



Föderation der Internationalen  
**DONAU-SYMPOSIA**  
über Diabetes mellitus  
Zentraleuropäische Diabetesgesellschaft

**22. Symposium der Föderation der Internationalen  
Donau-Symposia über Diabetes mellitus**

**- 2. Zentraleuropäischer Diabeteskongreß -**

**22nd Symposium of the Federation of International  
Danube-Symposia on Diabetes Mellitus**

**- 2<sup>nd</sup> Central European Diabetes Congress -**

**Insel Kos, Griechenland, 07. – 09. Juni 2007**  
**Island of Kos, Greece, 07 – 09 June 2007**

**Prof. Dr. Helmut Schatz, Bochum**  
Präsident der Zentraleuropäischen Diabetesgesellschaft - FID

**Prof. Dr. Erifili Hatziagelaki, Athen**  
Tagungspräsidentin

## **Programm**

## **Abstracts**

## **Vorabdruck aus Diabetologie und Stoffwechsel Heft 4/2007**

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**Präsident:** Univ. Prof. Dr. H. Schatz, Universitätsklinikum Bergmannsheil der Ruhr-Universität Bochum, Bürkle- de-la-Camp-Platz 1, D-44789 Bochum. Tel: +49-234-302-6324, Fax: +49-234-302-6315, [helmut.schatz@rub.de](mailto:helmut.schatz@rub.de);  
**Vizepräsident:** Prof. Dr. V. Pirags, Clinic of Internal Medicine, P.Stradins University Hospital, Pilsonu iela 13, Riga, LV 1002. Tel: +37-1-9237760, Fax: +37-1-7069955, [pirags@latnet.lv](mailto:pirags@latnet.lv); **Sekretär:** Univ. Doz. Dr. R. Weitgasser, Univ.Klinik f. Innere Medizin I, Paracelsus Medizinische Privatuniversität Salzburg, Müllner Hauptstr. 48, A-5020 Salzburg. Tel: +43-662-4482-2802, Fax: +43-662-4482-3429, [r.weitgasser@salk.at](mailto:r.weitgasser@salk.at); **Beisitzer:** PD Dr. M. Füchtenbusch, München; Prof. Dr.E. Hatziagelaki, Athen; PD Dr. R. Lehmann, Zürich; Dr. habil.med. D. Moczulski, Zabrze; Univ. Prof. Dr. M. Roden, Wien; PD Dr. T. Temelkova-Kurtschiew, Sofia  
**Homepage:** [www.fid.at](http://www.fid.at) oder: [www.donausymposium.at](http://www.donausymposium.at) oder: [www.donausymposium.de](http://www.donausymposium.de)

## 22. Symposium der Föderation der Internationalen Donau-Symposia über Diabetes Mellitus

### 2. Zentraleuropäischer Diabeteskongress

## 22nd Symposium of the Federation of International Danube-Symposia on Diabetes Mellitus

### 2nd Congress of the Central European Diabetes Association

**Ort/Datum:** Insel Kos, Griechenland, 07.–09. Juni 2007  
Island of Kos, Greece, 07.–09. June 2007

Präsident der FID: Prof. Dr. Helmut Schatz  
Tagungspräsidentin: Prof. Dr. Erifilli Hatziagelaki

#### Begrüßung

**Liebe Mitglieder und Freunde der Zentraleuropäischen Diabetesgesellschaft – FID, sehr geehrte Damen und Herren!**

Herzlich möchte ich Sie zum 22.Symposium der FID, der Föderation der Internationalen Donau-Symposia über Diabetes mellitus, auf die Insel Kos einladen, welches zugleich den 2. Zentraleuropäischen Diabeteskongress darstellt. Ich freue mich, Sie in Griechenland als Präsident begrüßen zu können, in welchem Land unsere Gesellschaft nun zum zweiten Mal tagt. Ich danke allen, die durch ihr Erscheinen die Richtigkeit der Idee unterstreichen, uns jetzt anstatt alle 2 Jahre jährlich zu treffen. Der neue Zusatz zum bisherigen Vereinsnamen FID, „Zentraleuropäische Diabetesgesellschaft“ wurde auf vielfachen Wunsch auf der Mitgliederversammlung in Riga 2006 einstimmig beschlossen und ist jetzt im Vereinsregister in Wien eingetragen.

Innerhalb Europas existieren 3 größere regionale Diabetesvereinigungen. Unsere Gesellschaft besteht seit 1969 und hält ihre Kongresse vorwiegend auf Deutsch, aber auch mit Beiträgen in Englisch ab, eine weitere Gruppierung tagt in französischer Sprache, und seit 1985 gibt es auch eine „Mediterrane Gruppe zum Studium des Diabetes“.

