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# Plasma Alpha–Tocopherol and Malondialdehyde Concentrations in Type 2 Diabetic Patients

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***Background and Aims.*** *Oxidative stress is considered to be a unifying link between diabetes mellitus (DM) and its complications, including retinopathy, nephropathy, neuropathy, and accelerated coronary artery disease. Plasma antioxidant level may be affected by this hyperglycemia-induced oxidative stress and cause the increased production of oxidative parameters including malondialdehyde (MDA). In the present study, the plasma MDA and a-tocopherol in fairly controlled Type 2 DM ( fasting plasma glucose [FPG] < 180 mg/dl ) or Tyoe 2 DM complicated with coronary artery disease ( CHD ) and poorly controlled Type 2 DM ( FPG > 180 mg/dl ) were investigated.*

***Materials and Methods.*** *A total of 65 Type 2 DM patients were subdivided into those with 26 fairly controlled, 19 poorly controlled and 20 Type 2 DM complicated with CHD. Plasma a-tocopherol, lipid profiles and MDA concentrations were estimated in all patients and in 20 nondiabetic healthy persons which FPG < 110 mg/dl. In all groups of DM, their results were compared with a control group by one-way ANOVA test.*

***Results.*** *The plasma MDA levels were significantly increased in all groups of Type 2 DM as compared to controls, ( $p < 0.05$ ). No significant difference of MDA level within groups of DM was found. Significantly decreased plasma a - tocopherol, a- tocopherol/total cholesterol and a-tocopherol/total lipid levels were found only in Type 2 DM complicated with CHD as compared to controls, ($p < 0.001$) and also showed significant difference when compared to fairly controlled and poorly controlled type 2 DM ($p< 0.001$). However, no significant difference of these a - tocopherol parameters was found in fairly controlled and poorly controlled Type 2 DM as compared to controls ($p > 0.05$)*

***Conclusion.*** *Results of the present study indicate that oxidative stress is increased and antioxidant defenses are compromised in Type 2 DM. These derangements are of a higher magnitude in patients of Type 2 DM with CHD. From this study, we conclude that antioxidant treatment may attenuate the hyperglycemia – induced oxidative stress to prevent cardiovascular complications in type 2 diabetic patients.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

PP 72

# Effect of Glucose on Human Serum Paraoxonase (PON1) GeneTranscription in Hepatocytes

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***Background and Aims.*** *Human serum paraoxonase (PON1) is associated with high-density lipoprotein, and inhibits oxidative modification of low-density lipoprotein. We and other investigators have shown that enzymatic activities of PON1 decreased in diabetic patients, however, an alteration in the hepatic PON1 synthesis under hyperglycemic condition remains unclear. We previously demonstrated that Sp1 is a positive regulator of PON1 transcription, and that an interaction between Sp1 and protein kinase C (PKC) is a crucial mechanism for the effect of Sp1 on PON1 transcription in cultured HepG2 cells. Since several PKC isoforms are known to be activated in hyperglycemic state, we examined an effect of D-glucose, which can activate diacylglycerol-PKC pathway, on the PON1 promoter activity.*

***Materials and Methods.*** *For a reporter gene assay, a DNA fragment of the promoter region of PON1 gene (-1230/-6) was amplified using a PCR method, and the DNA fragment was introduced into the firefly luciferase expression vector. For stable transfection experiments, a mixed polyclonal HuH7 human hepatocyte cell line incorporated with PON1-luciferase expression vector was established using a cationic lipid method. For statistical analyses, data were compared by one-way ANOVA with Fisher's protected least significant difference test. P values less than 0.05 were considered significant.*

***Results.*** *D-glucose, but not L-glucose or mannitol, enhanced PON1 promoter activity in a dose-dependent manner (the promoter activity after a treatment with 25 mM D-glucose for 24 hrs was 1.5~2.0-fold higher as compared to that with 5 mM D-glucose). The time-course study showed the effect of D-glucose reached a plateau at 12 hr, and slightly diminished after 72 hrs. Bisindolylmaleimide, a PKC inhibitor, significantly inhibited D-glucose-induced transactivation of PON1, and mythramycin, an inhibitor of Sp1, completely abrogated the transactivation. Insulin showed no significant effect on PON1 promoter activity.*

***Conclusion.*** *Our data suggest that D-glucose enhances PON1 promoter activity through Sp1 activation by PKC. However, the sustained exposure of D-glucose (after 72 hrs) decreased the PON1 transactivation, suggesting that chronic effect of high glucose may be different from its acute effect. Further work is required to clarify the regulation of hepatic PON1 synthesis in diabetes that is a long-standing hyperglycemic condition.*

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**PP 73**

# Plasma Apolipoprotein E is a Major Determinant of Phospholipid Transfer Protein Activity in Type 2 Diabetes Mellitus

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***Background and Aims.*** *Phospholipid transfer protein (PLTP) transfers phospholipids between lipoproteins and plays an important role in HDL metabolism. PLTP exists as a high-activity and a low-activity form in the circulation and the regulation of different PLTP forms and their activities are poorly understood. Recent in vitro studies have shown that apolipoprotein (apo) E is able to activate PLTP whilst the low activity form of PLTP tends to associate with apo AI. We have therefore investigated whether plasma apo AI, B and E concentrations are important determinants of plasma PLTP activity in type 2 diabetes, a condition known to be associated with increased plasma PLTP activity.*

***Materials and Methods.*** *Plasma PLTP activity was assayed by measuring the transfer of radiolabelled phosphatidylcholine from liposomes to HDL. Apolipoproteins AI and B were measured by rate nephelometry and apo E by a 2-point turbidimetric assay.*

***Results.*** *Type 2 diabetic patients (n=230) had higher apo B (1.03 ± 0.29 g/l vs 0.92 ± 0.27, p<0.01) and apo E (48.5 ± 19.6 mg/l vs 43.6 ± 17.0, p<0.05) and lower apo AI (1.27 ± 0.20 g/l vs 1.43 ± 0.27, p<0.01) than controls (n=97). Plasma PLTP activity was increased in diabetic patients (2374 ± 628 nmol/ml/h vs 1862 ± 585, p<0.01). In control subjects, PLTP activity correlated with apo AI (r=-0.20, p=0.05) and apo E (r=0.24, p<0.05) whereas in diabetic patients, PLTP activity correlated with apo AI (r=-0.21, p<0.01), apo B (r=0.16, p<0.05), apo E (r=0.45, p<0.01) and HbA1c (r=0.13, p=0.05). General linear model univariate analysis showed that plasma apo E concentration was the major determinant of PLTP activity in both controls and diabetic subjects.*

***Conclusion.*** *The associations between plasma apo AI and E concentrations and PLTP activity suggest that these apolipoproteins may regulate PLTP activity by influencing the distribution of the two forms of PLTP. The increase in PLTP activity in type 2 diabetes is partly related to the higher apo E and lower apo AI concentrations in these individuals.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

**PP 74**

# Association between Advanced Glycation End Products and Serum Cholesterol Efflux Capacity in Type 2 Diabetes Mellitus

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***Background and Aims.*** *Advanced glycation end products (AGEs), as ligands for scavenger receptor class B type 1 (SR-B1), have recently been shown to inhibit cholesterol efflux from Chinese hamster ovary cells to HDL in vitro (J Biol Chem 2001;276:13348-55). Hyperglycaemia leads to increased formation of AGEs, and serum and tissue concentration of AGEs are increased in diabetes. We have investigated whether the capacity of serum from type 2 diabetic patients to induce cholesterol efflux is related to serum levels of AGEs.*
***Materials and Methods.*** *Serum AGEs were assayed by competitive ELISA using a polyclonal rabbit antisera raised against AGE-RNase. Serum cholesterol efflux capacity was determined by measuring the transfer of [3H]cholesterol from SR-B1-rich Fu5AH cells to the medium induced by the test serum.*
***Results.*** *Type 2 diabetic patients (n=210) had higher plasma triglyceride ($p<0.01$) and lower HDL ($p<0.01$) than controls (n=87). Serum AGEs were increased in diabetic patients (4.29 ± 0.93 unit/ml vs 3.19 ± 0.81, $p<0.01$) whereas serum cholesterol efflux capacity was reduced (13.66 ± 3.10 % vs 14.56 ± 4.13, $p<0.05$). In diabetic patients, serum cholesterol efflux capacity was associated with HDL ($r=0.42$, $p<0.001$), apolipoprotein AI ($r=0.22$, $p<0.01$), log(triglyceride) ($r=-0.17$, $p<0.05$) and HbA1c ($r=0.14$, $p<0.05$). In contrast to the in vitro findings of AGEs inhibiting cholesterol efflux, serum AGEs showed a strong positive correlation with serum cholesterol efflux capacity ($r=0.43$, $p<0.001$). Forward stepwise linear regression analysis showed that AGEs and HDL were the main independent determinants of serum cholesterol efflux capacity in the diabetic patients, accounting for 20% and 13% of its variation respectively.*
***Conclusion.*** *The strong positive correlation between serum AGEs and cholesterol efflux capacity would suggest that inhibitory effect of circulating AGEs on SR-B1 mediated cholesterol efflux was small. Since cholesterol efflux induced by serum involves a number of enzymes and lipid transfer proteins in addition to the cellular cholesterol transporter SR-B1, it is likely that AGEs affect other steps in the cholesterol efflux pathway and this is currently being investigated. The low serum cholesterol efflux capacity in diabetic subjects is partly due to decreased HDL levels.* *Acknowledgement. This study was supported by grant awards from Hong Kong Research Grants Council (HKU7350/02).*

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**PP 75**

# TDR* 5: Current Status of Dyslipidemia in Thai Diabetic Patients

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***Background and Aims.*** *Cardiovascular disease(CVD) is the major cause of death in diabetic patient. In order to decrease CVD, management of dyslipidemia is very important. American diabetes association (ADA) recommended that plasma LDL cholesterol should be lower to less than 100 mg/dl. Plasma cholesterol must be lower by 30-40% together with LDL lower than 100 for primary and 70 for secondary CVD prevention. In order to survey current lipid management status and impact of new ADA recommendation, We conducted a multi-center registry of diabetic patients in 11 tertiary care hospitals and medical schools across country to examine present clinical status of these patients.*

***Material and Methods.*** *A registration of 9,419 diabetic patients expected to follow-up at least one year at 11 diabetic clinics in tertiary diabetic clinics in Bangkok and major provinces was performed form April to December 2003. Individual Demographic data including education and socioeconomic status were collected. Physical examination for complications screening and laboratory results include plasma lipid concentration within six months were recorded in the database. Prevalence of diabetes complications was examined and percentages of achievement in metabolic control were calculated based on the ADA guideline.*

***Results.*** *There were 8,922 (Age 59.5±13.3 years, 33.9/66.1% M/F) of a total of 9,419 diabetic patients who have complete demographic and plasma lipid concentration. They composed of 8,464 patients with type 2 diabetes and 383 with type 1 diabetes. In this group of patients, 8.0% and 4.3% had previous history of coronary artery disease and cerebrovascular disease. Plasma lipids profile were total cholesterol (196.9±42.0 mg/dl), triglyceride (148.9±99.3 mg/dl), HDL (53.9±15.3 mg/dl), and LDL (114.5±35.7 mg/dl). About two-third of patients(63.3%) had LDL cholesterol more than 100 mg/dl, but 32.1% and 37.5% had levels of HDL and triglycerides in dyslipidemic range respectively. More than half of patients (55%) were taking lipid lowering medications, but one-third(30%) did not take lipid lowering medication even though they needed. The patients who were on government supported health plan, were less chance to have lipid lowering medication (OR 0.65, 95%CI 0.57-0.75) than another health plan. Statin (76%) and fibrate (19%) were contributed almost all of medication and about 5% were used in combination. Only about 42% of medication taking patients, were reached LDL goal (<100 mg/dl). If we use current ADA recommend, we must treat 40% more patients together with 55% who had been treated with lipid lowering medication that mean about 95% of this group of diabetes need lipid lowering medication.*

***Conclusions.*** *Elevated LDL cholesterol was the most important dyslipidemia in the group of diabetes. Although 55% of patients were taking lipid lowering agent, 30% more patient also need medication. More than half of treating patients need more intensive lipid lowering to achieve LDL goal. If we change our recommendation to current ADA recommendation, we may need to treat up to 95% of diabetic patients with lipid lowering agents.*

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## PP 76

# Comparison of Glycemic Control and Lipid Profiles in Both Sexes among Type 2 Diabetes

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***Background and Aims.*** *Diabetes mellitus is a coronary heart disease (CAD) equivalent and eliminates the protective effect of female sex on the risk of CAD. We assessed sex difference in glycemic control and lipid profiles among patients with diabetes in a medical center clinic in Taiwan.*

***Materials and Methods.*** *This cross-sectional analysis included 196 type 2 diabetic patients who were randomized enrolled in a Diabetes Case Management Project from March of 2004 to March of 2005. There were 117 males and 79 females with age ranged from 42 to 89 years old (mean: 69) and 40 to 87 years old (mean: 63), respectively. All patients received blood sampling for plasma glucose, hemoglobin A1c (A1c), cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride, liver and renal function after overnight fasting for at least 8 hours. These biochemistry values were analyzed with independent-samples T test to evaluate the difference between the two groups of patients. The chi-square test was used for comparison the numbers between male and female patients who met the American Diabetes Association (ADA) recommended criteria. Statistical significance was defined as $P< 0.05$.*

***Results.*** *The average fasting plasma glucose and A1c for male were 147mg/dl and 7.5%; for female were 151mg/dl and 7.6%. There were 45% male and 44% female patients had their A1c below 7%. The average values of cholesterol, triglyceride, LDL-C and HDL-C in male and female were: 198 and 206 mg/dl; 167 and 175mg/dl; 120 and 117 mg/dl; 48 and 54 mg/dl; respectively. There were 34.2% male and 37.5% female patients had their LDL-C below 100mg/dl. Most of the male patients (71.8%) had their HDL-C above or equal to 40mg/dl, but only 52.5% female patients had their HDL-C above or equal to 50mg/dl. There were 59.0% male and 61.3% female patients had their value below 150mg/dl for serum triglyceride concentration. Comparing the glycemic control and lipid profiles, there were no sex difference in fasting plasma glucose, A1c, cholesterol, triglyceride and LDL-C. Fewer female patients met the HDL-C criteria recommended by ADA than male patients did ($P=0.007$).*

***Conclusion.*** *In this report, there was no sex difference between glycemic control and most of the lipid profiles in our diabetic patients. However, fewer female patients met the ADA recommended HDL-C levels. The female diabetics still had more CAD risk factors than the male diabetic patients.*

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## PP 77

# Reduction of Low-Density Lipoprotein Cholesterol (LDL-C) Decreases Cardiovascular Events in Hong Kong Chinese Diabetic Patients

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***Background and Aims.*** *Limited prospective clinical data in Chinese type 2 diabetic (T2DM) population is available to examine the relation between achieving LDL-c <2.6mmol/L and cardiovascular outcome. The aim of this study is to investigate whether LDL-c reduction to <2.6mmol/L can decrease cardiovascular endpoints in Chinese diabetic patients.*

***Materials and Methods.*** *Between 1995 and 2000, a consecutive cohort of 3571 Chinese T2DM, with no known history of macrovascular disease and were not on lipid lowering drugs, were recruited. Patients were categorised into two groups (<2.6 mmol/L or e"2.6mmol/L). Cardiovascular endpoints between the two groups were compared.*

***Results.*** *In this study cohort, mean age was 55.9±14.4 years. 44% were male. Mean duration of diabetes was 6.7±6.2 years. Mean glycosylated haemoglobin (HbA1c) was 7.7±1.9%. Only 22.7% had LDL-c <2.6mmol/L. Diabetes with LDL-c e"2.6mmol/L were older (mean age=56.9 ±13.9 versus 52.7±15.4 years, p<0.001), more obese (body mass index, BMI=24.9±3.9 versus 24.4±4.4 kg/m2, p=0.002; waist circumference, WC=84.5±10.2 versus 82.8±11.2 cm, p<0.001), higher blood pressure (systolic blood pressure=132±20 versus 128±19mmHg, p<0.001; diastolic blood pressure=77±11 versus 74±10mmHg, p<0.001), worse glycemic control (HbA1c=7.8±1.9 versus 7.4±1.8%, p<0.001; fasting plasma glucose=8.8±3.4 versus 8.1±3.2 mmol/L, p<0.001) and higher triglyceride level (1.4±0.7 versus 1.3±0.9 mmol/L, p<0.001). Higher frequency of metabolic syndrome was also observed in diabetes with LDL-c e"2.6mmol/L compared to those with LDL-c <2.6mmol/L (54.2% versus 46.1%, p<0.001). After a median follow-up of 41 months (interquartile range: 23.6-56 months), 3.5% (n=125) reached cardiovascular endpoints, with significantly more patients in the group with LDL-c e"2.6mmol/L (4.0%, n=110 versus 1.9%, n=15, p=0.003). After adjusted for age, sex and other known risk factors for cardiovascular events including systolic and diastolic blood pressure, duration of diabetes, HbA1c, obesity indices (BMI and WC), smoking status, high-density lipoprotein levels, diabetic patients with LDL-c e"2.6mmol/L remained significantly at higher risk for cardiovascular mortality and morbidity compared to diabetic patients with LDL-c <2.6mmol/L (hazard ratio 1.77, 95% CI 1.02-3.03, p=0.041).*

***Conclusion.*** *In Hong Kong Chinese, high percentage of T2DM had LDL-ce"2.6mmol/L. LDL-ce"2.6mmol/L was associated with higher frequency of metabolic syndrome and higher risk of developing cardiovascular events compared to diabetes with LDL<2.6mmol/L. Therapeutic interventions should be reinforced to achieve LDL-c <2.6 mmol/L in Hong Kong Chinese T2DM patients.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

## PP 78

# Atorvastatin Goal Achievement Across Risk Levels (AT-GOAL) Study

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***Background and Aims.*** *The AT-GOAL study was set-up to determine the percentage of Thai dyslipidemic subjects achieving their LDL-C target, defined by the NCEP ATP III,* across starting doses of 10-40 mg/day atorvastatin, as well as the safety and tolerability of atorvastatin.*

***Materials and Methods.*** *This was an 8-week prospective, multi-center, open label study. Outpatients (e"18 and d"80 years of age) with a diagnosis of dyslipidemia and eligible for lipid lowering therapy were included. At study start, subjects' LDL-C and individual CHD risk categorization were established, accordingly their atorvastatin starting dose and LDL-C targets were determined. Subjects who did not achieve LDL-C target by Week 4 were titrated up one step, otherwise subjects continued on their starting dose. Lipid parameters assessed at each visit. Safety and tolerability were assessed by adverse events (AEs) and abnormal clinical laboratory tests.*

