and alterations in a number of mechanisms involved in platelet activation occur in these platelets, which could contribute to the hypersensitivity. These alterations include increased presence of glycoprotein receptors for agonists and adhesive proteins on the platelet surface, increased fibrinogen binding, decreased membrane fluidity, enhanced arachidonate pathway activation with increased thromboxane A2 formation and increased phosphoinositide turnover leading to increased inositol triphosphate production. Ca^{2+} mobilisation and protein phosphorylation. There is some evidence for increased platelet activity in vivo in diabetes, but it is unclear whether this reflects platelet hypersensitivity or increased platelet turnover on already diseased vessels. Studies in diabetic animals indicate greater interaction of platelets with injured vessels and incorporation into experimentally induced thrombi, but it is unclear if this reflects changes in platelets or other factors. These changes could be contributing to the enhanced atherosclerosis and its clinical complications in diabetic patients.

Effects of contraceptive steroids on cardiovascular risk factors in women with insulin-dependent diabetes mellitus

Petersen KR. Skouby SO, Sidelmann J, Molsted Pedersen L, Jespersen J. Am J Obstet Gynaecol 1994; 171 : 400-5.

Objective: We evaluated established cardiovascular risk factors within lipoprotein metabolism, haemostasis and endothelial function in women with insulin-dependent diabetes mellitus who were using oral contraceptives.

Study Design: Twenty-five women with uncomplicated insulin dependent diabetes mellitus allocated to treatment with a monophasic combination of 30 micrograms ethinyl estradiol and 75 micrograms gestodene (treatment group, n = 12) or with non hormonal contraception (control group, n = 13), were prospectively followed up for 12 months. Non-parametric methods were used for statistical evaluation.

Results: No statistical differences in the biochemical risk markers were noted between the two groups at the start of the study. In the treatment group, serum levels of low density lipoprotein cholesterol decreased, whereas the concentrations of total cholesterol, high density lipoprotein-cholesterol, very low-density lipoprotein-cholesterol and triglycerides were unchanged. Within the coagulation system factor VII coagulant activity increased, while fibrinogen levels were unchanged. In the fibrinolytic system, we found unchanged activities but decreased antigen concentrations of tissue plasminogen activator and plasminogen activator inhibitor. The concentration of Von Willebrand factor increased, but no change in albumin excretion rates were found. In the control group, no changes in any of the variables were observed.

Conclusion: Intake of modern oral contraceptives does not deteriorate the cardiovascular risk profile in women with insulin-dependent diabetes mellitus, but our study indicates a risk of disturbances of the endothelial integrity, which needs further investigation

Increases in serum lipids during pregnancy in Type 1 diabetic women with nephropathy

Biesenbach G, Janko O. Stoger H, Zazgornik J. Diabet Med 1994; 11 : 262-7.

During pregnancy, women with Type 1 diabetes do not differ from normal women with respect to pregnancy associated changes in serum lipid levels. However, influence of diabetic nephropathy on lipoprotein metabolism in pregnancy has not been described previously. Changes in lipids were compared during and after pregnancy in 10 Type 1 diabetic women without macroproteinuria as well as in 5 diabetic women with macroproteinuria due to diabetic nephropathy. In the pregnant women with macroproteinuria, compared to the diabetic women without macroproteinuria, we observed both significantly higher total and percent increases in serum levels of total cholesterol (97% versus 48%) and of LDL cholesterol (137% versus 50%), which had risen progressively throughout gestation. The percent increases in serum triyglycerides (115% versus 128%) were similar in both patient groups. Metabolic control was improved during pregnancy in both groups of women. Renal function remained normal throughout pregnancy in the diabetic women without nephropathy and worsened during pregnancy in the proteinuric women. The mean protein excretion showed a physiological rise from 0.107 ± 0.040 g 24 h-1 before pregnancy to 0.336 ± 0.234 g 24 h-1 in the third trimester in the non-proteinuric women and an increase from 2.2 ± 1.0 to 7.1 ± 1 .7 g 24 h-1 during the same period in the women with macroproteinuria. Therefore, it is concluded that the greater increase in serum lipid levels during pregnancy in the women with pre-existing diabetic nephropathy can mainly be explained by the concomitant increase in proteinuria associated with development of the nephrotic syndrome in these patients.

Serum sialic acid, a risk factor for cardiovasculsr disease, is increased in IDDM patients with microalbuminuria and clinical proteinuria.