Die Aktivitäten der Zentraleuropäischen Diabetesgesellschaft sollen den Gedankenaustausch und die Kooperation aller am Diabetes beteiligten und interessierten Berufsgruppen über die Grenzen der FID-Länder hinweg fördern. Zu diesen Ländern zählen jetzt auch die baltischen Staaten. Unsere Gesellschaft vergibt Reisestipendien für die Teilnahme an den Kongressen sowie Hospitationsstipendien für mehrmonatige Studienaufenthalte in anderen FID-Ländern. Die genauen Details finden sich auf unserer homepage: [www.fid.at](http://www.fid.at); oder [www.donausymposium.de](http://www.donausymposium.de).

In der FID vollzieht sich gerade ein Generationswechsel und jetzt haben die Jüngeren die Idee weiterzutragen. So veranstaltete im vorigen Jahr Herr Professor Valdis Pirags, Riga, als Tagungspräsident höchst erfolgreich das 21. Donausymposium in der Hauptstadt Lettlands, welches zugleich der 1. Zentraleuropäische Diabeteskongress war. Im Jahre 2007 liegt die Tagungspräsidentschaft in den Händen von Frau Professor Erifilli Hatziagelaki, Athen. Ich danke ihr herzlich für die große Mühe der Organisation. Sie hat ein hervorragendes Programm für die Tagung auf der Insel Kos erstellt. Ich bin sicher, und wir alle wünschen ihr und natürlich auch uns allen, dass der Kongress ein voller Erfolg wird.

Bochum, im Juni 2007

Prof. Dr. Helmut Schatz  
Präsident der FID

## Introduction

Dear Friends and Colleagues,

after an interlude of twenty years, it is with great pleasure that we welcome you once again to the **“22nd International Symposium of the Federation of the International Donau-Symposia of Diabetes Mellitus”**.

This occasion is of a celebratory nature, not only for us as hosts, but also for our scientific society, F.I.D., as this symposium is being held for the second time under its new name, the **“Congress of the Central European Diabetes Association”**.

Of course this name change scarcely affects either the content of Professor Alois Beringer's original idea back in Vienna in 1969, or the forty year tradition of the “Symposium of the Federation of the International Danube-Symposia”. At that time certainly, the symposia offered a unique occasion for German-speaking doctors from both sides of the iron curtain to meet. However, the idea of communication at a professional level, accompanied by the exchange of thoughts and experience between teams and groups active in the field of diabetes from several countries, remains just as opportune today in an increasingly united Europe. The river Donau might still be the symbol of the union between Central and Eastern Europe, but not of today's approach by the member states within the expanded European Union and of course, not just contained in the scientific field. “Central Europe” as a name and symbol, represents the centre of the circle of a united Europe and the objective of our scientific society is to extend and unify this circle over time.

For this reason, we intentionally selected the location for our symposium this year to be held at a site in the region of this circle – a site even further from the centre of the circle than the **1987 Symposium in Porto Carras**, near Thessaloniki. Moreover, the island of Kos, homeland of Hippocrates, the father of medicine, is one more reason why this selection constitutes a meeting point of old and contemporary, as well as a luminous point to remind us of the constant efforts of mankind to progress medical science.

Consequently, we have utilised all our efforts to make this **Symposium in 2007 in Kos** firstly a meeting place for experienced, well-known diabetologists, as well as younger, active and promising scientists and secondly, to offer everyone the opportunity to present and discuss the results of their continuous efforts in the field of research, with a special extended session of free abstracts.

The island of Kos is also a preferred holiday destination, providing exceptionally well organised hotel infrastructures, a great number of monuments from ancient and contemporary history, beautiful landscapes, splendid beaches and a plethora of local gastronomic pleasures.

For the first evening together (Gesellschaftsabend) we have planned an introductory journey of the ancient and present day history of this beautiful island. Accompanying members will also have the opportunity to visit one or more of the surrounding islands, such as the well-known island of Rhodes or the island of Nisiros with its active volcano.

We cordially invite you to the island of Kos for a unique and unforgettable experience in one of the most beautiful spots in Europe.