***Results.*** *A total of 242 subjects entered this study, only 11 subjects (4.5%) discontinued prematurely. In the total sample, 82% of subjects reached their target LDL-C by Week 2; this was sustained at Week 4 (87%) and continued to Week 8 (89%). Only 10% (n=25) of subjects were titrated at Week 4. There were only 2 serious AEs recorded, both of which were not treatment related. The incidence of abnormal laboratory test results was unremarkable during the study*

***Conclusion.*** *Atorvastatin was found to be an effective, safe and well tolerated treatment for dyslipidemia in this Thai population. The appropriate assigned starting dose of atorvastatin treatment resulted in a quick achievement of LDL-C target and with minimal requirement for dose titration. *National Cholesterol Education Program Adult Treatment Panel III*

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**PP 79**

# Atorvstatin Does Not Affect Serum Adiponectin and Leptin Concentrations in Hyperlipidemic Type 2 DM Patients

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***Background and Aims.*** *To delineate the effect of statins on the serum concentrations of adiponectin and leptin in hyperlipidemic type 2 DM patients.*

***Materials and Methods.*** *A total of 29 patients fulfilled the criteria of 1) aged from 18-80 years; 2) HbA1C f" 10 %; 3) LDL-C g" 130 mg/dl; 4) triglyceride < 400 mg/dl. The patients were randomized to receive 10 mg (n=10), 20 mg (n=10) and 40 mg (n=9) of atorvastatin for 12 weeks. Evaluations were performed before and after atorvastatin treatment. The evaluations included body mass index (BMI), serum concentrations of total cholesterol (TC), low density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), triglyceride (TG), hemoglobin A1C (HbA1C), adiponectin and leptin.*

***Results.*** *Baseline Characteristics including age, BMI, serum concentrations of TC, LDL-C, HDL-C, TG, HbA1C, adiponectin and leptin were not different among these three treatment groups. The post-treatment concentrations of TC and LDL-C were lower than those of pre-treatment in the 10 mg (174.3 ± 10.6 vs 249.2 ± 8.3 mg/dl; 107.8 ± 8.9 vs 169.1 ± 7.8 mg/dl, respectively, P < 0.001), 20 mg (138.1 ± 10.1 vs 240.8 ± 7.7 mg/dl; 76.2 ± 7.8 vs 164.8 ± 6.3 mg/dl, respectively, P < 0.001) and 40 mg (137.4 ± 8.4 vs 235.3 ± 8.4 mg/dl; 80.9 ± 8.0 vs 164.3 ± 7.7 mg/dl, respectively, P < 0.001) treatment groups. The serum concentrations of TG was also decreased after 10 mg (101.5 ± 11.4 vs 160.9 ± 27.8 mg/dl, P = 0.007), 20 mg (110.7 ± 14.9 vs 173.5 ± 17.8 mg/dl, P = 0.002) and 40 mg (93.1 ± 13.7 vs 130.7 ± 20.1 mg/dl, P = 0.022) of atorvastatin treatment. No significant change of serum HDL-C and HbA1C levels were noted after each dose of atorvastatin treatment. Besides, post-treatment serum concentrations of adiponectin and leptin were not different compared with those of pre-treatment in the 10 mg (76.9 ± 14.7 vs 78.4 ± 11.9 mg/l; 84.4 ± 14.8 vs 79.8 ± 15.3 mg/l, respectively, P > 0.05), 20 mg (81.7 ± 27.0 vs 61.1 ± 17.0 mg/l; 96.1 ± 16.4 vs 104.1 ± 33.5 mg/l, respectively, P > 0.05) and 40 mg (66.7 ± 17.5 vs 68.9 ± 16.8 mg/l; 33.0 ± 7.3 vs 29.8 ± 5.9 mg/l, respectively, P > 0.05) treatment groups. The comparisons of the change from baseline showed that neither change of adiponectin (P = 0.149) nor change of leptin (P = 0.816) was found of significant difference after treatment of different dose of atorvatatin.*

***Conclusion.*** *Atorvstatin does not affect serum adiponectin and leptin concentrations in hyperlipidemic type 2 DM patients.*

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**PP 80**

# Two-Arm Study Comparing the Efficacy and Safety of Simvastatin and Simvastatin Plus Fenofibrate in Type 2 Diabetes with Dyslipidemia

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***Background and Aims.AIM.*** *To compare the efficacy and safety between simvastatin and simvastatin plus fenofibrate in type 2 diabetes with dyslipidemia.*

***Materials and Methods.*** *Seventy-nine subjects with type 2 diabetes and dyslipidemia who cannot achieve the optimal therapeutic goal with statins were enrolled and randomly assigned to two groups in this study. Group 1 (n=42) received a combination of simvastatin 20 mg/d and fenofibrate 200 mg/d, and group 2 (n=37) received simvastatin 40mg/d for 3 months following a period of 3 months with simvastatin 20mg/d. Lipid profiles were measured at three time points: 3 months before modification, before modification, and after modification. Generalized estimating equation models were employed to resolve repeated measurement problems.*

***Results.*** *After treatment modification for 3 months, there was no significant difference on lipid-lowering efficacy between the two groups. All subjects showed significant improvement in LDL (-21.2 mg/dL, p<0.05), HDL (9.7 mg/dL, P<0.05), and TG (-79.8 mg/dL, p<0.05). A 23.1-fold increased likelihood of achieving the LDL therapy target, a 5.26-fold increased likelihood of attaining the HDL target, and a 4.39-fold increased likelihood of achieving the TG target was demonstrated after treatment modification . One subject developed rhabdomyolysis after administration of simvastatin 40mg/d for 1 month. No subjects in group 1 showed adverse reactions.*

***Conclusion.*** *This study showed that the combined therapy of simvastatin 20 mg/d plus fenofibrate 200mg/d has the same efficacy as simvastatin 40 mg/d for patients with type 2 diabetes and dyslipidemia.*

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## PP 81

# The Hepatic Mechanism of Anti-Diabetic Effect by Fenofibrate in Oletf Rats

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***Background and Aims.*** *We hypothesized that fenofibrate treatment can reduce fat burden in liver and can prevent the development of diabetes in OLETF rats.*
***Materials and Methods.*** *Fenofibrate group was fed with LabChow diet containing fenofibrate (300 mg/kg/day) from 10-46 weeks of age. Paired feeding group was fed with LabChow diet only but same amount as in the fenofibrate group. Free diet group was fed freely with LabChow diet only.*
***Results.*** *The chronic treatment of fenofibrate prevented from gaining abdominal adiposity and maintained the blood glucose levels within normal range in the rats. However, all the control groups became obese and diabetic. The liver of fenofibrate treated rats showed increased oxidative phosphorylation (coupling) and uncoupling activities with newly expression of UCP-3. And they showed little pathologic change in the microscopic morphologic study. However, the liver of control rats demomstrated moderate to severe fatty changes with swollen mitochondria.*

**Table 1.** The blood levels of glucose, insulin, beta-ketone and the respiration rate.

| | Fenofibrate (n=10) | Paired feed (n=10) | Free diet (n=10) | P value |
|---|---|---|---|---|
| Glucose (mmol/L) | 8.5±0.9 | 22.4±3.0 | 16.9±3.7 | P=0.0001ßð |
| HOMA IR index | 5.5±0.5 | 22.0±1.6 | 22.0±2.3 | P=0.02ßð |
| beta ketone (mol/L) | 1.5±0.2 | 0.6±0.1 | 0.7±0.1 | P=0.01ßð |
| State-3 respiration rate (ul/hr) | 1416.5±17.5 | 239.5±12.3 | 225.0±23.0 | P=0.001ßð |
| State-4 respiration rate(ul/hr) | 391.5±11.0 | 211.0±4.5 | 186.5±11.5 | P=0.005ßð |

MEAN±SEM, ßFenofibrate vs Paired feed, ð Fenofibrate vs Free diet

***Conclusion.*** *We concluded that chronic fenofibrate treatment could prevent the development of diabetes in OLETF rats by relieving the fat burden on liver via increasing the mitochondrial bioenergetics (coupling and uncoupling processes) with ketogenesis to prevent hepatic mitochondrial dysfunction.*

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## PP 82

# TDR* 6: Hypertension in Diabetes: Prevalence, Associated Factors and Patterns of Antihypertensive Therapy

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Nattachet Plengvidhya, Supawadee Likitmaskul, Chaicharn Deerochanawong,
Sompong Suwanwalaikorn, Sutipong Wacharasindu, Thongchai Prathipanawatr,
Thanya Chetthakul, Sirinate Krittiyawong, Sayan Cheepudomwit,
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***Background and Aims.*** *Hypertension is very common in patients with diabetes and is a major contribution to both micro- and macrovascular complications. Most current guidelines recommend aggressive management of hypertension with target blood pressure of less than 130/80 mmHg. Drugs that inhibit renin-angiotensin system are usually recommended as first line agents in patients with diabetes. The objectives of this study are to determine the prevalence of hypertension and its associated factors in adult Thai diabetic patients in OPD setting. The achievement of target blood pressure control and patterns of antihypertensive agents were also analyzed.*

***Material and Methods.*** *A cross-sectional, multicenter, hospital-based diabetic registry was carried out from April to December 2003. Diabetic patients in diabetic clinics of 11 tertiary centers were registered. Blood pressure was measured twice, at least 30 second of time apart, by automated blood pressure machine (Omron T4). Mean values of both systolic and diastolic blood pressure were used to define blood pressure levels. Hypertension was defined by mean blood pressure levels equal to or more than 140/90 mmHg or the use of antihypertensive agents.*

***Results.*** *The number of diabetic subjects aged 18 years or older was 9,255 (3,137 males and 6,118 females). The prevalence of hypertension was 77.1%. The mean (SD) age of the patients was 60.2 (12.2) years. Age, body mass index, duration of diabetes, serum creatinine, dyslipidemia (increased triglycerides and decreased HDL) were independently associated with hypertension. Eighty-four per cent of all hypertensive patients currently received antihypertensive agents. Mean (SD) blood pressure levels among those receiving antihypertensive agents were 147.3 (22.4) / 79.0 (11) mmHg. The achievement of blood pressure control (less than 130/80 mmHg) among these patients was 14.27%. Systolic blood pressure target could be achieved in 20.7% and diastolic target in 52.7%. The mean (SD) number of antihypertensive agents was 1.81 (0.89). Most patients (45.5%) received single antihypertensive drug, while 21.4% received three or more drugs. ACE inhibitors were the most commonly prescribed antihypertensive agents (55%), followed by diuretics (43.4%) and calcium channel blockers (34.2%). Among patients who received antihypertensive monotherapy, ACE inhibitors were also most often prescribed (54%), followed by calcium-channel blockers (13.2%), diuretics (12%) and beta-blockers (12%)*

***Conclusions.*** *Hypertension was very common in adult patients with diabetes. The majority of patients still could not achieve good blood pressure control. Nearly half of hypertensive patients received only single antihypertensive drug. ACE inhibitors were among the most commonly used antihypertensive agents, both in mono- and combination therapy. More aggressive management of hypertension in these patients should be seriously considered.*

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**PP 83**

# Assessment of Hypertension in Diabetic Patient Undrer Follow Up in Moosabne Jafar Hospital in Ghochan-Iran

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***Background and Aims.*** *Nephropathy affects diabetic patient and antihypertensive treatment has been shown to retard its progression . Hypertension should be treated aggressively in diabetic patient particularly if there is evidence of renal disease. This report focuses specially on the assessment of BP and management of hypertension in diabetic patient.*

***Materials and Methods.*** *This is a retrospective study to assess hypertension in diabetic patient. Data Collection is done from 100 client document which were refer to moosabne jafar hospital which diagnosed type two diabetes. In this research BP e"140 / 90 or usage of antihypertensive drugs equivalent of hypertension.*

***Results.*** *70% had hypertension. Mean of age, FBS and BP at the firs and last day of residence was 62/9 years, 270/8 and 167/5 mg/dl, 129/77 and 120/75 mmHg.50% of patient used ACE agent and 30% used adalat and lasix. Most of them at least complain of one of these problem : CVA, IHD, DVT, CRF, CHF, Chest pain, and paresthesia.*

***Conclusion.*** *Hypertension in diabetic patient is associated with accelerated progression of both micro vascular (retinopathy and nephropathy) and macro vascular (arteriosclerosis) complication. Diabetic nephropathy is now the leading cause of ESRD and medical treatment has been shown to retarded its progression. The aim of blood pressure reduction includes retardation of progression and prevention of diabetic complication. ACE agent is one of the best medication in this patient*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

**PP 84**

# Improvement of Insulin Resistance by Angiotensin Type 2 Receptor Blocker and Calcium Channel Blocker Treatment in Hypertensive Patients with Hypertriglyceridemia

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***Background and Aims.*** *Hypertension, hyperlipidemia, glucose tolerance or diabetes mellitus, and obesity may have a close interrelation based on insulin resistance. The aim of this study was to investigate the effects of angiotensin type 2 receptor blocker (ARB) or calcium channel blocker (CRB) on insulin resistance in hypertensive patients with hypertriglyceridemia.*

***Materials and Methods.*** *We selected 160 hypertensive patients with hypertriglyceridemia were divided into two groups; the ARB treatment group received 20 mg/day of termisartan during 24 weeks, while the CRB treatment group received 5 mg/day of amlodipine during 24 weeks. Blood pressure, glycemic control, lipid control, hepatic function, serum level of insulin were measured during treatment period. The insulin resistance were calculated by HOMA-IR at each study period.*

***Results.*** *The blood pressure in each group fell significantly ($p<0.001$, respectively). The ARB decreased the serum levels of triglycerides (TG) ($p<0.05$), and Apo E ($p<0.05$), while the serum levels of total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), Apo A, and Apo B were not decreased significantly. On the other hand, the CRB were not decreased the serum levels of TG, TC, HDL-C, LDL-C, Apo A, Apo B, and Apo E. The plasma glucose level was not decreased significantly, but serum level of insulin, and HOMA-IR were decreased significantly ($p<0.05$) by the ARB treatment. On the other hand, these parameters were not decreased significantly by the CRB treatment.*

***Conclusion.*** *These results suggest that treatment with the ARB, but not with the CRB, may have a beneficial effect for improving insulin resistance even in hypertensive and hypertriglyceridemia.*

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**PP 85**

# The Analysis of Gene Polymorphisms in B3 Adrenergic Receptor and Uncoupling Protein-1 Genes in Papua New Guinea

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***Background and Aims.*** *Type 2 diabetes has been rapidly increasing in developing countries, particularly in Asia and the Pacific. Obesity is thought to be a crucial risk factor for type 2 diabetes. The prevalence of obesity, which varies with their environmental influences and genetic susceptibilities, is also increasing in these countries. We hypothesized that the people in these countries have the genetic predispositions to obesity. The purpose of this study is to evaluate their genetic susceptibilities of the obese subjects in Papua New Guinea (PNG) by analyzing the polymorphisms in b3 adrenergic receptor (AR) and uncoupling protein (UCP)-1 genes, which play crucial roles in the regulation of energy expenditure.*

***Materials and Methods.*** *Blood samples were collected from 252 Austronesian-speaking Balopa Islanders in PNG. To evaluate whether the polymorphisms in these genes were associated with obesity, genotype and allelic frequencies were compared between two groups: non-obese subjects (20f"BMI< 22.5) and obese subjects (30f"BMI). Polymerase chain reaction-restriction fragment length polymorphism method was used to analyze gene polymorphisms.*

***Results.*** *We analyzed Trp64Arg polymorphism in b3-AR gene in 175 subjects (106 in the non-obese and 69 in the obese). The genotype frequencies of Trp/Trp, Trp/Arg and Arg/Arg were 82.1, 17.0 and 0.9% in the non-obese subjects, and 64.6, 33.3 and 2.1% in the obese subjects, respectively. The allele frequencies of the Arg64 were 9.4% in the non-obese and 18.8% in the obese subjects. The genotype frequency of Trp/Arg and the mutation allele frequency were significantly higher in the obese than in the non-obese group. UCP-1 gene polymorphisms, -3826A/G, -112A/G, and Met229Leu, were analyzed in 234 subjects (124 in the non-obese and the 110 in obese). The genotype frequencies of A/A, A/G and G/G at -3826 were 6.5, 38.7 and 54.8% in the non-obese subjects, and 12.7, 44.5 and 42.7% in the obese subjects, respectively. Although the genotype A/A was presented much in the obese subjects, the significant difference was not found between two groups. The A allele frequency was 25.8% in the non-obese and 35% in the obese subjects. The A allele frequency was significantly lower in the non-obese. The G allele frequency at -112 in UCP1 gene was 1.5% in the non-obese and 1.4% in the obese subjects. There was no substitution of Met229Leu in UCP1 genotype in both non-obese and obese subjects. No significant difference was detected between these two types of allele frequencies.*

***Conclusion.*** *The polymorphisms of –112A/C and Met229Leu in UCP-1 gene were not involved in the obesity in PNG, whereas the A allele in UCP-1 gene at –3826 and the substitution of Trp64Arg in b3AR seems to be associated with obesity in PNG. Our observation on –3826 A/G was not consistent with biological data showing that the substitution of A to G in UCP-1 gene at –3826 resulted in decreased expression level of UCP-1 and energy expenditure. It was considered that the –3826 A/G polymorphism had little importance in the pathogenesis of obesity in PNG. In conclusion, the substitution of Trp64Arg in b3AR was associated with susceptibility to obesity in PNG.*

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## PP 86

# Supportive Molecular Observations for Increasing Prevalence of Type 2 Diabetes in Indonesia and Papua New Guinea (PNG)

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***Background and Aims.*** *Type 2 diabetes has been rapidly increasing in developing countries. We hypothesized that the people in these countries have the genetic predispositions, beside westernization of their life-style. This was evaluated by analyzing PPAR,,2 Pro12Ala and ,3-adrenergic receptor Trp64Arg substitutions that are considered to be associated with obesity and type 2 diabetes.*

***Materials and Methods.*** *Blood samples were obtained from 238 subjects in Yogyakarta, Java and 86 subjects in Sembiran, Bali, Indonesia, and 252 subjects in Balopa islands, Papua New Guinea. Polymerase chain reaction (PCR) –restriction fragment length polymorphism (RFLP) method was used to analyze gene polymorphism.*