Crook MA, Earle K, Morocutti A, Yip J, Viberti G, Pickup JC. Diabetes Care 1994; 17: 305-10.

Objective: An elevated serum sialic acid concentration has recently been shown to be a potent cardiovascular risk factor in the general population. Because clinical proteinuria is associated with a high frequency of cardiovascular disease and because microalbuminuria predicts the development of renal and cardiovascular disease in diabetes. we investigated whether serum sialic acid levels are increased in insulin-dependent diabetes mellitus (IDDM) patients with microalbuminuria or clinical proteinuria.

Research design and methods: We studied 23 patients with IDDM who had a normal urinary albumin excretion rate, 23 patients who had microalbuminuria and 23 patients with clinical proteinuria. The patients were matched for age, sex, duration of diabetes, GHb levels and body mass index (BMI). Fasting blood samples were taken for measurement of sialic acid, cholesterol, triglyceride, creatinine and GHb.

Results: Serurn sialic acid was significantly higher in the microalbuminuric patients compared with the normoalbuminuric group (mean ± SD: 1.93 ± 0.26 vs. 1.76 ± 0.27 mM, P < 0.01). Moreover, serum sialic acid was also significantly higher in the group with clinical proteinuria compared with the microalbuminuric patients (2.34 ± 0.24 vs. 1 .93 ± 0.26 mM, P < 0.001). Serum sialic acid was not related independently to age, BMI, diabetes duration, GHb, blood pressure, serum cholesterol, triglyceride or creatinine concentration in any of the diabetic groups.

Conclusions: These observations suggest that the serum sialic acid concentration is raised in IDDM patients with both rnicroalbuminuria and clinical proteinuria and may play a role as a cardiovascular risk factor or disease rnarker in these conditions.

Effects of NIDDM on lipoprotein(a) concentration and apolipoprotein(A) size.

Rainwater DL, MacCluer JW, Stern MP, VandeBerg JL, Haffner SM. Diabetes 1994; 43 : 942-6.

We investigated the effects of non-insulin-dependent diabetes mellitus (NIDDM) on lipoprotein(a) (Lp[a]) and apolipoprotein(A) (apo[A]) in a population of Mexican-Americans. In plasma samples from 536 subjects, we measured Lp(a) concentrations and we estimated apo(A) isoform sizes following immunostaining of plasma proteins resolved using sodium dodecyl sulfate electrophoresis. We identified 81 diabetic subjects who had 108 distinct apo(A) isoform bands. We then identified 81 non-diabetic subjects from the remainder who were closely matched for apo(A) phenotype (i.e., number and size of apo(A) isoform bands). As expected, the diabetic group had higher levels of glucose and insulin (both fasting and 2 h after glucose challenge) and triglycerides and lower levels of high density lipoprotein (HDL)-cholesterol when compared with the matching non-diabetic group. Moreover, the diabetic group also had significantly lower Lp(a) concentrations than the non-diabetic subjects (10.6 vs. 13.6 mg/dl, P = 0.045) using a paired *Student's t test.* To detect the effects of diabetes on apo(A) size, we identified by pedigree analysis the non-diabetic family members who possessed alleles identical to those in the diabetic group. When we compared the average sizes for each allele, we found that apo(A) isoforms averaged 4.1 kDa larger in diabetic subjects than the genetically identical apo(A) measured in non-diabetic subjects (P = 0.044, n = 36 alleles). In summary, we have detected significant effects of NIDDM both on Lp(a) concentrations and on apo(A) size.

Body fat distribution and its association with metabolic and hormonal risk factors in women with angiographically assessed coronary artery disease. Evidence for the presence of a metabolic syndrome.

Hauner H, Bognar E, Blum A. Atherosclerosis 1994; 105 : 209-16.