**Professor Erifili Hatziagelaki**  
President of the Congress

Programm	
Donnerstag, 7. Juni 2007	
12:30 – 14:00	<b>Industrie-Symposium</b>
14:00 – 15:00	Mittagspause
15:00 – 17:00	<b>1. Sitzung:</b> Jenseits des Typ-1 und Typ-2 Diabetes Vorsitz: E. Standl, München; G.A. Spinas, Zürich
15:00 – 15:30	Gene und Umwelt in der Pathogenese der $\beta$ -Zelldysfunktion und -zerstörung N. Stefan, Tübingen
15:30 – 16:00	Hyperglykämie bei Kindern und Jugendlichen – Differentialdiagnose, Weiterbehandlung und genetische Familienberatung O. Kordonouri, Hannover
16:00 – 16:30	Neue Konzepte zur Pathogenese und Therapie des Gestationsdiabetes M. Füchtenbusch, München
16:30 – 17:10	Diagnostik und Therapie des LADA W. Scherbaum, Düsseldorf – P. Pozzilli, Rom
17:10 – 17:30	Kaffeepause
17:30 – 19:30	<b>2. Sitzung:</b> Neuere Erkenntnisse für die Pathophysiologie und ihre Bedeutung für die Prävention des Typ 2 Diabetes. Vorsitz: J. Sieradzki, Krakau; V. Pirags, Riga
17:30 – 18:00	Ursachen und Folgen der Fettleber H.-U. Häring, Tübingen
18:00 – 18:30	Postprandiale Hyperglykämie: Warum, wann und wie behandeln? T. Temelkova-Kurktschiev, Sofia
18:30 – 19:00	Ergebnisse der DREAM- und anderen Studien der letzten Jahre zur Prävention des Diabetes und seiner Komplikationen V. Karamanos, Athen
19:00 – 19:30	Ernährungsaspekte in der Diabetologie A.F.H. Pfeiffer, Berlin
19:30 – 20:30	<b>Eröffnung:</b> H. Schatz, Bochum E. Hatzigelaki, Athen Grußworte <b>Festvortrag:</b> „Asklepios – Ippokrates – Asklepieia“ S. Geroulanos, Athen
20:30 – 21:30	<b>Generalversammlung</b>
ab 21:30	<b>Gesellschaftsabend</b> (Griechischer Abend)
Freitag, 8. Juni 2007	
09:00 – 11:30	<b>3. Sitzung:</b> Stellenwert der gegenwärtigen und kritische Analyse der neueren oralen Antidiabetika Vorsitz: R. Lehmann, Zürich; H. Mehnert, München
09:00 – 09:30	Orlistat, Acarbose und klassische Sekretagoga A. Kautzky-Willer, Wien
09:30 – 10:00	Metformin: Vom Teufel zum Engel G. Schernthaner, Wien
10:00 – 10:30	Die Rolle der Glitazone in der Prävention und Therapie des Typ 2 Diabetes M. Roden, Wien
10:30 – 11:00	Inkretin-Mimetika und Gliptine: Was steht fest, auf was kann man hoffen? J. B. Gallwitz, Tübingen
11:00 – 11:30	Kaffeepause
11:30 – 14:00	<b>4. Sitzung:</b> Insulinersatztherapie und ihre Überwachung Vorsitz: S.A. Raptis, Athen; H. Schatz, Bochum
11:30 – 12:00	Vorteile der langwirkenden Insulinanaloge. Klinische Studien und Metaanalysen K. Kantartzis, Athen
12:00 – 12:30	Inhalatives Insulin – wann inhalieren statt spritzen? H. Schatz, Bochum
12:30 – 13:00	Pumpentherapie und kontinuierliche Blutglukosemessung: Wie weit sind wir noch vom closed-loop-künstlichen Pankreas entfernt? R. Weitgasser, Salzburg
13:00 – 13:30	Fortschritte der Pankreas- und Inseltransplantation M. Brendel, Gießen
13:30 – 14:00	Therapie zur Betazellregeneration – Perspektiven. R.G. Bretzel, Gießen
14:00 – 15:00	Mittagspause
15:00 – 16:00	<b>Posterbegehung</b> Vorsitz: E. Hatzigelaki, Athen; D.Moczulski, Lodz, K. Kantartzis, Athen
16:00 – 17:00	<b>Debate:</b> Vorsitz: W. Waldhäusl, Wien; A. Alaveras, Athen Metabolic Syndrome: Myth or Reality? E. Standl, München; E. Gale, UK
17:00 – 17:30	Reduction of the cardiometabolic risk by rimonabant, a specific antagonist of CB1 receptors A. Scheen, Belgien
19:30 – 21:00	<b>Aufführung im antiken „Asklipion“-Theater von Kos</b>
ab 21:00	<b>Gala Dinner</b>
Samstag, 9. Juni 2007	
10:00 – 12:30	<b>5. Sitzung:</b> Pathogenese, Prävention und Behandlung der diabetischen Folgeerkrankungen Vorsitz: N. Katsilambros, Athen; I. Klimes, Bratislava
10:00 – 10:30	Klinische Aspekte der diabetischen Retinopathie I. Vergados, Athen
10:30 – 11:00	Fortschritte in der Therapie der Nephropathie und der arteriellen Hypertonie bei Diabetikern I. Stefanidis, Larissa
11:00 – 11:30	Proteinstoffwechsel bei Typ-2-Diabetes P. Halvatsiotis, Athen
11:30 – 12:00	Neue Erkenntnisse für die Behandlung der Dyslipidämie A.G. Yalouris, Athen
12:00 – 12:30	Diagnose und Behandlung der diabetischen Neuropathien N. Tentolouris
12:30	<b>Einladung</b> zum 23. Internationales Donausymposium über Diabetes mellitus – Zentraleuropäischer Diabeteskongreß 2008 – T. Temelkova-Kurktschiev, Sofia