***Results.*** *(1) All samples revealed wild genotype in Pro12Ala substitution of PPARã2 except six cases of Yogyakarta showing heterozygote. This mutant allele frequency in Yogyakarta was 0.03. There was no significant difference in this allele frequency among these three islanders.(2) In Balopa islands where no substitution of PPARã2 genotype was detected in both non-obese (BMI<25kg/¡3) and obese (BMIg"25kg/¡3) subjects, allele frequency of Trp64Arg substitution of â3-adrenergic receptor was analyzed and its frequency was 0.13. It was similar to that in Mexican or African Americans. In obese subjects it was 0.12 , whereas 0.09 in non-obese ones. The former was higher (p<0.05).*

***Conclusion****. Since PPARã2 Pro12Ala polymorphism has been indicated to possess protective effect against development of type 2 diabetes under high fat diet, the present observations imply that the people in these developing countries appear to have susceptibility to type 2 diabetes. They may become more susceptible to it through obesity causing insulin resistance when additional genetic trigger such as mutation of â3-adrenergic receptor is present. Thus, in the near future the prevalence of type 2 diabetes in Indonesia and Papua New Guinea would come close to its current high level reported in the developed countries.*

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**PP 87**

# Human Peroxisome Proliferator-Activated Receptor Delta Gene Polymorphism is Associated with Visceral Obesity, Insulin Resistance and Lipid Metabolism in Chinese

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***Background and Aims.*** *Recent studies on peroxisome proliferator-activated receptor (PPAR) ä have shown its importance on the lipid metabolism. The purpose of this study is to investigate the association between the polymorphism (-87T>C) of the human PPARD gene and phenotypes related to lipid and glucose metabolism.*
***Materials and Methods.*** *A total of 663 unrelated Chinese in Shanghai were studied. Among them, 287 were newly diagnosed type 2 diabetes mellitus patients (sex ratio: 142 males, 145 females; age: 55.00±9.48 years old) and 376 were nondiabetic control subjects (sex ratio: 173 males, 203 females; age: 58.08±12.29 years old) over 40 years old. Clinical data collected were: height, weight; waist, hip and femoral circumstance; systolic blood pressure and diastolic blood pressure; plasma glucose level, serum insulin and C peptide levels of blood obtained both at 0 and 120 minute during a standard 75 grams glucose oral glucose tolerance test (OGTT); serum lipid level including total cholesterol, triglyceride, high-density and low-density lipoprotein cholesterol. Percentage and distribution of body fat were measured by bioelectrical impedance analysis and magnetic resonance image (MRI). Genotype of PPARD -87 T>C polymorphism were detected through PCR-RFLP.*
***Results.*** *The C allele carriers had more abdominal visceral adipose tissue (P=0.0224). Among the T2DMs, the C allele carriers had higher fasting and 2-hour plasma glucose levels (fasting plasma glucose: P<0.0001; 2-hour plasma glucose: P=0.0007), elevated HOMA-IR (P=0.0044) and lower insulin sensitivity index (ISI)-Gutt (P=0.0033). While among the NGTs, we found the similar association between the C allele carriers and fasting plasma glucose level (P=0.0148), HOMA-IR (P=0.0238) and ISI-Gutt (P=0.0223) respectively. Moreover, the C/C homozygotes had higher serum levels of total cholesterol (P=0.0033), triglyceride (P=0.0027) and low-density lipoprotein cholesterol (P=0.0003).*
***Conclusion.*** *Human PPARD gene is associated with visceral obesity and glucose and lipid metabolism.*

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## PP 88

# Effects of PGC-1· GENE G482S Variant on Body Fat Content, Glucose and Lipid Metabolism in Chinese

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***Background and Aims.*** *To make ensure if PPAR-ã coactivator ·(PGC-1á) Gly482Ser variant has any effect on body fat content and its distribution ,energy balance,lipid and glucose profile,insulin secretion and function in Chinese.*

***Materials and Methods.*** *302 Chinese subjects participated in the study, include 107 normal weight subjects and 195 overweight/obesity subjects(include 103 DM subjects).Fat Mass(FM),Fat Free Mass(FFM) and Fat content(%) were measured by Bioelectrical Impaired Analysis(BIA);Regional body fat were measured by Magnetic Resonance Imaging(MRI) and were expressed as subcutaneous fat area(SA),visceral fat area(VA) and femoral fat area(FA);Resting energy expenditure was measured by indirect calorimeters and was expressed as resting energy per kilogram(REE/kg).BMI(body mass index),waist circumference, fasting serum lipids were measured. Plasma free fatty acid(FFA) , glucose,insulin and C-peptide in the fasting state or during an OGTT were estimates too. The discrepancy of these clinical characteristics among different genotypes of the gene variant were also investigated.*

***Results.*** *1)The allele frequency of G482S was different from that in other studied population. 2)A allele carriers had higher level of FFA in normal weight subjects than A allele non-carriers as to G482S variant (P=0.032). 2h FFA inhibition rate was lower in A allele carriers (P=0.015). FPG level had the same tendency. 3) G482S variant was associated with fasting serum TG in overweight/obesity subjects(P=0.029), A allele carriers had higher levels than A allele non-carriers. Moreover, fating serum C peptide levels also had same discrepancy in the two group(P=0.029). 4) The overweight/obesity subjects accompanied with DM with A allele carriers had higher level of TG than A allele non-carriers(P=0.002). A allele carriers have higher level of FFA in this group too(P=0.019). 5) Stepwise regression analysis was revealed that the indepent variants to G482S variant were FFA,TG and FCP in normal weight subjects and overweight/obesity (whether DM or not).*

***Conclusion.*** *1) The allele frequence of G482S variant in PGC-1á is different from that in other races. 2) The G482S variant in PGC-1á is associated with obesity phenotype, lipid metabolism and insulin secretion. A allele carriers have significant higher level of FFA,TG and C peptide than A allele non-carriers.*

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**PP 89**

# The Molecular Pathology of Visceral Obesity and Glucose Intolerance in Follicle Stimulating Hormone Receptor Knockout (FORKO) Female Mice

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***Background and Aims.*** *Obesity is associated with increased susceptibility to type 2 diabetes, cardiovascular risk, cancers and other disorders. In FORKO mice, the lack of gonadal follicle stimulating hormone receptor (FSHR) signaling causes ovarian underdevelopment inducing chronic estrogen deficiency. By 3 months of age null mutants show signs of obesity with increased deposition of abdominal fat as in postmenopausal women. Null females also exhibit age dependent glucose intolerance. To investigate the mechanism of development of visceral obesity and glucose intolerance caused by estrogen deficiency, we focused our study on the two major regulators of fat storage, PPARã and adiponectin. Peroxisome proliferator- activated receptor (PPAR) gamma is considered important regulator of fat depot by its effect on differentiation of adipocytes. Adiponectin, a novel adipocytokine, is reportedly down regulated in obesity/diabetes.*

***Materials and Methods.*** *Our study focused on the follicle stimulating hormone receptor knockout ( FORKO ) female mice. We weighed the bodyweights and gonadal fat pads weights of homozygous female mice, hetorozygous female mice and wild type female mice at their different age and caculated the ratio of gonadal fat pad weight and bodyweight respectively. Glucose tolerance test was performed among the three genotype female mice at the age of three months old and eight months old respectively. RT-PCR and Western-blot were performed to measure the express of adiponectin and PPARã in white adipose tissue and serum in FORKO female mice. Histology was used to observe the shape and size of certain cells.*

***Results.*** *By 3 months of age null mutants show signs of obesity with increased deposition of abdominal fat as in postmenopausal women. Null females also exhibit age dependent glucose intolerance. The expression of mRNA for both adiponectin and PPARã were significantly higher in null females than those in wild type females. The expressions of adiponectin both in white adipose tissue and in serum were significantly higher in null female than those in wild type ( WT ) female.*

***Conclusion.*** *The results suggest that supraphysiological activity of PPARã and adiponectin dysfunction caused by estrogen deficiency could contribute to visceral obesity and glucose intolerance in FORKO female mouse. These changes in hormonal background during aging or deficiency states could alter regulatory genes that impact on adipocyte proliferation, differentiation and metablism. The FORKO female provides an interesting experimental paradigm to determine their interrelationships.*

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**PP 90**

# Association of Non-Alcoholic Fatty Liver Disease with Insulin Resistance in Non-Diabetic, Normal Weight Subjects

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***Background and Aims.*** *It is well known that non-alcoholic fatty liver disease (NAFLD) is associated with type 2 diabetes, obesity, and dyslipidemia. NAFLD is frequently found in non-diabetic, normal weight adults, but the meaning of it is not fully investigated. The aim of the present study was to elucidate the association of NAFLD with insulin resistance in non-diabetic, normal weight subjects.*
***Materials and Methods.*** *Sixty, aged 20-70, subjects participating in medical check-up were recruited. Hepatitis B and C serologies were negative, and not having the history of alcohol abuse. Liver ultrasound was carried out by experienced radiologist.*
***Results.*** *Their age were 43 ±13.5 years, and BMI were 21.1 ±1.4 kg/m2. The clinical characteristics and biochemical profiles of control (n=42) and NAFLD group (n=18) were compared. The NAFLD group had significantly higher serum triglycerides and uric acid levels and lower HDL cholesterol concentrations compared with the control group. HOMA-IR was also higher in NAFLD group ($p<0.01$).*
***Conclusion.*** *NAFLD is associated with insulin resistance in non-diabetic, normal weight adults.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

**PP 91**

# Insulin Sensitivity and Abdominal Fat in Non-Obese, Non-Diabetic Thai Men with Non-Alcoholic Fatty Liver Disease

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***Background and Aims.*** *The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus changed the lower limit of IFG from 110 to 100 mg/dl in order to equalize the prevalence of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) as well as the risk for developing diabetes mellitus (DM). However, there are few studies that validated this change in Asian populations. The aim of this study was to describe the agreement in glucose tolerance status between the fasting and 2-h plasma glucose criteria.*
***Materials and Methods.*** *Anthropometric measurement and 75-g oral glucose tolerance test were performed in 954 Thai adults not known to be diabetic. Of these, 319 (33.8%) were males, and 626 (66.2%) were females. Their mean (±SD) age and body mass indices were 50 ± 11 years and 24.5 ± 3.7 kg/m2*
***Results.*** *Based on the fasting plasma glucose levels, the prevalence of normal fasting glucose (NFG), IFG, and DM were 87.4%, 10.8%, and 1.8%, respectively. According to the 2-h plasma glucose levels, the prevalence of normal glucose tolerance (NGT), IGT, and DM were 57.8%, 34.6%, and 7.6%, respectively. One-third of NFG subjects had IGT, whereas only 3.8% of NGT had IFG. Of those with IFG, 20.6% had NGT, whereas 84.1% of IGT subjects had NFG*
***Conclusion.*** *In conclusion, our results clearly demonstrated that even when the lower limit of IFG was changed from 110 to 100 mg/dl, there is poor agreement between the fasting and 2-h plasma glucose criteria in classifying glucose tolerance status*

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## PP 92

# The Research on the Effect of Oral Hypoglycemic Agents Upon Fat Distribution and Fatty Liver in Patients with Type 2 Diabetes Mellitus

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***Background and Aims.*** *Along with the advanced research on type 2 diabetes mellitus, people are cognizant of that in the drug treatment in type 2 diabetes mellitus the keystone is not only glucose control but also improving insulin resistance, protecting â-cell function, improving fat distribution and weight loss. Therefore, it is of great importance to explore the effect of oral hypoglycemic agent upon the fat distribution and fatty liver in type 2 diabetes mellitus. The objective of our research is to observe the change of the adipose content in abdomen, thigh and liver after the treatment of oral hypoglycemic agents and to give some advice to drug selection.*

***Materials and Methods.*** *We selected a total of 73 subjects with type 2 diabetes mellitus from out-patient department of Shanghai Sixth People's Hospital, the diagnosis of type 2 diabetes mellitus was based on 1999 WHO standard. Each subject aged between 30 to 70 years and his/her HbA1c was higher than 6.5%. Each one had no hypoglycemic or hypolipidemic treatment and had no severe disease in alimentary canal, heart, liver or kidneys. The subjects were divided into 4 groups randomly and there was no difference between each group in age, blood pressure, HbA1c, FPG, 2hPG, BMI and WHR. Each group took a 24 weeks' hypoglycemic treatment, rosiglitazone(group A), repaglinide(group B), metformin(group C) and glipizide(group D). We evaluated adipose content in abdomen & thigh by MRI and in liver by ultrasound histogram at –2w and 24w. We examined HbA1c, FPG, 2hPG at -2w, 12w and 24w.*

***Results.*** *1) Compared with the first week, HbA1c, FPG and 2hPG were decreased in all groups after 24 weeks' treatment. 2) After 24 weeks' treatment in group A, the decline of total abdominal adipose tissue, visceral adipose tissue, adipose tissue beneath the fascia of thigh and intermuscular adipose tissue had significant difference ($P<0.01$). In group C, visceral adipose tissue and adipose tissue beneath the fascia of thigh had significantly declined($P<0.05$). 3) After 24 weeks' treatment in group A, the decline of adipose content in liver had significant difference ($P<0.01$)*

***Conclusion.*** *1) It was viable of using ultrasound histogram technology to half measure hepatic fat content. 2) In patients with type 2 diabetes mellitus rosiglitazone and metformin showed great effect on the decline of adipose content in abdomen(especially in visceral adipose tissue) and thigh(adipose tissue beneath the fascia of thigh and/or intermuscular adipose tissue). 3) Rosiglitazone reduced the adipose deposition in liver.*

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**PP 93**

# Liver Enzymes as a Predictor for Incident Diabetes Mellitus in a General Japanese Population: The Hisayama Study

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***Background and Aims.*** *Several prospective studies have found that high levels of hepatic enzymes are associated with the later development of diabetes. However, very few studies examined this issue in Asian populations. We investigated the associations between liver enzymes and future diabetes in a general Japanese population, taking into account comprehensive risk factors for diabetes.*

***Materials and Methods.*** *In 1988, a screening survey for the present study was performed in Hisayama Town in southern part of Japan. A total of 1,804 community-dwelling subjects, aged 40 to 79 years and without diabetes (according to the ADA fasting criteria), were stratified into four groups on the basis of quartiles of liver enzymes, including gannma-glutamyltransferase (GGT), alanine aminotranferease (ALT), and aspartate aminotransferase (AST), by sex and followed up prospectively for mean 9.0 years.*

***Results.*** *During the follow-up period, 135 subjects (71 men and 64 women) developed diabetes. In both sexes, the age-adjusted cumulative incidence of diabetes increased significantly as the quartiles of each liver enzyme increased. In multivariate analyses, the risk of developing diabetes was significantly higher in the highest GGT quartile than in the lowest quartile after adjusting for age, family history of diabetes mellitus, high-sensitive C-reactive protein (HS-CRP), fasting insulin, body mass index, waist-to-hip ratio, total cholesterol, HDL-cholesterol, triglycerides, hypertension, current drinking, current smoking, physical activity, and other liver enzymes (odds ratio [OR], 2.54; 95% confidence interval [CI], 1.03-6.26) for men; OR, 5.73; 95% CI, 1.62-20.19 for women). Similar results were observed for quartiles of ALT (OR, 2.32; 95% CI, 0.91-5.92 for men; OR, 4.40; 95% CI, 1.38-14.06 for women), but not for quartiles of AST (OR, 1.87; 95% CI, 0.77-4.53 for men; OR, 1.26; 95% CI, 0.55-2.92 for women). In the receiver operating characteristic (ROC) analyses, the area under the ROC curve of GGT and ALT was significantly larger than that of AST, waist-to-hip ratio, fasting insulin, and HS-CRP. However, the significant difference of ROC curve area between GGT and ALT was not observed.*

***Conclusion.*** *Our findings suggest that serum GGT and ALT concentrations are strong predictors of diabetes mellitus independent of known risk factors in the general Japanese population.*

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## PP 94

# Reciprocal Association between Adiponectin, HS-CRP, and Fasting Insulin Levels in Subjects with Dysglcaemia

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***Background and Aims.*** *Dysglycaemia - impaired fasting glucose, and impaired glucose tolerance - is associated with high risk of coronary heart disease. Previous prospective studies indicate a relation between low levels of adiponectin and high hs-CRP levels in subjects with diabetes mellitus as well as those with coronary heart disease. The purpose of this study is evaluating the correlation between these two markers, and fasting insulin subjects with dysglycaemia.*

***Materials and Methods.*** *Subjects were from our EIDEG study for the screening of diabetes mellitus. One hundred and twenty six subjects were selected for complete examination, including physical and laboratory examinations. After 12 – hour fasting, OGTT was performed to all subjects. Lipid profiles, free fatty acid, fasting insulin, hs-CRP, and adiponectin were also examined. ). They were classified into two groups, normal glucose tolerance, and impaired fasting glucose / impaired glucose tolerance as the dysglycaemia group. Statistical analysis was performed by either one-way ANOVA or Chi-square analysis, and conducted with SPSS for Windows 13.0 software (SPSS, Inc.).*

***Results.*** *Twenty five subjects belong to normal glucose tolerance group and the rest 121 subjects to the dysglycaemia group. There was a significant difference between age, BMI, and systolic blood pressure, being higher in the dysclycaemia group. Fasting insulin, free fatty acid, and hs-CRP were significantly higher in the dysglycaemia group 13,6 + 12,6 uL/ml vs. 5,6+5,8 uL/ml (p< 0,0001), 0,9+0,5mmol/L vs. 0,5+0,2mmol/L (p< 0,01), and 6,1+4,3mg/dl vs. 2,1+1,3 mg/dl subsequently. On the contrary the adiponectin levels were significantly lower in the dysglycaemia group compared to normal glucose tolerance group, 10,1+5,6ng/ml vs. 17,6+6,3.ng/ml.*

***Conclusion.*** *There is a reciprocal association between adiponectin levels and hs-CRP levels and fasting insulin levels in the dysglycaemia subjects. These may support that the dysglycaemia subjects have inflammatory process which more prone to coronary heart disease.*

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**PP 95**

# Relation between Adiponectin, and HS-CRP, in Obese Subjects with Insulin Resistance

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***Background and Aims.*** *Low levels of adiponectin, as well as high level of hs-CRP both are predictor factors for diabetes mellitus and coronary heart disease. Most of the obese subjects have insulin resistance. The aim of this study is to find out the relation between adiponectin, hs-CRP, in obese subjects with insulin resistance measured by HOMA-IR.*

***Materials and Methods.*** *Subjects were collected from the East Indonesia Diabetes Epidemiology Group (EIDEG). Obese subjects were defined as those with BMI > 25 kg/ m2. After 12-h fasting, blood was taken for lipid profiles including free fatty acids, fasting insulin, fasting plasma glucose, adiponectin and hs-CRP. Insulin was determined by RIA methods, and insulin resistance was measured using HOMA-IR formula. Statistical analysis was performed by either one-way ANOVA or Chi-square analysis, and conducted with SPSS for Windows 13.0 software (SPSS, Inc.).*