The aim of this study was to investigate the pattern of body fat distribution and its association with metabolic and hormonal cardiovascular risk factors in women undergoing coronary angiography. Thirty of the 51 women exhibited significant coronary artery disease (CAD) (group A), whereas the remaining 21 subjects were tree of major coronary stenoses (group B). Twenty five healthy women without clinical signs of CAD served as a control group (group C). Despite comparable age and body mass index the women ot group A had a significantly higher waist-to-hip ratio (WHR), a measure of the pattern of body fat distribution, than those of group C (0.88 ± 0.07 vs. 0.78 ± 0.06, P < 0.01). In an oral glucose tolerance test a high prevalence of impaired glucose tolerance or diabetes was found in groups A and B (53 % and 63% respectively) compared with group C (4%, each P < 0.01). The women of groups A and B showed significantly higher blood pressure and triglyceride levels as well as lower HDL-cholesterol than those of group C. whereas total and LDL-cholesterol were not different between the groups. The serum concentrations of testosterone, sex hormone binding globulin (SHBG) and cortisol were comparable between the three groups and correlation analysis revealed positive associations between androgens and WHR (r = 0.36, P < 0.01) and serum insulin (r = 0.34, P < 0.01) respectively. These findings indicate that women with angiographically confirmed CAD and those with clinical signs of CAD but without significant stenosis. frequently exhibit a metabolic syndrome

characterised by a cluster of metabolic abnormalities which may underlie the atherosclerotic process.

Plasma t-PA and PAI-1 antigen concentrations in non-insulin-dependent diabetic patients: implication for diabetic retinopathy.

Cho YW, Yang DN, Oh DY, Baick SH, Kim SK, Kim SJ, Hong SY Diabetes Res Clin Pract 1994; 22 : 123-8.

Parameters of fibrinolysis, including basal plasma tissue type plasminogen activator (t-PA) and plasminogen activator inhibitor type 1 (PAI-1) antigen levels were studied in 49 non-insulin dependent diabetic patients (23 men, 26 women: ages 51.3 ± 14.9 years) and 16 age-matched non-diabetic subjects (9 men, 7 women, ages 49.8 ± 12.2 years) as a control group. Compared to a control group, the diabetic patients had a significantly higher mean plasma t-PA antigen (4.94 ± 2.68 vs. 3.20 ± 2.30 ng/ml) and PAI-1 antigen (34.86 ± 16.71 vs. 17.60 ± 15.36 ng/ml) levels ($P < 0.05$). Significant univariate correlations were observed between t-PA and body mass index (BMI) ($P = 0.0009$, $r = 0.7217$) and PAI-1 were positively correlated with BMI and FBS (fasting blood sugar) in the total diabetic patients ($P = 0.0003$, $r = 0.7217$; $P = 0.0477$, $r = 0.2858$ respectively). In diabetic patients with proliferative diabetic retinopathy, both PAI-1 and t-PA antigen levels were significantly lower than those of diabetic patients with negative or background retinopathy ($P = < 0.05$). There were no significant differences of the plasma t-PA and PAI-1 levels between diabetic patients with micro and macroproteinuria. This study conducted on non-insulin-dependent diabetic patients suggests that they have significantly higher t-PA and PAI-1 antigen levels than do control subjects and these findings appear to correlate negatively with proliferative retinopathy observed among the patients studied.

Risk factors for cardiovascular disease in IDDM. A study of identical twins.

Dubrey SW, Reaveley DR, Seed M, Lane DA, Ire land H, O'Donnell M, O'Connor B, Noble MI, Leslie RD. Diabetes 1994; 43: 831-5.

Patients with insulin-dependent diabetes mellitus (IDDM) have an excess mortality, predominantly attributable to cardiovascular disease. To determine the effect of IDDM on potential risk factors for cardiovascular mortality, we studied subjects from the British Diabetic Twin Study Group. Forty-five identical twin pairs discordant for IDDM were recruited in addition to 45 matched non-diabetic singleton control subjects. All were selected to be normotensive and to have normal albumin excretion rates. Four variables differed significantly between the diabetic twins and their non-diabetic identical co-twins: diabetic twins had higher systolic blood pressure (sBP) ([mean ± SD] 127 ± 17 vs. 123 ± 18 mmHg, $P < 0.05$), high density lipoprotein (HDL)-cholesterol (1.36 ± 0.31 vs. 1.25 ± 0.29 mM, $P < 0.05$) and fibrinogen (3.23 ± 0.81 vs. 2.98 ± 0.71 mg/ml, $P < 0.05$) but lower factor VII (114 ± 34% vs. 122 ± 31%, $P < 0.05$). All four of these risk factors were significantly correlated ($P < 0.001$) within the identical twin pairs, as were the other risk factors. These significant correlations within twins for the risk factors studied reflects the impact of shared genetic and environmental influences. IDDM affects sBP, HDL-cholesterol, fibrinogen and factor VII, but only sBP and fibrinogen are affected adversely.

Atherosclerosis and juvenile dyslipidaemias.