***Results.*** *We studied 87 obese subjects with mean BMI of 29.5+3.2 kg/ m2. There was a significant negatively correlation between adiponectin levels (r=0.478, p=0.000), HDL-cholesterol level (r=0.401, p=0.000) with obesity. A significant positively correlation were found between fasting plasma glucose (r=0.528, p=0.000), triglyceride levels (r=0.319, p=0.003), free fatty acid (0.377, p=0.001), fasting insulin (r=0.382, p=0.000), HOMA value (r=0.408, p=0.000) and hs-CRP level (r=0.352, p=0.001) with obesity.*

***Conclusion.*** *There was a significant correlation between low adiponectin, high hs-CRP and insulin resistance in obese subjects.*

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## PP 96

# Serum Adiponectin Levels are Independently Predicted by Visceral Fat in Non-Diabetic Obesity and by Low Density Muscle in Diabetic Obesity

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***Background and Aims.*** *Clinical aspects of diabetes and obesity are somewhat different, even at similar levels of insulin resistance. The purpose of this study was to determine differences in body fat distribution and serum adiponectin concentrations in diabetic and non-diabetic obese participants. We were also interested in identifying the characteristics of insulin resistance in these two groups, particularly from the standpoint of adiponectin.*

***Materials and Methods.*** *Adiponectin concentrations of 112 type 2 diabetic obese participants and 124 non-diabetic obese participants were determined. Abdominal adipose tissue areas and midthigh skeletal muscle areas were measured by computed tomography. An HOMA-IR score was calculated to assess insulin sensitivity. The relationships between serum adiponectin, body fat distribution and clinical characteristics were also analyzed.*

***Results.*** *Both abdominal subcutaneous and visceral fat areas were higher in the non-diabetic obese group, while midthigh low-density muscle area was higher in the diabetic obese group. The HOMA-IR score was similar between groups, whereas serum adiponectin was lower in the diabetic obese group. In the non-diabetic obese group, the following were correlated with serum adiponectin: age ($\hat{a}$ = -0.529, p = 0.006), sex ($\hat{a}$ = -0.254, p = 0.030), total cholesterol ($\hat{a}$ = -0.303, p = 0.041), triglycerides ($\hat{a}$ = -0.345, p = 0.032), HOMA-IR ($\hat{a}$ = -0.177, p = 0.038), visceral fat area ($\hat{a}$ = -0.381, p = 0.012), VSR ($\hat{a}$ = -0.290, p = 0.043), and low-density muscle area ($\hat{a}$ = -0.218, p = 0.026). Among the diabetic obese group, adiponectin was significantly inversely related to the following: age ($\hat{a}$ = -0.512, p = 0.003), sex ($\hat{a}$ = -0.221, p = 0.032), weight ($\hat{a}$ = -0.267, p = 0.027), body mass index (BMI) ($\hat{a}$ = -0.298, p = 0.038), HbA1C ($\hat{a}$ = -0.478, p = 0.018), HOMA-IR ($\hat{a}$ = -0.213, p = 0.021), visceral fat area ($\hat{a}$ = -0.228, p = 0.044) and low-density muscle area ($\hat{a}$ = -0.413, p = 0.013).*

***Conclusion.*** *Therefore, factors involved in pathophysiology, including different serum adiponectin level and body fat distributions are believed to be responsible for differences in clinical characteristics, even at similar levels of insulin resistance in both diseases.*

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## PP 97

# Relationship of Serum Ghrelin and Adipokines Levels with Obesity, Coronary Atherosclerosis in Type 2 Diabetic Patients

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***Background and Aims.*** *Ghrelin, a peptide isolated from the stomach, could be involved in energy homeostasis. Ghrelin was recently detected in cardiovasculat tissues, but its role was not clearly studied. Adipose tissue secretes many kinds of adipokines, which may affect insulin action and vascular function.*

***Materials and Methods.*** *We measured fasting serum total ghrelin, leptin, adiponectin and resistin levels in type 2 diabetic patients to investigate the relationship of ghrelin and adipokines with obesity, coronary atherosclerosis. The diabetic patients were subdivided into 2 groups, those without (n=47) and with coronary artery disease (CAD, n=36). Patients who had organic stenosis of at least 1 major coronary artery, or who had developed myocardial infarction, or had undergone PCI or CABG were classified as having CAD. Insulin resistance was determined using homeostasis model assessment (HOMA-R).*

***Results.*** *Ghrelin was negatively correlated with body mass index (BMI, r=-0.253, p<0.05). There were significant correlations between leptin and age (r=0.361, p<0.05), BMI (r=0.333, p<0.005), waist (r=0.372, p<0.005) and hip (r=0.514, p<0.001) circumference, insulin (r=0.653, p<0.001), adiponectin (r=0.254, p<0.05), or HOMA-R (r=0.418, p<0.001). Adiponectin was positively correlated with age (r=0.359, p<0.001), and negatively with cholesterol (r=-0.286, p<0.05). Resistin did not show correlation with BMI, insulin or HOMA-R. Serum leptin, resistin, and insulin levels were significantly higher in patients with CAD when compared with those without CAD (leptin, 11.4+2.2 vs. 6.4+0.8 ng/mL, p<0.05; resistin, 5.7+0.6 vs. 2.5+0.4 ng/mL, p<0.001; insulin, 15.2+1.7 vs. 10.6+1.2 uIU/mL, p<0.005). No difference was found in serum ghrelin or adiponectin levels between the two groups. A regression analysis showed that resistin was significantly associated with coronary atherosclerosis.*

***Conclusion.*** *These results suggest that ghrelin and leptin are related to obesity, and that higher levels of resistin is associated with coronary atherosclerosis in type 2 diabetic patients.*

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**PP 98**

# Effect of Pouring Leptin Into SD Rates on Insulin Secretion

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***Backgrounds and Aims.*** *In order to observe the effect of pouring leptin into SD rates on insulin secretion.*
***Material and Methods****. 144 male Sprague-Dawley rats, 6 weeks of age (average weighing-200g), were used for the experiment. Among these, all rats was divided into 2 groups (a group that underwent vagotomy, a group that underwent both vagotomy and i.v. glucose load) were used for pre-experiment, which is in order to find out the obvious effectual concentration of leptin to the insulin secretion. All rats, which underwent catheterrization of the femoral vein, were divided into 6 groups (an intact , a group that underwent vagotomy, a group that underwent both vagotomy and chemical sympathectomy, a group that was subjected to an i.v. glucose load, a group that underwent both vagotomy and i.v. glucose load, a group that underwent vagotomy and chemical sympathectomy and i.v. glucose load). Rats from each group received a bolus injection of leptin (10nmol/kg ) or a control PBS or an i.v. glucose load .Afterward , artrial blood was withdrawn at 0, 3, 6 and 30min for the determination of plasma insulin levels.*
***Result****s. There is no significant effect by leptin on plasma insulin in intact rats and both vagotomy and chemical sympathectomy. Leptin significantly suppressed an increase in plasma insulin concentration in vagotomized rats, especially i.v. glucose load.*
***Conclusion.*** *Leptin suppressed insulin secretion through activation of the sympathectic nervous system. There is a close relation between leptin and insulin.*

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**PP 99**

# The Effect of Insulin on the Synthetic and Secretion of Leptin in Adipose Cells of Rat

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***Background and Aims.*** *Earlier study suggested that insulin play a vital role in increasing expression and secretion of leptin. The location of leptin in adipose cells and wheather insulin can directly increase the release from these cells by double-labling immunofluorescence in vitro were studied in this paper.*
***Materials and Methods.*** *Adipose cells were extracted and purified from SD rat epididymal fat pads and incubated in vitro in presence or absence of insulin for 0,15,60 min respectively. These cells were incubated with primary polyclonal anti-calnexin and anti-leptin antibodies and then with fluorescence-labled secondary antibodies in time order. Wrote down the change of fluorescence staining of these cells and analysis quantity by scanning imaging system*
***Results.*** *After 15 min, despite insulin treatment or not, the cell fluorescence staining is dimmer than that at beginning, but no difference between each other group. However, after 60 min of insulin treatment, the amount of cell-associated leptin was higher than that of non-insulin treatment and that at 0 min.*
***Conclusion.*** *There are no obvious effect of insulin on acute discreasing of leptin amount in adipose cells in vitro. But we can draw that insulin can increase leptin production if we prolong the observed time. That is, insulin can not directly increase leptin release from adipose cells, but can directly increase leptin secreted by stimulating production.*

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## PP 100

# Expression of the Long and Short Leptin Receptor Isoforms in Mononuclear Cells

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***Backgrounds and Aims.*** *Leptin receptors which include the long isoform, the short isoform and the soluble leptin receptor are present in hypothalamus and many peripheral tissues in human. In this experiment, we would mainly demonstrate the expression levels of the long isoform leptin receptor (OB-$R_L$) and the shortest membrance bound variant (OB-$R_S$) in mononuclear cells from the obese individuals and the lean individuals.*
***Materials and Methods.*** *Peripheral blood was obtained from 50 healthy individuals (30 obese individuals, BMI 18.9~25kg/m$^2$; 20 lean individuals, BMI 25~47.2kg/m$^2$). Mononuclear cells was isolated from peripheral blood with lymphocyte isolated reagent. We report the quantification by reverse transcriptase-polymerase chain reaction(RT-PCR). Leptin levels were measured in the serume from all individuals using a human leptin radioimmunoassay kit.*
***Results.*** *Ob-$R_S$ was expressed in all individuals. OB-$R_L$ was expressed in 38 individuals, OB-$R_L$ was not expressed in 12 individuals who were obese with a BMIÿ39kg/m$^2$. The predominance of OB-$R_S$ over Ob-$R_L$ was apparent in all samples and ranged from 4- to 27-fold. There was no significant difference in the expression of either isoform between men and women. The relative expression of both OB-$R_S$ and OB-$R_L$ isoforms was significantly lower and the serum leptin levels was significantly higher in the obese subjets (BMIÿ25kg/m$^2$), compared with the lean subjects (BMI"ÿ25kg/m$^2$).*
***Conclusions.*** *Both OB-$R_S$ and OB-$R_L$ were coexpressed in peripheral blood mononuclear cells from the lean and the medium obese subjects with a consistent predominance of OB-$R_S$. This several-fold higher expression of the OB-$R_S$ over the OB-$R_L$ leptin receptor splice variant was observed in both men and women, whether the lean or the obese individuals. Compared with the lean individuals, the expression of OB-$R_S$ and OB-$R_L$ leptin isoforms appears to be reduced in human mononuclear cells from the obese individuals, with OB-$R_S$ remaining the predominant leptin receptor isoform. There was an overall significant inverse correlation of both leptin receptor transcripts with the BMI and the serume leptin levels.*

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## PP 101

# Comparison the Accountability of Diabetes Care between Two Different Settings in a Regional Hospital

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***Background and Aims.*** *The prevalence of Diabetes is increasing world wide as well as in Taiwan. It account for more than one million peoples in this region. The quality of diabetes care is related to the long term morbidity and mortality. The Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) showed that with a better control in the A1c level there were a significant decrease in development of retinopathy, nephropathy, neuropathy, and macrovascular disease in type 1and type 2 diabetic patients. There are evidence showed that good professional accountability is related to better glycemic control and lower mortality. The aim of this study is to compare the accountability of diabetes care between two different settings within a regional hospital.*

***Materials and Methods.*** *Diabetes patients who has regular visit at our hospital for more than three times during the year of 2003 were used as the sampling pool. Among them, about 3000 patients were treated at the diabetic specialist out-patient clinics; about 900 patients were treated at the general internal medicine out-patient clinics. We use proportional random sampling methods to collect total 200 patients, 150 patients were in the diabetic specialist group and 50 patients were in the general internal medicine group. Retrospective charts review and data collection were done by three trained nurse specialists.Patient's characteristics including sex, age, BMI, duration of DM, education of diabetes…were recorded for compares.Lab. Data such as ac, pc sugar, A1c, cholesterol,, TG, HDL, LDL,… was compared between groups.The professional accountability defined as at least one time exam during the year and the frequency of tests were used for comparison.*

***Results.*** *Regarding to patients sex, age, weight, BMI, smoking, there were no significant differences between two groups, except that the duration of diabetes is longer in the diabetes specialist group (7.79 vs. 4.82 ys. P<0.001). Patients in the diabetes specialist group have significant higher mean frequency of annual exam in BP (5.13 vs.3.92 p=0.024), Ac sugar (6.87 vs. 3.14 p<0.001), Pc sugar (1.01 vs. 0.52 p=0.011), A1c (3.09 vs. 1.00 p<0.001), LDL (0.61 vs.0.14 p<0.001), HDL (0.75 vs. 0.53 p<0.001), SMBG (13.1 vs. 3.28 p=0.001).There were no differences in the total cholesterol and TG exam (1.43 vs. 1.18 p=0.196; 1.43vs. 1.16 p=0.156 respectively).The professional accountability was significantly higher in the diabetes specialist group in BP (92.7% vs. 84% p=0.024), Ac sugar (100% vs. 96% p<0.001), Pc sugar (44.3% vs. 38% p=0.011), A1c (99.3%vs. 68% p<0.001), LDL (54.7% vs. 12% p<0.001), HDL (60% vs. 22% p<0.001), urine protein (67% vs. 26% p=0.032), eye exam (79% vs. 16% p<0.001), foot exam (59% vs. 0% p<0.001), except for total cholesterol and TG (76%vs. 64% p=0.196; 76% vs. 62% p=0156 respectively).The proportion of A1c<7% (15% vs.30.3%), HDL >40mg/dl (14%vs. 44.7%), LDL<100mg/dl (2% vs. 11.3%), TG <150mg/dl (22% vs. 44.0%), and total Cholesterol <200 mg/dl (14%vs. 34%) is also significantly higher in the diabetes specialist group, but there is no difference in terms of SBP and DBP control (35% vs. 34.7% and 47% vs.53%).*

***Conclusion.*** *The chronic complications of diabetes can be avoided by striving for normal levels of serum glucose, blood pressure, and lipids. They can be effectively treated, but only if they are detected; the earlier they are detected, then the greater the chance of successful treatment. Better accountability can prevent or ameliorate the progression of diabetic complications. Strategy concerning accountability improvement needed to be implanted to non diabetic specialist care setting.*

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## PP 102

# What the Public Knows About what the Standard of Care of Diabetes Should be

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***Background and Aims.*** *With a high prevalence of diabetes in Singapore it is the norm that everyone either is related or knows someone with diabetes even if he/she is unaffected by the disease. It is paramount in our fight against this disease that public awareness is raised in this disease and especially in the ways in which complications can be prevented.In the Ministry of Health Clinical Practice Guidelines for diabetes, quality indicators for monitoring the diabetes management was recommended as : a) Glycated haemoglobin (HbA1c) 2 – 4 times a year) Body weight at least quarterly) Urine albustix, urinary protein or microalbumin at least yearly) Serum lipids at least annually) Serum creatinine at least annually) Eye examination at least annually) Foot examination at least annually) Patient education at diagnosis and reinforced regularly. The objective of the study was to determine the public perception of how frequently people with diabetes need to carry out assessments of their body weight, blood pressure, glycated haemoglubin (HbA1c), cholesterol, urine protein test, eye and foot examination require. This was used as a marker of patient education about diabetes in the general population as well as people with type 2 diabetes.*

***Materials and Methods.*** *The survey was conducted during the health screening event in conjunction with World Diabetes Day in Tan Tock Seng Hospital for people with and without diabetes. The questionnaires which took around < 5min to complete was either self administered or conducted through interview by the healthcare volunteers using different languages such as Malay, Mandarin, Tamil and other dialects. No poster or pamphlets information of Health Clinical Practice Guidelines for diabetes were displayed during the event.*

***Results.*** *472 people without diabetes and 56 with diabetes responded to the surveys. The number of questions answered correctly between people who do not suffer from diabetes and patients who do differed significantly. People with diabetes mellitus were more likely to answer more questions correctly. Although it was disturbing to note that in both groups the majority of people failed to get at least half the questions correct.*

***Conclusion.*** *To face this disease head-on, much more needs to be done in terms of public education, but more importantly people with known diabetes need to be better educated regarding their disease and its complications.*

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## PP 103

# Thailand Diabcare-Asia 2003: Patients' Insigh Into Diabetes and the Glycemic Outcome

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***Background and Aim***. *Diabetes can affect well-being and quality of life (QoL). This study aims to determine the relationship between the status of glycaemic control and the sense of well-being and QoL in diabetic patients managed by specialists/endocrinologists in Thailand.*

***Materials and Methods***. *Diabcare-Asia 2003 study is a cross-sectional survey study done in 9 countries in Asia with support from Novo Nordisk, BioRad and IDF-WPR. Thailand's data were analyzed separately. The patients who were managed for at least 12 months in 21 participating diabetes clinics were randomly recruited. Valid data were collected from 2953 patients retrospective-prospectively through review of medical records and personal interview. WHO-5 well-being assessment and quality of life (QoL) adapted from Diabetes Attitudes, Wishes and Needs questionnaire (9-items) were translated to Thai language, verified and used for assessment. $HbA_{1c}$ was standardized and measured by one central laboratory. All data were scanned electronically and validated using scanning software and the SAS system. The relation between well-being or QoL with glycaemic indices was tested using Kruskal-Wallis test.*

***Results***. *The majority (95.1%) of the patients were type 2 diabetes with preponderance of female (70.3%). The mean age (± SD) was 59.8 ± 11.6 years and the mean duration of diabetes was 10.2 ± 7.1 years. Mean ±SD of $HbA_{1c}$ and fasting plasma glucose (FPG) were 7.9±1.8% and 8.5±3.1 mmol/L, respectively. Only 34.1% of the patients had $HbA_{1c}$ <7% and 36.4% had FPG d" 7.2 mmol/L. For psychological well-being, the larger proportion of patients felt cheerful and relaxed (61%), active (62%), fresh and rested (61%), life filled with interest (64%), despite having diabetes. The outcome on QoL was congruent with the positive outlook; less than half of patients (range: 15.2–42.7%) felt that QoL had suffered as a consequence of diabetes. There was no trend to suggest that control of glycaemia was better in patients reporting positive well-being or good QoL. Median $HbA_{1c}$ and FPG levels were comparable in those who reporting positive well-being or good QoL and those did not. Insulin initiation was of great concern in many patients (69.2%). But, the patients who worried about insulin initiation had comparable glycaemia to those did not, median $HbA_{1c}$ 7.3 vs 7.1% and FPG 7.8 vs 7.7 mmol/L. However, the patients who felt that diabetes was not well-regulated (17.3%) had significantly higher median $HbA_{1c}$ (8.3 vs 7.4%) and FPG (9.2 vs 7.7 mmol/L).*

***Conclusion***. *Control of glycaemia in majority of Thai diabetic patients was not optimal though they appeared to hold positive attitudes or claimed no effect on QoL. There did not appear to be a relation between control and overall well-being or QoL. It is possible that patients concentrate only in their feelings but ignore the target of treatment.*

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**PP 104**

# Diabetic Management 1997 to 2003 at Maharat Nakhon Ratchasima Hospital

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***Background and Aims.*** *Diabcare-Asia, the largest, multicenter observational study in Asia, was established (in 1996 as DCDCP) to monitor the status of diabetic control among Asian diabetic patients. Maharat Nakhon Ratchasima Hospital was randomly selected to represent Thailand in the collaboration.*

***Materials and Methods.*** *This was a cross-sectional study carried out in the Diabetic Clinic of Maharat Nakhon Ratchasima Hospital, in Nakhon Ratchasima province, Northeast Thailand. We recruited 200, 100 and 204 diabetic patients cared for and treated at the Out-Patient Department for at least 12 months in 1997, 1998 and 2003, respectively.*

***Results.*** *Most (93 per cent) of the patients had type 2 diabetes. Patients with a BMI [3]25 kg/m2 increased from 38, 45 and 47 percent in 1997, 1998 and 2003, respectively. Annual check-ups for diabetic complications increased to nearly 100 per cent by 2003; however, only 72 per cent were examined for diabetic retinopathy, but that number is up from the 33 per cent in 1997. In our hospital, diabetic retinopathy was detected in 8, 16 and 25 percent of patients, respectively. Diabetic nephropathy (urine albumin [3]1+ by urine strip) decreased from ~50 per cent in 1997/98 to 19 per cent in 2003. Patients were able to achieve the target blood sugar better than in the past. The number of patients with HbA1C < 7 per cent and FPG d"130 mg/dL was 8, 21, 38 and 30, 39 and 40 percent in 1997, 1998 and 2003, respectively. The proportion of patients who achieved the American Diabetic Association blood pressure, total cholesterol and LDL-C targets in 2004 was < 50 per cent.*

***Conclusion.*** *Diabetic control at Maharat Nakhon Ratchasima Hospital improved between 1997 and 2003. A similar hospital-based diabetic care system should be implemented at other Thai hospitals for the early identification and prevention of diabetic complications.*

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## PP 105

# Explore the Psychological Barriers that Inhibit Type-2 Diabetics Patients with Poor Glycaemic Control to Initiate Insulin Injection

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***Background and Aims.*** *Oral hypoglycaemic agents are the main pharmaceutical agents to type-2 diabetic patients. However, with times, despite maximum dose of oral hypoglycaemic agents (OHA) will fail to control blood sugar. It is a phenomenon commonly known as secondary OHA failure. Upon this stage, either insulin add-on therapy or insulin replacement therapy is indicated. However most patients will encounter a long struggle and dilemma when they are suggested to initiate insulin injection. Study conducted by Guthie and Guthrie (1997) explained that the administration of insulin had often been presented with fear, anxiety and self-pity. Objectives: To explore the psychological barriers of type-2 diabetic patients with secondary OHA failure to insulin injection.*

***Materials and Methods.*** *It is a retrospective survey of type-2 diabetic patients with secondary OHA failure, referred from specialty out-patient department (SOPD) in one local hospital, to diabetes nurse. This study period was between 1st September 2004 and 31st March 2005. Patients and their carers were interviewed by diabetes nurse in a structured format which consisted of (1) metabolic domain ie. blood sugar, HbA1c, lipid.. etc., (2) social domain ie. activity daily living, and (3) psychological domain ie. relaxation strategy.*

***Results.*** *A total of 73 patients were recruited. 31 were male and 42 were female. Over 85% of the patients had a mean age of 62.3. The mean of duration of diabetes was 12 years. The most common worries and concerns were: (1) fear of pain over the injection site, (2) stigma as Intra-venous drug addict, (3) intestinal injury caused by injection needles, (4) poor eye vision, (5) unstable hand movement and (6) expensive injection devices. In response to relieve their worries, a holistic approached was adopted to (1) educate on the natural history of disease progress and its management, (ii) clarify misconception of insulin injection, (iii) demonstrate injection devices, and (iv) assess family support system and financial status.*

***Conclusion.*** *Understanding patients' psychological needs is able to diminish their fear to injection and enhance insulin compliance.*

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**PP 106**

# Comparison of Self-Care Behavior, Self-Efficacy, and Hrqol Between Personality Type A and B in Diabetes Patients

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***Background and Aims.*** *The purpose of this study was to compare the self-care behavior, self-efficacy, HbA1c, and health-related quality of life between type A and type B personality in diabetes patients.*
***Materials and Methods.*** *The subjects consisted of 190 diabetes patients who regularly visited the endocrinology outpatient clinic. The self-care, self-efficacy, and components of HRQOL (SF-36) were measured by self-reported questionnaires and HbA1c was tested. The scale for personality groups were used to classify type A and type B personality. The scores of self-care and self-efficacy and level of HbA1c were compared between two groups.*
***Results.*** *The general and clinical characteristics were not statistically different between personality type A and B. There were no differences in scores of self-care, self-efficacy, and HbA1c. The type B personality showed significantly higher scores in Role Emotional, and Mental Health components of HRQOL (SF-36) than type A personality ($p < .05$).*
***Conclusion.*** *This study showed some relations between personality types and quality of life and the change of personality from type A to type B would be helpful to improve the quality of life in diabetes patients.*

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**PP 107**

# Individually Catered Consulting Method for Insulin Therapy

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***Background and Aims.*** *Insulin therapy is one of the important methods of controlling the plasma glucose level in both type 1 and 2 diabetes. However, quite a few diabetic patients who need insulin therapy are elderly and/or have paresis due to cerebral infarction, which means that they may have trouble understanding the need for insulin therapy and/or injecting insulin by themselves. Using diabetics who required insulin therapy, we examined the effectiveness of providing individualized instructions for each patient.*

***Materials and Methods.*** *The subjects were 90 diabetic patients who were being treated at our hospital and required insulin therapy. We randomly assigned 45 patients to the group receiving conventional instructions (conventional group) and 45 patients to the group given individualized instructions (experimental group). The patients in the experimental group were given numerical scores for the following: (1) the history of insulin therapy for the patient and family members, (2) the presence/absence of upper-extremity paresis, (3) the patient's understanding of the need for insulin therapy, and (4) the patient's understanding of the procedures for insulin injection. Based on their scores, the patients were divided into the following four groups: (a) outpatient guidance; (b) in-hospital guidance; (c) detailed instructions about insulin injections; or (d) family members given instructions about insulin injections.*

***Results.*** *Based on the scores of patients in the experimental group 3, 20, 19, and 3 fell into categories (a), (b), (c), and (d) respectively. After the start of insulin therapy, 3 patients lost the requirement for insulin in the experimental group versus none in the conventional group. None of the patients from the experimental group stopped therapy due to noncompliance, but 4 patients dropped out of the conventional group. At 6 months after the start of therapy, the HbA1c level was significantly decreased from 10.6% to 7.4% in the experimental group and from 10.5% to 8.0% in the conventional group (both $p<0.001$). The reduction in the experimental group was significantly greater than that in the conventional group ($p<0.01$).*

***Conclusion.*** *When considering how insulin therapy should be provided to diabetics, an individualized method of providing instructions about insulin may achieve more stable glycemic control than standard methods.*

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**PP 108**

# Comparison of Quality of Life between Diabetic Foot Ulcer Patients and Diabetes-Related Below Knee Amputees

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***Background and Aims.*** *Diabetic foot ulcer is a common problem among people with diabetes. It is usually chronic and the rate of amputation is high. This study aims to compare the quality of life (QoL) between diabetic foot ulcer patients and diabetes-related below knee amputees with prosthesis as refer to the control (diabetic neuropathy patients).*

***Materials and Methods.*** *Ninety diabetes-related foot problem cases (30 diabetic foot ulcers, 30 diabetes-related lower extremity amputations and 30 diabetic peripheral polyneuropathy as control) were recruited from foot clinic, diabetic clinic, vascular clinic and minor surgery clinic at the Faculty of Medicine Siriraj hospital between February-May 2005. Information on QoL were collected using the SF-36 questionnaires (Thai-version).*

***Results.*** *Patients with diabetic foot ulcer and diabetes-related below knee amputee with prosthesis had all dimensions score lower than the control. When compared with the diabetic foot ulcer group, the diabetes-related below knee amputee with prosthesis group had statistically significant lower scores in the dimensions of physical functioning, role-physical and role-functional emotion. The dimensions of bodily pain, general health perception, general mental health, social functioning and vitality were not statistical difference.*

***Conclusion.*** *QoL were significantly impaired in diabetic foot ulcer patients and diabetes-related below knee amputees with prosthesis compared to the control. In addition, the dimensions of physical functioning, role-physical and role-functional emotion were more impaired in diabetes-related below knee amputees with prosthesis than diabetic foot ulcer patients. This study demonstrates the importance of foot ulcer prevention and limb preservation in diabetic persons.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

## PP 109

# Influencing Factors on HRQOL in Diabetes Patients

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***Background and Aims.*** *One of the major goals of diabetes treatment is to maintain and improve health related quality of life. The aim of this study was to describe and explore influencing factors on health related quality of life in diabetes patients.*

***Materials and Methods.*** *The subjects consisted of 190 diabetic patients who regularly visited the endocrinology outpatient clinic. The association among general and medical characteristics, diabetes self-care score, diabetes self-efficacy score, and components of HRQOL (SF-36) were investigated from the self reported responses. The association was analyzed by Pearson's correlation.*

***Results.*** *Physical functioning in HRQOL was associated with age, diabetes self-efficacy, self-care scores on exercise practice and score on self medication. Role Physical in HRQOL was related to age. General health in HRQOL was correlated with BMI index, self-care score on exercise practice and self medication score. Vitality in HRQOL was not associated with other factors except the components of HRQOL. Social Functioning and Role Emotional in HRQOL were correlated with age and BMI index. Mental health in HRQOL was associated with BMI index and self-care scores on exercise practice. The blood glucose level was not correlated with any components of HRQOL but negatively correlated with age.*

***Conclusion.*** *The self-efficacy, self care, and BMI were modifiable variables among influencing factors and it is suggested that the strategies to control these factors should be developed to improve the quality of life in diabetes patients.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

**PP 110**

# Quality of Life and Glycemic Control of People with Diabetes at Medical Out Patient Unit, Ramathibodi Hospital

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***Background and Aims.*** *Diabetes is a chronic disease that threaten to quality of life, because of alternation of blood glucose level and it's complications. Control of hyperglycemia delays or prevents complications and improves quality of life of diabetes, but many persons with diabetes do not achieve optimal glycemic control. The purpose of this descriptive study was to assess quality of life and glycemic control in people with diabetes, who attended at medical out patient unit, Ramathibodi Hospital between May and December 2004.*

***Materials and Methods.*** *Purposive sampling was used to recruit a sample of 497 adults aged 15 years or older. The instruments used in this study included a demographic data record form, a physiologic parameters, and the Diabetes Quality of Life Measure (DQOL) developed by the Diabetes Control and Complications Trial Research Group and translated into Thai.*

***Results.*** *The results revealed that the sample consisted of 71.4% of females and 28.6% of males. Their age ranged from 17 to 91 years with a mean of 57.43 ± 13.80 years. Of total, 90.3% are persons with type2 diabetes. The mean duration of being diagnosed as diabetes was 10.20 ± 7.98 years and most of them have had the diabetes for 6-10 years. Most of the sample (83%) perceived a high level of their overall quality of life, while 11.7% perceived a moderate level of their overall quality of life. Approximately, almost half of the sample had higher levels of fasting plasma glucose (FPG) and glycocylated haemoglobin (HbA1C) than the targeted levels. However, 37% and 25% of the sample had the targeted level of FPG and HbA1C, while 27.8% had an acceptable level of HbA1C, and 7.3% had lower than the targeted level of FPG. In addition, the analysis showed that the patients with high quality of life were significantly associated with married status, low educational level, having affordable medical expense, having reimbursement scheme for medical expense, and having type 2 diabetes. Quality of life was associated with older age, lower level of FPG and lower level of HbA1C.*

***Conclusion.*** *This study demonstrates that about half of the sample could not control their glycemic level well, although most of them perceived good quality of life. Encouragement this population to improve their glycemic control for reducing complications by health care providers are necessary.*

** This study was supported by research grant from the Faculty of Medicine, Ramathibodi Hospital, Mahidol University, 2004, No.47001*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

**PP 111**

# Internet-Based Blood Glucose Management System (IBGMS) Using Personal Digital Assistants (PDA) in Rural Heath Subcenter

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***Background and Aims***. *To evaluate the efficacy of web-based diabetes management system using personal digital assistants (PDA) with glucose monitoring device in care of the diabetic patients of rural health subcenter*

***Materials and Methods.*** *We previously developed the Internet-based Blood Glucose Monitoring System (IBGMS) and reported its efficacy for management of type 2 diabetic patients. Here we applied PDA with glucose monitoring device into IBGMS in rural area where diabetic patients have fewerer chances to get medical help from health care provider. Fifty seven patients with type 2 diabetes mellitus who had their glycated hemoglobin levels below 11% were enrolled and randomized into the intervention and the control group. In the intervention group, Community Health Nurse Practitioner (CHNP) checked patient's blood glucose levels using PDA regularly and sent the data including patient's medication, amount of meal, and degree of exercise to IBGMS. Then endocrinology specialist, dietitians, and nurses sent recommendations for individualized diabetes management to CHNP. In the control group, CHNP just checked patient's blood glucose levels and gave general information about diabetes management without any helps or contact with IBGMS. Laboratory tests including lipid profiles and glycated hemoglobin (HbA1c), and a survey about dietary habits and exercise were performed before and after the study.*

***Results.*** *A total of 52 diabetic patients completed this study. Fasting plasma glucose level of the intervention group was significantly improved from 156.4±46.1 mg/dl to 137.6±31.8 mg/dl after 3 months of study period compared with that of the control group ($p<0.05$). Among the patients with their HbA1c of 7% or higher at baseline, IBGMS with PDA significantly improved HbA1c of the intervention group after 3 months compared with that of the control group (from 8.51±1.0% to 8.46±1.1% in the intervention group vs. from 7.96±0.9% to 8.96±1.3% in the control group, $p<0.05$). Several parameters regarding dietary habits and exercise were also significantly improved in the intervention group.*

***Conclusion.*** *This study results suggested that IBGMS using PDA was effective management system for diabetic patients in rural health subcenter. And PDA with glucose monitoring device was a useful tool for caring the diabetic patients with limited medical helps.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

**PP 112**

# Whether Self Monitoring of Blood Glucose (SMBG) Can Reflect Glycemic Control in Type 2 Diabetes Mellitus Using Glycoxylated Hemoglobin $HbA_{1C}$ as Gold Standard

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***Background and Aims.*** *To investigate the relationship between self monitoring of blood glucose (SMBG) and glycosylated hemoglobin (HbA1c) in type 2 diabetes mellitus patients in a regional hospital.*
***Materials and Methods.*** *Glycemic profile by SMBG at fasting, pre-lunch and pre-dinner were obtained in 53 type 2 diabetes mellitus patients in an ambulatory setting over 3 month duration. They were on either diet therapy alone or on oral hypoglycemic agents (i.e. sulphonylurea; biguanide; a-glucosidase inhibitor; peroxisome proliferators-activated receptor PPAR) +/- once-a-day insulin. Exclusion criteria: 1.Type 2 diabetes mellitus patients with secondary oral hypoglycaemic agent failure who were on twice daily or multiple dose insulin regimes. 2. Pregnant patients. 3. Patients with blood loss, surgery, sepsis or nutrition correction during the study period. 4. Patients with hemoglobinopathy. (based on the Mean Cell Volume (MCV) in the blood picture and the past medical records) SMBG profile were performed preferably once to twice per week, the minimum frequency being once in 2 weeks. The total plasma glucose exposure was calculated by area under curve model and the mean plasma glucose level calculated by dividing the total plasma glucose exposure over time. The plasma glucose values at different time points and the mean plasma glucose value were correlated with HbA1c.*
***Results.*** *The fasting plasma glucose was 6.81+/-1.71mmol/L. The pre-lunch plasma glucose was 8.34+/-2.68mmol/L and pre-dinner plasma glucose was 9.13+/-2.66mmol/L. Mean plasma glucose MPG was 8.13+/-1.90mmol/L. The lowest plasma glucose occurred at fasting in the morning and the highest plasma glucose occurred at pre-dinner time. The mean HbA1c of the subjects was 8.34+/-1.19%. The hemoglobin level ranged from 9.4 to 15.4g/dL with hematocrit value ranged from 0.29 to 0.45. Pre-lunch plasma glucose and mean plasma glucose correlated significantly with HbA1c. Linear regression analysis demonstrated linear relationships: 1) between pre-lunch plasma glucose and HbA1c ($r=0.545$, $p<0.001$), and 2) between mean plasma glucose and HbA1c ($r=0.365$, $p=0.007$). The stronger correlation was between pre-lunch plasma glucose and HbA1c. Collinearity was noted between pre-lunch plasma glucose and mean plasma glucose. After multiple regressions analysis with stepwise elimination, the only independent factor retained in the final model was the pre-lunch plasma glucose level.*
***Conclusion.*** *Despite the small sample size, pre-lunch plasma glucose and mean plasma glucose correlated significantly with HbA1c. Pre-lunch plasma glucose was the only independent predicting factor for HbA1c. Prediction of HbA1c from SMBG was not feasible due to the limitations of the study and the large prediction interval. Nevertheless SMBG conveys important unique information not available in HbA1c measurement and is an essential component in the monitoring and management of type 2 diabetes mellitus.*

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**PP 113**

# Effectivenss of Diabetes Phone on Glucose Control Via Telecommunication is as Good as the Glucose Monitoring System Via Internet

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***Background and Aims.*** *Last year we reported the effect of Internet based glucose monitoring system (IBGMS) on glucose control for 3 months. Recently a cell phone with the capacity to measure glucose level and send those to web server directly was developed. We investigated the effectiveness of diabetes phone on glucose control and compared to that of IBGMS.*