Calvani M. Recenti Prog Med 1994; 85: 204-11.

Large scale and systemic epidemiological, pathological and experimental studies emphasised and documented the childhood origin of atherosclerosis. There is increasing consensus that lipid levels in children to a large extent determine the rate of coronary artery disease (CAD) in the adult population. Minimal sudanophilic intimal deposits and the presence of intracellular and extracellular lipid and a slight increase in interstitial ground substance in 3 years of age or older patients are found. In the Bogalusa Hearth Study, aortic fatty streaks were strongly related to the antemortem levels of both total cholesterol and low density lipoprotein-cholesterol (LDL-C) independent of race, sex and age and were negatively correlated with the ratio of high density lipoprotein (HDL-C) to low density plus very low density lipoprotein-cholesterol (LDL-C+VLDL-C). The potential for primary prevention is real and the strongest piece of evidence for it is the remarkable trend in CHD mortality rates in recent times, rapidly downward in many western countries. A number of factors influence plasma levels of lipid and lipoproteins in newborn, in infants, in children and adolescents and their relevance as possible predictors of adult coronary artery disease. They are certain inherited disorders of dyslipoproteinaemia (familial hypercholesterolaemia, familial combined hyperlipidaemia, hyperapobetalipo-proteinaemia and hypoalphalipoproteinaemia) and secondary causes of hyperlipidaemia (congenital biliary atresia, glycogen storage diseases, hypothyroidism, diabetes mellitus and nephrotic syndrome etc).

Relative risk of factors for coronary heart disease in population with low cholesterol levels.

Onat A. Senocak MS. Int J Cardiol 1994; 43 : 51-60.

We studied the odds ratios of 7 leading risk variables in a population essentially having a 'low' cholesterol concentration. In a cross-sectional population-based study of 3689 Turkish adults, 20 years of age or over, 90 men and 83 women were diagnosed to have definite or suspected coronary heart disease. The criteria were based on history, cardiovascular examination and on Minnesota coding of electrocardiograms. Potential risk factors studied were: plasma total cholesterol (≥ 240 mg/dl), fasting triglycerides (≥ 200 mg/dl), diabetes mellitus, hypertension (systolic ≥ 160 mmHg, diastolic ≥ 95 mmHg or both or subjects reporting to take antihypertensive medication), smoking currently or in the past, obesity (body mass index ≥ 30 kg/m^2) and physical inactivity. Hypertension and lack of physical exercise constituted the most important risk factors in both sexes being valid for all age groups and having high attributable risks; odds ratios in men and women respectively, were 3.16 and 2.6 for hypertension and 2.16 and 3.49 for physical inactivity. Hypertriglyceridaemia followed these factors in men with an odds ratio of 2.15. In women an additional significant factor was obesity (odds ratio 1.76), while diabetes and hypercholesterolaemia revealed to be significant only in those aged 20-59 years and smoking in women aged 30-59 years. Among men, smokmg was a borderline significant risk factor for coronary disease whereas hypercholesterolaemia did not prove to be so. These findings, somewhat at variance with those of industrialised nations, may have significance for a policy of cardiovascular disease prevention in third-world populations.

Hyperinsulinaemia and hypertriglyceridaemia.

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Hyperinsulinaemia and hypertriglyceridaemia are frequently associated. This may be as a part of the syndrome of insulin resistance or in diabetes, particularly non-insulin-dependent diabetes (NIDDM). The importance of this association lies in the fact that atherosclerosis is the most frequent complication of diabetes, that hypertriglyceridaemia is a risk factor for coronary artery disease in diabetic populations and that

hyperinsulinaemia also appears to be a risk factor for atherosclerosis. Hypertriglyceridaemia, even without obesity, is associated with resistance to insulin. This can result in compensatory hyperinsulinaemia. Chronic hyperinsulinaemia has been shown to increase the production of triglyceride (TG)-rich lipoproteins. The vast majority of particles in the TG-rich lipoprotein spectrum are in the intermediate density lipoprotein (IDL) range. Furthermore, increased levels of TG result primarily from increased numbers of these particles rather than from increased particle size. This is important because at least in non-diabetic individuals, increased levels of IDL are associated with increased atherosclerosis. Thus, there may be a vicious cycle of insulin resistance, hyperinsulinaemia, hypertriglyceridaemia and atherosclerosis. We have found that by reducing plasma TG levels alone, one can increase sensitivity to insulin and break this cycle.