***Materials and Methods.*** *We conducted a randomized clinical trial involving 70 patients who visited the outpatient clinic at the Kangnam St. Mary's Hospital for 3 months. Participants were assigned to two groups, 'Diabetes phone' group and 'Internet' group (35 subjects in each group). 'Diabetes phone' group was treated using telecommunication and internet for 12 weeks, and the 'Internet' group using internet only for the same period. HbA1c and other laboratory tests were performed twice, once at the beginning of the study and again at the end of the study.*

***Results.*** *The test results from the beginning of the study established that there were no significant differences between the two groups with respect to age, sex, diabetes duration, BMI, blood pressure, HbA1c, and other laboratory data. On follow-up examination 12 weeks later, HbA1c levels of 'Internet' group and 'Diabetes phone' group were significantly decreased from 7.5 to 6.8% and 8.0 to 6.9% ($P<0.01$). At the end of the study, there was no significant difference in HbA1c level between both groups. In survey of satisfaction and the adherence of the doctor's order, most subjects in both groups answered good or excellent (80.6% and 76.4% of subjects, respectively in 'Internet' group; 79.2% and 82.7% in 'Diabetes phone' group).*

***Conclusion.*** *Use of diabetes phone showed good results as IBGMS in HbA1c reduction and compliance.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

**PP 114**

# Effectiveness of Surveillance System in Prevention of Hospital Hypoglycemia

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***Background and aims.*** *Hypoglycemia is the common problem among hospitalized diabetic patients with oral hypoglycemia drug and/or insulin treatment. Hospital hypoglycemia, which has been evaluated by a limited number of studies, associated with in-hospital increased mortality.*
***Main outcome measures.*** *Comparison the incidence of hospital hypoglycemia before and after surveillance indicated by1. Rate of hospital hypoglycemia per all diabetic patients 2. Rate of hospital hypoglycemia per high risk diabetic patients 3. Level of clinical impacts of hospital hypoglycemia.*
***Results:*** *Incidence of hospital hypoglycemia per all diabetic patients reduced after the surveillance of hospital hypoglycemia by multidisciplinary team from 5.01% to 4.28%. As well as incidence of hospital hypoglycemia per high risk diabetic patients decreased from 19.08% to 11.74% with relative risk reduction 38.5% after the surveillance. Less severity of clinical impacts of hospital hypoglycemia also demonstrated.*
***Conclusion.*** *This study is a part of hospital accreditation process, clinical risk management. Hospital hypoglycemia in diabetic patients is the priority watch list of incident reports. The surveillance of hospital hypoglycemia by multidisciplinary team decreased rate of hospital hypoglycemia and severity of clinical impact.*

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## PP 115

# Hypoglycemia and Eating Attitude in Diabetics

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***Background and Aims***. *Hypoglycemia is often induced by unfavorable eating behavior in diabetics. Therefore, the analysis of eating attitude of diabetics is interesting to prevent the hypoglycemia.*
***Materials and Methods***. *Thirty-four outpatients with diabetes were subjected to the questionnaire study using "The Hypoglycemia Fear Survey "(Cox DJÿ1987) and "The Eating Attitude for Diabetes Mellitus Inventory" ÿIsao Fukunishi, 1997 ). Frequency of hypoglycemic episodes and the average HbA1c level during the latest one year as indicator of blood glucose control were assessed.*
***Results.*** *1. The average HbA1c level had a positive correlation with the score of "Impulsive Eating Behavior" that is one of the factors in the questionnaire "Eating Attitude for Diabetes Mellitus Inventory" (p=0.046, r=0.345). 2. Among diabetics having one to twelve hypoglycemic episodes per month, those with average HbA1c of <7% had a tendency to show lower score of "Impulsive Eating Behavior" in the questionnaire "Eating Attitude for Diabetes Mellitus Inventory" than those with average HbA1c of g"7% (p=0.072). They also showed the higher scores of the quiz "Eat something as soon as I feel the first sign of low blood sugar" in the questionnaire "The Hypoglycemia Fear Survey" (p=0.004).*
***Conclusion***. *Prevention of hypoglycemia seems to be achievable by educational reduction of the excessive hypoglycemia fear and impulsive eating behavior from the cognitive- behavioral point of view.*

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## PP 116

# Pharmacokinetic Profile of a New Fixed-Dose Combintion of Glimepiride and Metformin in Healthy Volunteers in Korea

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***Background and Aims.*** *The aim of this study was to evaluate the relative bioavailability of the two different treatments, fixed-dose versus free combination of glimepiride and metformin, by comparing their pharmacokinetic (PK) profiles.*

***Materials and Methods.*** *In this single-center, randomized, open, single-dose, two-way crossover study, total 32 healthy adults volunteers (16 males and 16 females) were randomized into two groups (16 subjects per group), and the subjects were treated, in a crossover way, with one tablet of fixed-dose combination (glimepiride 2 mg/metformin 500 mg) and each tablet of glimepiride 2 mg and metformin 500 mg co-administered following one-week wash-out. Plasma concentrations of glimepiride and metformin were analyzed by LC/MS/MS method.*

***Results.*** *The study treatments were well tolerated. PK parameters including AUC and $C_{max}$ of fixed-dose combination were comparable to those of free combination (Table). The CV's (Coefficients of Variation) of the parameters ranged from 20 % to 30 % suggesting low inter-subject variability.*

| | Parameter | Fixed combination | Free combination | Logarithmic mean change (90% CI) | Note (Equivalence range) |
|---|---|---|---|---|---|
| Glimepiride | $C_{max}$(ng/mL) | 205±56 | 202±51 | 0.0056 (-0.0927 ~ 0.1039) | Consistent with BE (-0.2231 ~ 0.2231) |
| | $AUC_{last}$(ng*h/mL) | 879±228 | 900±245 | -0.0227 (-0.0788 ~ 0.0335) | Consistent with BE (-0.2231 ~ 0.2231) |
| Metformin | $C_{max}$(ng/mL) | 1084±305 | 1122±291 | -0.0388 (-0.1366 ~ 0.0591) | Consistent with BE (-0.2231 ~ 0.2231) |
| | $AUC_{last}$(ng*h/mL) | 6293±1364 | 6516±1272 | -0.0380 (-0.1058 ~ 0.0298) | Consistent with BE (-0.2231 ~ 0.2231) |

***Conclusion.*** *This study establishes bioequivalence of both, glimepiride and metformin, following two different treatments, fixed-dose and free combination of glimepiride and metformin. Both treatments were safe and well tolerated in healthy adults.*

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**PP 117**

# Muraglitazar (PARGLUVA(TM)), a Dual (α/γ) PPAR Activator: A Randomized, Double-Blind, Placebo-Controlled, 24-Week Monotherapy Trial in Adult Patients with Type 2 Diabetes

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***Background and Aims.*** *Peroxisome proliferator-activated receptors (PPAR) present a therapeutic target and simultaneous activation of PPARα and PPARγ may provide improvement in glycemic control and dyslipidemia in patients with type 2 diabetes. The objective of this study was to evaluate the efficacy and safety of muraglitazar (PARGLUVA(TM)), a dual (α/γ) PPAR activator, in adult patients with type 2 diabetes.*
***Materials and Methods.*** *This was a randomized, double-blind, placebo-controlled, 24-week monotherapy study in drug-naive type 2 diabetes patients.*
***Results.*** *Participants (N = 340) had mean baseline A1C values of 8.0%. Monotherapy with muraglitazar 2.5 mg and 5 mg significantly reduced A1C (–1.05% and –1.23%, respectively), compared with placebo (–0.32%, P < 0.001). At week 24, 58%, 72%, and 30% of patients receiving muraglitazar 2.5 mg, 5 mg, and placebo, respectively, achieved A1C <7%. Plasma FPG, free fatty acids, and insulin levels significantly decreased during muraglitazar treatment (P < 0.001), suggesting an increase in insulin sensitivity. Muraglitazar 2.5 mg and 5 mg provided significant improvement from baseline in triglyceride (–18% and –27%), HDL cholesterol (+10% and +16%), apolipoprotein B (–7% and –12%), and non-HDL cholesterol levels (–3% and –5%; P < 0.05 versus placebo for each). In a parallel, open-label cohort of 109 drug-naive patients (mean baseline A1C, 10.6%), muraglitazar 5 mg decreased A1C from baseline by –2.62% (LOCF) and –3.49% (patients completing 24 weeks). Changes in lipid parameters with open-label treatment were similar to those observed during double-blind treatment. Muraglitazar was generally well tolerated. Mean weight change during double-blind treatment was +1.1 kg (2.5 mg), +2.1 kg (5 mg), –0.8 kg (placebo, P < 0.0001) and +2.9 kg (5 mg open-label). Edema-related adverse effects of mild to moderate severity occurred in 8% to 11% of patients in all groups.*
***Conclusion.*** *In this study, muraglitazar was an effective treatment option for patients with type 2 diabetes.*

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**PP 118**

# Effects of Aging and Diabetes on Resting and Post Occlusive Hyperemia of the Forearm; the Impact of Rosiglitazone

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***Background and Aims.*** *A growing body of evidence has demonstrated a strong interrelationship between the metabolic syndrome of insulin resistance and endothelial dysfunction. A primary contributor towards coronary atherogenesis in patients with diabetes is endothelial cell dysfunction. The insulin sensitizer and peroxisome proliferator-activated receptor g (PPARg ) ligand rosiglitazone (RSG) has been shown to improve endothelial function in preclinical and clinical trials.*

***Materials and Methods.*** *Thirty control subjects and twelve subjects with type 2 diabetes participated in a series of experiments to examine the interrelationships between age, diabetes and endothelial cell function. RSG was administered for 1 year. Resting forearm flows and blood flows after 4 min of vascular occlusion (an index of endothelial cell function) were measured. Resting forearm flows were measured by venous occlusion plethysmography and were negatively correlated to both age and diabetes.*

***Results.*** *Using linear regression analysis, blood flows in patients with diabetes correlated with non-diabetic counterparts who were 23 years older. (Figure 1) Administration of RSG after 1 year improved endothelial function similar to age matched controls. Total post occlusive flows in control subjects compared to subjects with diabetes before RSG averaged 56.58 +/- 12.57 and 13.6 +/- 8.01 cc/100ml tissue per min respectively, and were significantly different ($p<0.01$). After 12 months on RSG, differences between flows in the two groups were no longer evident, averaging 51.8+/-12.6 cc/100ml/min for subjects with diabetes and 56.7+/-14.3 cc/100ml/min for controls.*

***Conclusion.*** *RSG may help to promote reversal of accelerated endothelial cell dysfunction seen in patients with diabetes similar to age matched non-diabetic controls*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

**PP 119**

# Improvements in Thermoregulation after Six Months of Treatment with Rosiglitazone in Individuals with Type 2 Diabetes

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***Background and Aims.*** *Pilot data in 5 diabetics showed improvement in thermoregulation post-intake rosiglitazone (RSG). We hypothesized that the RSG would improve thermoregulation (skin flow, sweat rate, and body temperature) in a larger diabetic cohort through its peroxisome proliferator-activated receptor-ã activity on the endothelial micro-vasculature in the skin circulation and autonomic nervous system.*
***Materials and Methods.*** *Lower limb cutaneous flow was measured by a laser Doppler flow meter. Mean body temperature was calculated as a function of core and mean skin temperature. Sweat was measured by a sweat hygrometry system on the forearm, chest, forehead and calf. RSG, 4 mg was given daily for four weeks to 11 insulin resistant diabetics. Baseline characteristics included: n = 9 male, n = 2 female, age 61.3 + 10.6 years, body mass index 31.7 + 8.0, duration of diabetes 8.6 + 7.5 years and HbA1c 9.1 + 2.8.*
***Results.*** *After RSG, sweat rates increased after 4 weeks from 0.050 mg/cm2/min to 0.147 mg/cm2/min. The mean cutaneous flow at baseline was 104 +/- 28.2 flux units and at week 4 increased to 120.7 +/- 35.5 flux units (p < .01). Prior to RSG, mean body temperature rose to 35.8 ± 0.4ºC after 30 minute heat exposure. Attenuation in mean body temperature was demonstrated at week 2, 35.7 ± 0.3ºC (p =.02) and week 4 35.6 ± 0.4ºC (p=.01). Mean post occlusive (3-5 seconds) flows at baseline were 6.39 cc +/- 2.82 per 100g tissue/min. 4 weeks flows increased to 15.30 +/- 3.67 cc/100 grams tissue/min (P<.01).*
***Conclusion.*** *Improvements in thermoregulation were demonstrated post initiation of RSG and corresponded to improvements in the endothelial function.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

## PP 120

# Comparison of the Efficacy and Safety of Fixed-Dose versus Free Combination of Glimepiride and Metformin in Patients with Type 2 Diabetes in Korea

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***Background and Aims.*** *A couple of sulfonylurea/metformin combined tablets are now available for use in type 2 diabetes in the market. Recently, a new fixed-dose combination of glimepiride and metformin has been developed in Korea. This study was designed to compare the efficacy and safety of the fixed-dose versus free combination of glimepiride and metformin in patients with type 2 diabetes.*

***Materials and Methods.*** *In this 16-week, randomized, multicenter, open, parallel-group study, 202 subjects were randomly assinged to receive either fixed-dose (n=101) or free combination (n=101) of glimepiride and metformin. Doses were then titrated every 2 weeks with the intention to achieve fasting blood glucose d"140 mg/dL. The primary endpoint was change in HbA1c level from baseline to the last visit: secondary endpoints included change in FPG and PPG2h levels, response rate based on HbA1c, and subject compliance.*

***Results.Baseline.*** *characteristics were similar between the fixed-dose and free combination groups (mean age: 54.6±9.7 vs 54.3±8.9 years; BMI: 24.8±2.6 vs 25.2±2.6 kg/m2; HbA1c: 7.99±0.71 vs 7.88±0.75% [±SD]). HbA1c levels decreased in both groups over the study period (-1.09% vs -1.08%). Two-sided 95% confidence interval (-0.21%, 0.19%) for the difference of the changes in HbA1c of the two groups existed in pre-defined equivalence range (-0.5%, +0.5%). Decrease in FBG and PPG2h was similar in the fixed-dose versus free combination (mean change 35.4±41.4 vs 37.3±44.2 mg/dL; p=0.8486, 49.1±84.2 vs 49.8±77.3 mg/dL; p=0.2992). The response rate based on HbA1c (% of patients with HbA1c < 7.0%) did not show the statistically significant difference between the two treatment groups (53.5% vs 57.4%; p=0.5917). Compliance was slightly higher in the fixed-dose combination group (94.6%) than the free combination group (91.4%) showing no statistically significance (p=0.1511). The occurrence rates of symptomatic hypoglycemia (36.4% vs 37.4%; p=0.9947) and treatment emergent adverse events (TEAEs, 38.2% vs 42.4%; p=0.5734) were comparable. The mean daily doses at the end of the study were similar as well between the two groups (glimepiride/metformin, 4.1 mg/ 1024 mg vs 3.8 mg/947 mg).*

***Conclusion.*** *The fixed-dose combination of glimepiride and metformin is considered to be equally safe and effective for the treatment of type 2 diabetic patients compared to the free combination therapy of glimepiride and metformin already widely used in current medical practice.*

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**PP 121**

# Single Dose Safety, Pharmacokinetics (PK), and Pharmacodynamics (PD) of Sitagliptin, an Inhibitor of Dipeptidyl Peptidase-IV (DPP-IV), in Healthy Male Japanese Subjects

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***Background and Aims.*** *Sitagliptin (MK-0431) is an orally active, potent and selective DPP-IV inhibitor under investigation for the treatment of type 2 diabetes. DPP-IV inhibitors enhance levels of active GLP-1 and other incretins, facilitating glucose-dependent insulin secretion. The objective of this study was to investigate the safety, PK, PD of sitagliptin in healthy male Japanese subjects following single oral doses, and to compare the PK and PD profile of sitagliptin in healthy male Japanese subjects to healthy male non-Japanese subjects.*
***Materials and Methods.*** *In this randomized, double-blind, placebo-controlled, 2-panel study (3 periods each), 18 healthy Japanese male subjects, 20 to 46 years, received single oral sitagliptin doses ranging from 5-to 400-mg.*
***Results.*** *Sitagliptin was generally well tolerated with no episodes of hypoglycemia or serious adverse experiences. Over the dose range studied plasma AUC0-" increased approximately dose proportionally; plasma Cmax increased in a slightly greater than dose-proportional manner; and Tmax exhibited a slight trend toward shorter Tmax with increasing dose. Median Tmax ranged from 2 to 6 hours (h) over the dose range evaluated and apparent terminal tΩ decreased slightly with increasing dose, with harmonic means ranging from 9.07 to 13.8 h. The fraction of dose excreted unchanged in the urine ranged from 0.730 to 1.00 and tended to increase slightly with increasing dose. There was no significant difference in renal clearance (ClR) across the dose range of 12.5 to 200 mg (averaging 430 mL/min). ClR exceeded the typical glomerular filtration rate for healthy young males (approximately 125 mL/min), suggesting that sitagliptin was renally eliminated through a net active secretion process. Food (a traditional Japanese breakfast) did not affect the PK of sitagliptin in a clinically meaningful manner. There was a dose-related increase in the percent inhibition of plasma DPP-IV enzyme activity over the dose range studied. A greater than 80% difference from placebo in the DPP-IV weighted average inhibition (WAI) through 24 h postdose was observed for doses of 100 mg and above. Comparisons between Japanese and non-Japanese subjects revealed that the PK as well as the plasma DPP-IV inhibition profiles were generally similar over the dose range studied. The correlation between DPP-IV activity and plasma sitagliptin concentrations was also similar between Japanese and non-Japanese subjects4. Using an Emax model, the EC50 for plasma DPP-IV inhibition was approximately 25.7 nM.*
***Conclusion.*** *Single doses of sitagliptin were generally well tolerated. Sitagliptin PK and PD data (i.e., plasma DPP-IV inhibition) following single oral sitagliptin doses are similar in Japanese and non-Japanese historical control subjects. 4Stevens C, Van Dyck K, Yi B, Bergman A, De Smet M, Snyder K, Hilliard D, Tanaka W, Wang A, Zeng W, Musson D, Winchell G, Ramael S, Gottesdiener K, Wagner J, Herman G. Single doses of MK-0431, an inhibitor of dipeptidyl peptidase-IV, raise active GLP-1 levels without causing hypoglycemia in healthy subjects (abstract). Diabetes 2005; 54 (suppl 1).*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

**PP 122**

# TDR* 8: Glycemic Control in Type 2 Diabetes and Its Relation to Hypoglycemic Agents Use

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***Background and Aims.*** *Good glycemic control reduces microvascular complications in type 2 diabetes as shown in UKPDS. After failure of diet control and exercise, initial drug therapy is either sulfonylurea (SU) or metformin. However, in order to achieve $HbA_{1C}$ less than 7 % , a number of patients has to use various combination therapy of oral agents and/ or insulin. The objectives of this study were to determine the pattern of hypoglycemic agents use in Thai type 2 diabetes in relation to BMI , and duration of disease. The achievement of target glycemic control by various modalities of treatment were also analyzed.*

***Material and Methods.*** *A cross-sectional, multicenter registry of 9,419 diabetic patients in 11 tertiary care hospitals and medical shools was carried out from April to December 2003. Only type 2 diabetes were analyzed for achievement of target glycemic control in various modalities of treatment including diet control alone , monotherapy wtith SU, metformin, repaglinide, alpha-glucosidase inhibitors(AGI) , thiazolidinedione(TZD) , insulin,and combination therapy. Body mass index (BMI) and duration of diabetes were also assessed in each group.*

***Results.*** *There were 8913 type 2 diabetes. The percentage of patients treated with metformin, SU and insulin were 70.8, 68.7 % and 25.3 %, respectively. Only 7.0 %, 5.7 % and 1.1 % of patients received AGI, TZD and repaglinide, respectively while 3.2 % was on diet control alone. Metformin and SU was the most common combination therapy in 39.5 % of patients. Target glycemic control was achieved in 57.6 %, 37.1 %, 52 %, 16.7 %, 62.5 % , 52 % and 16.9 % of patients who were on diet control only, monotherapy with SU , metformin, TZD, AGI , repaglinide and insulin, respectively. BMI $\geq$ 25 $kg/m^2$ was found in 61. 7 % of patients treated with metformin only where as less than 45 % in other monotherapy. Mean duration of diabetes in the patients treated with metformin alone was 5.9 $\pm$ 5.5 years , less than in SU- and insulin-treated patients. (8.3 $\pm$7.1 years, 14.8 $\pm$ 9.0 years, respectively)*

***Conclusions.*** *Metformin is still the most common oral hypoglycemic agents used in type 2 diabetes, especially in the obese patients. Mean duration of diabetes in the patients treated with metformin only was shortest which may contribute to the better glycemic control when compare with other hypoglycemic agents.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

**PP 123**

# Effects of Different Medicine on Body Weight Fat Mass Fasting Serum Ghrelin Level of High-Fat Diet Induced Obese Rats

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***Background and Aims.*** *Ghrelin identified recently is synthesized predominantly in the stomach, which appears to play a role in longer-term appetite regulation and energy balance. Topiramate, a novel anticonvulsant, may result in weight loss. Fenofibrate, a hypolipidemic drug, activates the peroxisome proliferator-activated receptor alpha and may also increase energy expenditure. To assess the effects of sibutramine0fenofibrate0metformin and topiramate on the body weight0fat mass0fasting serum glucose0insulin and ghrelin levels of high-fat diet induced obese Wistar rats.*

***Materials and Methods.*** *3-week-age Wistar male rats with body weight from 63.7gram to 99.9 gram were randomly divided into two groups: rats of one group received high-fat diet, and those of another group reveived normal diet. 19 weeks later, we got 7 normal ratsÿnormal diet,mean weight 496.43±55.43 g ÿand 35 obese rats ÿdiet-induced obese rat, DIO rat ÿÿmean weight 535.03±41.26 g ÿ ,15 obese resistance ratÿdiet-induced obese resistance rat, DIO-R rat ÿÿmean weight 418.46±15.73 g ÿ. Divide all of the 35 DIO rats into five groups randomly according to their body weight. Rats of these five groups were treated with water0sibutramineÿ10mg/kg ÿ0fenofibrateÿ83.4 mg/kg ÿ0metformin ÿ400 mg/kg, and topiramateÿ53.6 mg/kg ÿindividually. Both DIO-R rats and the DIO rats received high-fat diet as of old, and normal rats went on receiving their foregoing diet. Eight weeks later, all rats were executed. Scale the length from nose to anus of rats in order to calculate the Lee's index, collect the fasting blood samples and measure the viscus fat. Detect the fasting serum ghrelin and insulin levels by EIA (Phoenix Pharmaceuticals. Ins, USA) and RIA respectively.*

***Results.*** *(1) The body weight(418.46±15.73 g vs. 496.43±55.43g) and fasting insulin level(56.361±31.7 mIU/L vs. 112.656±39.279 mIU/L, both P"(0.01") of DIO-R rats were markedly lower than those of normal cohort, and the HDL-C level was markedly higher(0.968±0.07 mmol/L vs. 0.764±0.079 mmol/L, P"ÿ0.001"ÿ. Fasting serum ghrelin level has no difference between two groups (2.657±2.416ng/ml vs.1.656±0.141 ng/ml, P>0.05). (2) Fasting serum ghrelin level of DIO-R rats and normal rats was prominently negatively correlated to fasting insulin level (r=-0.73,P= 0.001)0TG(r=-0.629, P=0.007)0fasting glucose(r=-0.625,P=0.007) and fat mass(r=-0.517 P=0.023) according to simple correlation. But multiple regression analysis showed that none of them can determine the level of fasting ghrelin. (3)All of the four medicine could induce body weight loss. The fat mass of the groups of rats treated by sibutramine (12.144±3.285 g vs.16.659±3.123 g, P"ÿ0.05)and fenofibrate(9.845±4.245 g vs.16.659±3.123 g, P-0.01) decreased notably. Compared with fasting serum ghrelin level of obese cohort, that of rats treated by metformin(3.545±4.339 ng/ml), sibutramine(3.670±1.800 ng/ml), topiramate(6.187±6.271 ng/ml),and fenofibrate(1.637±0.152 ng/ml vs.2.167±1.186 ng/ml ) didn't change, there were no statistical significances between them. P>0.05 ) (4)Fasting serum ghrelin level of rats treated by medicine was prominently negatively correlated to fasting insulin level(r=-0.536 P=0.001) 0TG(r=-0.465 P=0.008) and Lee's index(r=-0.361 P=0.028) according to simple correlation. Multiple regression analysis showed that fasting insulin level can affect the fasting ghrelin level, meanwhile TG level and Lee's index can't. Partial correlation analysis revealed that the relationship between TG 0Lee's index and ghrelin level were cooperated with the effect of fasting insulin.*

***Conclusion****. All of sibutramine0fenofibrate0metformin and topiramate were effective on the treatment of obesity, furthermore, the effects of sibutramine and fenofibrate on reducing fat mass were noticeable. Fasting serum ghrelin levels of rats treated by four drugs may not related with the weight loss, but fasting insulin level.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

## PP 124

# An Investigation of the Quality and Performance of Glimepiride Generic Versus Amaryl®

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***Background and Aims.*** *The use of generic copies of drugs is one method of reducing health care costs. However, the quality and performance of these generics should be carefully evaluated. Glimepiride (Amaryl®; Amarel®; Solosa®) is a third generation sulfonylurea. The aim of this study was to compare the quality and performance of commercially available generic forms of glimepiride versus Amaryl®.*

***Materials and Methods.*** *Samples of Amaryl® and 23 glimepiride generics (all 2 mg) were analysed at Day 0 for content of active compound, levels of impurities, levels of residual solvent and dissolution profile. De-blistered samples were stored at 60ºC for 21 days in order to mimic temperature stressed conditions. Content of active compound, levels of impurities and dissolution profiles were again measured at Day 7 and Day 21. All analytical results were compared against Amaryl® specifications.*

***Results.*** *74% (17/23) of the generics evaluated were not of equivalent quality or performance compared with Amaryl®. In one generic, the mean content of active compound was below Amaryl® specifications (1.80–2.10 mg) at Day 21. Levels of the degradation product glimepiride–sulfonamide (GS) were ?1% in all products at Day 0 but increased to above Amaryl® specifications (d"2.5%) in two generics at Day 7 and four generics at Day 21. GS levels were five times greater for one generic product versus Amaryl® at Day 0 (1 vs 0.2%) and 12.5 times greater at Day 21 (15 vs 1.2%). Total levels of other impurities were above Amaryl® specifications (d"1.0%) in two generics at Day 0; one generic product contained 2.8% total other impurities versus 0.1% for Amaryl®. High levels of residual solvents, above Amaryl® specifications (>1400 ppm), were detected in two generic products. At Day 0, the dissolution of 12 generics (52%) failed to meet Amaryl® specifications (e"85% dissolved in 15 minutes); this trend was confirmed at Day 21. The dissolution profiles of 15 generic products (65%) were not considered comparable to that of Amaryl®.*

***Conclusions.*** *This study indicates that a relevant percentage of generic copies may present poor quality and performance when compared with the original drug. The results highlight the need for the evaluation and certification of generics in order to guarantee safe and effective therapeutic activity.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

## PP 125

# Preliminary Result of Comparison of the Efficacy of Insulin Glargine in Non-Obese versus Obese Type 2 Diabetes in Korea

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***Background and Aims***. *Type 2 diabetes mellitus (T2DM) is a complex metabolic disorder characterized by relative insulin deficiency and decreased insulin sensitivity. Obesity is one of the most important factors for insulin resistance to affect on the glycemic outcome of insulin therapy. The aim of this study was to compare the efficacy of insulin glargine in non-obese versus obese Korean type 2 diabetes.*

***Materials and Methods***. *We analyzed mean changes in HbA1c in relation with mean daily dose of insulin glargine in 2,869 patients (mean age: 57.6 ±11.4 years; body mass index (BMI): 23.8±3.0 kg/m2; duration of diabetes: 10.9±7.4 years [±SD]) with type 2 diabetes who were enrolled in the uncontrolled observational study and treated with insulin glargine for 16 weeks. Decisions related to the doses, other ancillary treatments, and follow-up interval were made at the physicians' discretion.*

***Results.*** *There was no significant difference in the mean age and duration of diabetes between the two groups. As expected, BMI was significantly lower in the non-obese group (defined as BMI <25 kg/m2) than the obese group (22.2±1.9 vs 27.2±2.0 kg/m2, p<0.0001). HbA1c at baseline was significantly higher in the non-obese group than the obese group (9.22±1.84 vs 9.03±1.63%, p=0.0077). Overall, HbA1c decreased by 1.14%, after 16 weeks' treatment with insulin glargine of which mean daily dose was 26.1±11.0 IU at the last visit. There was no significant difference in the mean change in HbA1c adjusted with baseline value (-1.14 vs -1.14%, p=0.9420 by ANCOVA) between the two groups. Meanwhile, the mean daily dose of insulin glargine was significantly lower in non-obese group than obese group at the last visit.*

| Group by | BMI (kg/m$^2$) | | *p* |
|---|---|---|---|
| | < 25 (Non-obese) n=1,944 | ≥ 25 (Obese) n=925 | |
| Age (years) | 57.4±11.6 | 58.1±11.2 | 0.1345* |
| BMI (kg/m$^2$) | 22.2±1.9 | 27.2±2.0 | <0.0001* |
| Duration of diabetes (years) | 10.8±7.3 | 11.2±7.5 | 0.1702* |
| HbA1c at baseline (%) | 9.22±1.84 | 9.03±1.63 | 0.0069* |
| Adjusted mean change in HbA1c (%) | -1.14 | -1.14 | 0.9926[ß] |
| Daily dose of insulin glargine (IU) | 25.2±11.0 | 28.2±10.8 | <0.0001* |

***Conclusion***. *These data suggest that insulin glargine should be equally effective in improving glycemic control for both non-obese and obese type 2 diabetes. In addition, the higher dose of insulin glargine should be required for the HbA1c reduction of similar extent for obese than non-obese type 2 patients, which means we need to pay more attention to find appropriate dosage for each group to achieve glycemic target.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

**PP 126**

# Effects on Glycated Hemoglobin ($HbA_{1C}$) after Switching to Human Insulin Analogues

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***Background and Aims.*** *There has been an increasing use of the newer insulin analogues in our hospital, and this study therefore aimed to review and audit the usage of these insulin analogues in the diabetic outpatients in NUH. To study (i) if there were reasons given for the switch from conventional insulin to insulin analogues; (ii) the frequency of diabetes related hospitalizations before and after switching; (iii) the effectiveness in glycemic control after switching to human insulin analogues based on the differences in glycated hemoglobin (HbA1c).*

***Materials and Methods.*** *This was a retrospective study. Case notes of all patients who were prescribed human insulin analogues at the outpatient diabetic clinic from January to September 2004 were reviewed. The change in mean HbA1c, the frequency of hospitalizations at least 3 months before and after switching to insulin analogues was counted, and the reason(s) stated by the clinician for switching to the insulin analogues was obtained.*

***Results.*** *A total of 141 patients were prescribed human insulin analogues: Lispro (N=27), Aspart (N=79), Glargine (N=54) in the study time period. Patients who were switched to Aspart showed 27.3% reduction in the number of hospitalizations as compared to before switching. For patients who were switched to Aspart with a given reason, this review showed a reduction in absolute mean HbA1c of 0.53 % (p=0.001). The differences in HbA1c and number of hospitalizations with the other insulin analogues, and for patients where there was no given reason for the switch were all not statistically significant, but this may be due to the smaller sample size.*

***Conclusion.*** *The diabetes control for patients, who had a given reason for switching to insulin analogue Aspart, had shown to be improved significantly.*

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## PP 127

# Relationship between Serum Amylin and Insulin, Body Composition in Type 2 Diabetic Patients

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***Background and Aims***. *Amylin is a peptide hormone cosecreted with insulin from the pancreatic fl-cell. It inhibits glucagon secretion, delays gastric emptying, and acts as a satiety agent. However, there have been no studies on the association of Amylin with fasting insulin, HOMA-IR, and body composition in type 2 diabetes mellitus (T2DM). To study the change of serum amylin level and the relations of it to serum insulin, HOMA-IR and body composition in patients with newly-diagnosed type 2 diabetes mellitus.*

***Materials and Methods***. *29 newly-diagnosed T2DM patients and 20 controls were measured for body height, waist circumference, blood pressure, serum lipid, fasting blood glucose, fasting amylin, fasting insulin, HOMA-IR and body composition by bioelectrical impedance analysis, and correlation was analyzed between amylin and other indexes.*

***Results***. *Fasting serum amylin level was lower (43.48% P< 0.05) in T2DM patients than that in controls. The levels of insulin and HOMA-IR are higher in T2DM patients than that in controls. Fasting amylin concentrations were positively associated with age, and negatively associated with fasting insulin, HOMA-IR, fat-free mass, basic metabolic rate and total body water in patients with 2-DM.There is no relation between Amylin and body composition in controls.*

***Conclusion***. *Amylin reduction may occur before the reduction of Insulin in newly-diagnosed T2DM patients Low amylin may contribute to the onset and development of T2DM and the change of body composition.*

**Table 1** Parameters of patients with 2-DM and controls

| Parameters | 2-DM | Control | P |
|---|---|---|---|
| BMI (Kg/m2) | 29.26±5.91 | 21.48±2.84 | P<0.05 |
| SBP (mmHg) | 133.05±17.81 | 107.14±14.96 | P<0.01 |
| DBP (mmHg) | 85.59±11.22 | 76.43±12.49 | P<0.05 |
| Waist (cm) | 98.91±13.60 | 73.20±11.90 | P<0.01 |
| Fat % | 36.01±8.50 | 26.67±8.51 | P<0.01 |
| BMR (KJ) | 6469.62±998.00 | 5792.57±1069.87 | P<0.05 |
| Fat mass (Kg) | 30.25±12.80 | 16.67±7.08 | P<0.01 |
| FFM(Kg) | 52.19±11.04 | 44.79±7.90 | P<0.05 |
| TBW(Kg) | 38.41±7.99 | 32.77±5.77 | P<0.01 |
| CH (mmol/ L) | 5.50±1.02 | 4.66±0.97 | P<0.01 |
| HDL-c (mmol/ L) | 1.39±0.36 | 1.52±0.25 | P>0.05 |
| LDL-c (mmol/ L) | 3.37±0.82 | 2.72±0.68 | P<0.01 |
| TG (mmol/ L) | 2.56±2.52 | 1.20±0.88 | P<0.01 |
| Glucose (mmol/ L) | 8.23±2.54 | 5.17±0.48 | P<0.01 |
| Insulin (uU/ml) | 9.67±5.72 | 6.48±3.15 | P<0.05 |
| HOMA-IR | 5.19±4.09 | 1.91±1.05 | P<0.05 |
| Amylin(ng/ml) | 0.13±0.09 | 0.23±0.12 | P<0.01 |

**Table 2** Correlation between serum Amylin and other variables in patients with 2-DM

| Parameters | r | P |
|---|---|---|
| Age | 0.713 | 0.000 |
| insulin | 0.619 | 0.006 |
| HOMA-IR | -0.562 | 0.015 |
| FFM(Kg) | -0.447 | 0.019 |
| TBW(Kg) | -0.471 | 0.013 |
| BMR(KJ) | -0.532 | 0.004 |

## PP 128

# Effects of Amylin on Serum Ghrelin, MRNA Expression of Adiponectin and TNF-α in Visceral Adipose Tissue in High-Fat Diet Induced Obese Rats

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***Background and Aims***. *Both ghrelin and amylin belong to gut hormones. A recent study showed that single subcutaneous injection of amylin can decrease serum ghrelin level in rats, but the effect of subcutaneous injection of amylin on the endocrine function of adipocyte remains unknown. Thus, the aim of this study was to examine the changes of serum ghrelin level and expression of adiponectin mRNA and TNF-α mRNA in visceral adipose tissue after physiological dosage of amylin had been administrated subcutaneously to rats for 19 days, in order to explore the relation of amylin to obesity and type 2 diabetes mellitus.*

***Materials and Methods.*** *Fourteen fat-rich diet induced obese male wistar rats were divided randomly into two groups (n=7 in each group) according to their weights: vehicle control (0.9% saline), amylin treatment(amylin, 10ug.kg-1.d-1 Bachem Ins, USA). Amylin and saline were injected subcutaneously once daily for 19 days. Food intake and body weight were recorded daily. On the twentieth day, all rats were killed for measurement of serum ghrelin, retroperitoneal and perinephric fat depot weight, adiponectin mRNA and TNF-αmRNA expression in visceral adipose tissue through RT-PCR.*

***Results***. *(1)Three days after starting the injection,the weight decrease of amylin group was clearly different from that of saline group (12±8.37g vs. 3±5.7g , P=0.036).This difference lasted to the end of the experiment. On the twentieth day, the weight decrease was 48±10.95g and 33.75±4.78g respectively (p=0.0083); (2) The visceral fat weight of amylin group was lower than that of saline group (15.52±4.03g vs. 27.03±10.15g,P=0.0164); (3) Food intake of amylin group declined continually, and reached the plateau after 10 days injection(30% reduction from baseline). Contrarily, food intake of saline group remained unchanged; (4)Serum ghrelin level of amylin group was higher than that of saline group at the end of experiment(8.82±2.82 VS 3.29±3.43, p=0.0064); (5) Compared with saline group, amylin upregulated adiponectin mRNA expression by 46% (p=0.0000), downregulated TNF-α mRNA expression by 50.4% (p=0.0006).*

***Conclusion***. *Amylin of physiological dosage by subcutaneous injection to fat-rich diet induced obese rats can reduce food intake, body weight, visceral fat depot, upregulate adiponectin mRNA expression ,and downregulate TNF-α mRNA expression in visceral fat. Increase of serum ghrelin level by Amylin injection may be a feedback of body weight reduction.*

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**PP 129**

# The Effects and Mechanisms of GLP-1 and Its Analogue Exendin-4 on the Differentiation of Pancreatic Neuroacinar AR42J Cells

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***Background and Aims.*** *The glucagon-like peptide-1(GLP-1) and Exendin-4 (an analog of GLP-1) have been shown to promote an increase in pancreatic beta cells mass via proliferation of islet cells and differentiation of non-insulin-secreting cells. In this study, we have characterized some of the events that lead to the differentiation of non-insulin-secreting cells in response to treatment with GLP-I and Exendin-4.*
***Materials and Methods.*** *AR42J cell line was cultured in the presence of 10nM GLP-1 or 0.1nM Ex-4. Cell proliferation was examined by MTT. Cell cycle was analyzed by FACS. mRNA expression of PDX-1 and insulin was studied by RT-PCR. Immunohistochemical statining with insulin antibody was performed.*
***Results.*** *MTT assay showed that GLP-I or Ex-4 reduced cell proliferation. Exposure of cells to GLP-1 or Ex-4 induced a significant decrease in the percentage of cells in S phase and an increase in the percentage of cell in G0-G1 phase of the cell cycle by FACS. Cells treated with GLP-1 or Ex-4 showed more activation of insulin by immunocytochemistry analysis and induced a time-dependent expression of insulin, PDX-1 mRNA.. GLP-1 and Ex-4 induces a cell cycle re-distribution with a decreased in cell proliferation rate prior to promoting the differentiation of cells.*
***Conclusion.*** *In conclusion, GLP-1 and Ex-4 induces a differentiation from AR42J cell line to insulin producing cells by a cell cycle re-distribution with a decreased in cell proliferation rate and increase of mRNA expression of insulin and PDX-1 gene*

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**PP 130**

# Beneficial Effects of Soy Protein Isoflavons on Lipid Levels and Blood Glucose in Type 2 Diabetic Subjects

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***Background and Aims***. *Consumption of soy protein has recently been shown to improve the blood lipid levels in nondiabetic subjects. The purpose of this study was to evaluate if a dietary soy protein isoflavones affects lipid levels and blood glucose in type 2 diabetic subjects.*

***Materials and Methods***. *26 type 2 diabetic patients refferd to Ahvaz Jondishapour University diabetes center, because of uncontroled diabetes, participated in this study. They complited a trial of dietary supplementation with 25gr/day of a processed defated meal contain soy protein 48g/100g and isoflavones 195mg/100gr, for 3 months. FBS, HbA1C, Serum total cholesterol, Triglycerid, HDL and LDL and Blood pressure were checked before soy protein consumption and monthly thereafter.*

***Results***. *A total of 26 (17 female & 9 male) type 2 dibetic patients complited the study. Age of patients were between 39 to 70 years .Duration of diabetes was between one month to 15 years). There were significant differences in mean FBS (152 vers 178 mg/dl ,P< 0.015), HbA1C (8.8 versus 9.5 , P<0.001), Triglycerid (228 versus 267 mg/dl P<0.008) and Total cholesterol level (196 versus 207 mg/dl, P<0.002) before and after three months consumption of this soy protein isoflavones dietary supplement. No significant changes occurred in HDL and LDL cholestrol, blood pressure and patient's weight*

***Conclusion***. *These results indicate beneficial effects of dietary supplementation with soy protein isoflavones on lipid and blood suger levels, in type 2 diabetic subjects.*

***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

**PP 131**

# Positive Effects of Brown Rice on Glycemic Index of Two High Iron-Dense Rice Strains of Thailand: A Study in Type 2 Diabetic Patients*

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***Background and Aims.*** *Evidence suggests that increased postprandial blood glucose and insulin concentrations are deleterious factors for diabetic patients and even apparently healthy people. The glycemic index has been proposed as a standard way to assess the quality of food that may affect diabetes and cardiovascular risk. Consumption of foods with low glycemic index such as whole grains has been recommended. Since Thai rice is the staple food for millions across the world, two high Fe-dense rice strains were developed by integrated biotechnology. The aim of this study is to determine the glycemic index (GI) of polished and brown (unpolished) rice of two high Fe-dense Thai rice strains which are strain 313-19-1-1 (313) and strain 1000-11-2-26 (1000).*

***Materials and Methods.*** *On five occasions with 1 or 2-weeks intervals, 16 Type 2 diabetic patients (F12, M6) consumed 5 breakfast meals containing 50 g carbohydrate of glucose solution (control) and 4 cooked rice as followed; polished and brown rice strain-313, polished and brown rice strain-1000, eaten with fried chicken with sweet basil and chilli. Blood samples were collected before and after meal ingestion at 0, 30, 60, 120, 180 and 240 min and analyzed for plasma glucose and insulin, and the incremental areas under the curves (AUC) were calculated. The rice samples were determined for carbohydrate, protein, fat, amylose, amylopectin and fiber contents. Total antioxidant capacity of water- (ACW) and lipid-soluble substances (ACL) of the rice were also measured by photochemiluminescent method (Photochem).*

***Results.*** *Incremental AUCs for glucose but not insulin response of 4 test meals of cooked rice were significantly lesser than glucose load. Only mean values of 1-h glucose of all cooked rice were significantly lower than glucose load ($p<0.05$). The 1-h glucose values (mean + SEM, mg/dL) were 218 + 13 (n=14) for brown-313, 229 + 13 (14) for brown-1000, 231 + 15 (13) for polished-313, 242 + 15 (14) for polished-1000 and 297 + 21 for glucose load (15). It is remarkable that brown rice displayed lower post-prandial glucose and insulin responses than polished rice, and brown rice-313 showed the lowest responses. The comparison between glycemic index of the meals showed that brown rice-313 had the significantly lowest GI (GI = 58). There were no statistically significant differences between GI of brown -1000 (GI = 62), polished-313 (GI = 72) and polished-1000 (GI = 74).*

***Conclusion.*** *The glycemic index of 4 traditional Thai meals compared between brown and polished rice of 2 rice strains, showed clinical importance of brown rice-313. Moreover, cooked rice of brown-313 had ACW equaled to 23.8 mg ascorbic acid equivalent/100g and ACL equaled to 40.4 mg Trolox equivalent/100g. Therefore, brown rice-313 could be an integral part for dietary advice to diabetic patients in Thailand and countries sharing similar food traditions.*

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# The Hypoglycemic Activity of Combretum Decandrum Ethanolic Extract in Diabetic Rats

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***Background and Aims.*** *The diabetes therapy is extremely costly. Thus the investigation of new compounds including plant extracts for anti-diabetic effect is mandatory. Sa-Kae-Krur (Combretum decandrum Roxb) is widely used as a medicinal herb for diabetes in northeast region of Thailand. This study aimed to examine the anti-diabetic effect of Combretum decandrum Roxb (CD) in both normal rats and type 1 diabetic rats. The effect of CD on oral glucose tolerance test (OGTT) and insulin secretion were investigated.*

***Materials and Methods.*** *Male Sprague-Dawley rats were induced to be diabetic by intraperitoneal injection of streptozotocin 55 mg/kg BW. Plasma glucose was measured by glucose oxidase method. Pancreatic isolets were isolated from ICR mice and were cultured in RPMI 1640 medium. The concentration of secreted insulin was measured by a rat specific radioimmunoassay.*

***Results.*** *It was found that after oral administrations of the CD leaf ethanolic extract at the doses of 0.5, 0.75 and 1.0 g/kg BW/day for 3 consecutive days, the blood glucose level of type 1 diabetic rats were significantly ($p<0.05$) decreased as compared to before extract administration. The percentages of decrease were 42.02 $\pm$5.97, 58.75 $\pm$ 11.32 and 37.72 $\pm$ 5.13 respectively. However the CD extract did not show this hypoglycemic effect in normal rats. In an OGTT in type 1 diabetic rats, the administration of the extract at 1.0 g/kg BW for 3 days had no effect on the blood glucose level after receiving 3.0 g/kg BW of D-glucose orally. In contrast, the CD extract significantly ($p<0.01$, as compared to distilled water) decreased the blood glucose in the normal rats at 30, 60 and 120 minutes after receiving D-glucose. The CD extract at the concentration of 100 mg/ml did not enhance the glucose-stimulated insulin secretion.*

***Conclusion.*** *It is concluded that the extract of CD has the anti-diabetic effect only in the type 1 diabetic rats but not in the normal rats. However, the CD extract could improve the glucose tolerance in the normal rats. The hypoglycemic activity of CD may not be mediated via an increase in insulin secretion.*

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## PP 133

# Effects of a Traditional Medicine for Diabetes on Glucose Metabolism in Vitro

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***Background and Aims.*** *Traditional medicines (TM) represent a potential source of new leads for insulin resistance and type 2 diabetes therapeutic agents. We have previously shown that a TM used in the South Pacific improved the diabetic condition in Psammomys obesus, a polygenic model of obesity and type 2 diabetes. To determine how the TM extract has improved the diabetic condition in P. obesus, we have proceeded to investigate its effects on glucose metabolism in cellular model.*

***Materials and Methods.*** *Differentiated 3T3-L1 adipocytes were treated with the TM extract (0.005–2% w/v) for 90 min in 14C-glucose incorporation into lipid (lipogenesis) assay or for 20 min in 14C-deoxyglucose uptake assay, and its effects were measured. Furthermore, as a key mechanism in glucose transport, translocation of GLUT4 to permeable membrane was measured by using HA-tagged GLUT4 translocation assay1 in 3T3-L1 adipocytes. In addition, effect of the TM extract on a rate-limiting enzyme in hepatic glucose production, PEPCK, was assessed using a dual luciferase promoter-reporter assay in rat FAO hepatomas. The FAO cells over-expressed both, the internal control, renilla luciferase under thymidine kinase promoter and the firefly luciferase under PEPCK promoter. These cells were then treated with dexamethasone and cAMP analogue (CPT-cAMP) to activate PEPCK. Co-treatments with the 0.5% TM extract were performed to measure effects on activated PEPCK. Data was statistically analysed by ANOVA to test for effects of the TM.*

***Results.*** *In 3T3-L1 adipocytes, the TM extract caused dose-dependent increase in glucose incorporation into lipid by up to 55% ($p<0.05$; $n=2$), and glucose uptake by up to 80% ($p<0.05$; $n=3$) in the presence of 1 nM insulin. The TM extract (0.5% w/v) stimulated translocation of HA-GLUT4 to the PM by 35-70% ($n=3$) when compared to basal level of HA-GLUT4 at the PM. These results indicate that this TM increases glucose disposal in 3T3-L1 adipocytes, and support the previous in vivo findings of P. obesus using this TM. Moreover, the TM extract (0.5% w/v) also suppressed PEPCK promoter activity by 40% ($n=4$) when compared to the activation by dexamethasone and CPT-cAMP in the FAO cells.*

***Conclusion.*** *Our results suggest that this TM possesses insulin-sensitising and insulin-mimetic activities. We are currently undertaking a chromatographic fractionation of the TM, and further studies will involve assessment for bioactivity in these fractions to identify effective components of this TM as potential source of novel compounds for treatment of type 2 diabetes. 1 Grovers R., et. al. Molecular Cell Biology. 2004, 24(14)6456*

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## PP 134

# The Influence of Diabetes Mellitus and Aging on Pulmonary Tuberculosis in Singapore

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***Background and Aims.*** *The incidence of pulmonary tuberculosis (PTB) is decreasing in Singapore, but it is still prevalent in the elderly. Although the prevalence of diabetes mellitus in adults has also decreased from 9% to 8.2% in the last 6 years its prevalence increases with age. This study aims to examine the clinical characteristics of patients admitted to a secondary hospital in Singapore with smear-positive pulmonary tuberculosis, especially the association of PTB with diabetes mellitus and increased age.*

***Materials and Methods.*** *Demographic and clinical records were reviewed for 79 patients admitted between 1999 and 2004 for PTB to the medical wards of Changi General Hospital in Singapore. In particular, data was collected on the prevalence and severity of diabetes mellitus, and severity of PTB as measured by radiographic and biochemical criteria. Statistical analysis was conducted using SPSS 10.0 for Windows.*

***Results.*** *Our patients were aged 19 to 78 years, with a mean of 52.1 years, and 26 (32.9%) were over 60 years of age. There were 34 (43%) diabetics. All patients had at least moderately advanced PTB, with more than half (43 patients, 54.4%) having far advanced disease.Far advanced PTB was significantly more prevalent in diabetic (20 of 34 patients, 58.8%) than in non-diabetic patients (16 of 45, 35.5%; p = 0.034). Tuberculosis was also more likely to involve the lower lobes (7 of 34 diabetics, 20.6%, compared to 3 of 45 non-diabetics, 6.7%; p = 0.017) and to be bilateral (10 of 34 diabetics, 29.4%, compared to 8 of 45 non-diabetics, 17.7%; p = 0.047) in diabetic patients.Among diabetic patients, most (23 patients, 67.6%) were on oral hypoglycaemic agents, with two on insulin and nine on diet control alone. The mean age of the diabetics (58.0 years) was higher than the mean age of non-diabetic patients (47.6%), though this difference was not statistically significant. The duration of diabetes ranged from newly diagnosed (6 patients) to 20 years, with a mean of 7.3 years. Five patients (14.7%) had fair glycaemic control (HbA1c 7-7.9%), and 13 (38.2%) had poorly controlled diabetes (HbA1c > 8%). The severity of PTB was not significantly associated with glycaemic control or the duration of treatment.There was a higher proportion of elderly patients (aged over 60 years) in our study population than in the general population of Singapore. Elderly patients were less likely to have fever (p = 0.015), and more likely to have dyspnoea (p = 0.012) and far advanced PTB (p = 0.043) than younger patients. Older patients were also more likely to have a longer duration of cough at presentation (p =0.017).*

***Conclusion.*** *Diabetes is more prevalent amongst PTB patients than the general population. In the presence of diabetes, PTB tends to be more severe and to present with atypical radiological features. Older patients with PTB tend to be afebrile. A high index of suspicion on the basis of our findings would facillitate earlier diagnosis in these 2 population groups who present with suggestive symptoms.*

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## PP 135

# Rabies Vaccine in Type 2 Diabetes

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***Background and Aims.*** *The number of diabetics increases worldwide including Thailand, one of the rabies' endemic areas. The most important life-saving measure for rabies is vaccination. Certain immune defects in diabetics such as T cell lymphocyte dysfunction and impairment in macrophage's phagocytosis can affect the immunogenicity of vaccines, especially protein vaccine. Since rabies is a life-threatening disease and its vaccine is also a protein, it is crucial to know the immunological response of rabies vaccine in diabetics.*
***Materials and Methods.*** *Thirty-three type 2 diabetics without other active illnesses were enrolled. All patients received three doses of 0.5 ml purified Vero cell rabies vaccine(PVRV) intramuscularly on day 0, 7 and 28. Rabies neutralizing antibody (Nab) titers were determined by the rapid fluorescent focus inhibition test(RFFIT) on day 0 (before vaccination), day 42 (2 weeks after vaccination) and 1 year post-vaccination. Nab titer of more than 0.5 IU/ml were considered acceptable for rabies protection.*
***Results.*** *The mean age was 47 years and 64 percents of the group were women. The mean diabetic duration was 7 years and 93 percents of patients had HbA1c more than 7%. There were 6.1 and 45.5 percents of macrovascular and microvascular complication in patient group, respectively. Subjects did not have neutralizing antibody before vaccination. All of them were able to develop protective antibody against rabies on day 42 (2 weeks after vaccination). Geometric mean titers(GMTs) of Nab were 20.8 IU/ml (range 2.0-92.5). At 1 year after vaccination, GMTs from 23 available patients were 2.3 IU/ml (range 0.4-8.6). One of these patients had the Nab titer below protective level. This patient was a 42-years-old-woman with diabetes for 9 years and microalbuminuria. In this study nobody had serious adverse reaction after vaccination.*
***Conclusion.*** *All diabetics had protective antibody at 2 weeks after intramuscular pre-exposure rabies vaccination. Mean antibody level was lower but still protective at 1 year after vaccination except one of 23 remaining patients whose the rabies neutralizing antibody level was not protective. Further studies are needed to determine the duration of protection and/or to evaluate efficacy of booster vaccination in diabetic patients.*

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## PP 136

# Caloric Restriction Reduces Oxidative Stress in Type 2 Diabetic Model Oletf Rats

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***Background and Aims.*** *Oxidative stress can cause cellular injury and tissue damage by promoting several cellular reactions, e.g. lipid peroxidation. Type 2 diabetes may be especially prone to acute and chronic oxidative stress which enhances the development of late diabetic complications. Previous studies have shown that restriction of caloric intake lowers steady-state levels of oxidative stress. The aim of this study was to evaluate the effect of low calory diet on oxidative stress in obese Type 2 diabetic OLETF rats and to compare it with the results obtained in non-diabetic rats.*

***Materials and Methods.*** *OLETF and LETO(genetic control for OLETF) rats were used. By applying caloric restriction(CR) at 30% below ad libitum levels for 3 weeks. The thiobarbituric acid reactive substance(TBARS) concentration, as an index of oxidative stress, and antioxidant enzyme activities were measured in liver and skeletal muscle.*

***Results.*** *Caloric restriction(CR) showed significant effect on reducing body weight and blood glucose concentrations in both rats($P<0.001$). The TBARS concentration significantly decreased by CR in liver of both rats. The activities of catalase and superoxide dismutase were enhanced by CR in liver of LETO rats. However, the changes of antioxidant anzyme activities in liver of OLETF rats were not shown significantly. In skeletal muscle, CR did not produce any significant effect on the TBARS concentrations and activities of antioxidant enzyme in both rats.*

***Conclusion.*** *This results suggest that caloric restriction can reduce oxidative stress regardless of the presence of diabetes, especially in liver.*

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