## Abstracts

1

**High postprandial blood glucose is associated with prevalent cardiovascular disease independent of HbA1c in well controlled type 2 diabetic patients**

Brix J, Feder A, Krzyzanowska K, Mittermayer F, Scherthaner G  
 Department of Internal Medicine I, Rudolfstiftung Hospital, Vienna, Austria

**Background/Aims:** HbA1c is a well known predictor for diabetic complications. Postprandial blood glucose levels were also discussed to be responsible for the occurrence of cardiovascular events in patients with type 2 diabetes (T2DM). In the present study we investigated if high postprandial blood glucose levels are associated with the prevalence of cardiovascular disease (CHD, PAD, previous MI, previous stroke) independent of HbA1c levels. **Methods:** We included 431 patients with T2DM (mean age 61 yrs., 196 female) in a cross-sectional study. Blood glucose levels (2 hours postprandial) and HbA1c were measured by standard procedures. Patients were allocated to six different groups according to tertiles of HbA1c. Group 1 (n=51): HbA1c <6.9%, glucose <140 mg/dl; Group 2 (n=90): HbA1c <6.9%, glucose >140 mg/dl; Group 3 (n=53): HbA1c =6.9% and <8.2%, glucose <140 mg/dl; Group 4 (n=85): HbA1c =6.9% and <8.2%, glucose >140 mg/dl; Group 5 (n=28): HbA1c =8.2%, glucose <140 mg/dl and Group 6 (n=124): HbA1c =8.2% and glucose >140 mg/dl. In each group the prevalence of cardiovascular disease was assessed. Furthermore total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides and creatinine were measured. **Results:** Cardiovascular disease was reported in 5.9% of the patients in group 1, 70.0% in group 2 (P<0.001 vs. group 1), 28.3% in group 3 (P=0.003), 25.9% in group 4 (P=0.004), 25.0% in group 5 (P=0.015) and 29.0% in group 6 (P<0.001). According to a logistic regression analysis an increase of postprandial glucose by 1 mg/dl was associated with an odds ratio of 1.007 (95%CI: 1.001 – 1.012; P=0.014) for the prevalence of cardiovascular disease after adjustment for age, sex, HbA1c, antidiabetic treatment, systolic blood pressure, triglycerides and LDL-cholesterol. **Conclusions:** Postprandial blood glucose levels >140 mg/dl are associated with a high prevalence of cardiovascular disease independent of HbA1c, suggesting that the postprandial glucose could play a more important role for cardiovascular disease than HbA1c in well controlled type 2 diabetic patients.

2

**APGAR scores are lower in offspring from mothers with type 1 diabetes – results from the BABYDIAB study**

Füchtenbusch M, Hummel M, Knopff A, Wentzel A, Bonifacio E, Ziegler A  
 3<sup>rd</sup> Medical Department, Schwabing Hospital, Munich, Germany

Infants born to women with type 1 diabetes (T1D) are at increased risk of neonatal morbidity. Intrapartum monitoring is therefore essential to minimize complications. We analyzed APGAR scores after 5 and 10 min. in BABYDIAB offspring from mothers with T1D (n = 1047) compared to offspring from non-diabetic mothers whose partners had T1D (n = 592). Sectio rates in mothers with T1D were increased more than two-fold (48.1%) compared to mothers w/o T1D (21.4%, p < 0.0001). 16 of 927 offspring (1.7%) suffered from initial asphyxia as defined by an APGAR (5') < 7. Neonates from mothers with T1D had lower mean APGAR scores compared to offspring from non-diabetic mothers (p < 0.0001). Translated into clinical practice, that was a lower rate of maximally good APGAR scoring of 10 (47%) in children from mothers with T1D compared with offspring from non-diabetic mothers (71.8%, p < 0.0001) while rates of early asphyxia were not different (1.9% vs. 1.7%). Since mean APGAR scores were decreased in offspring delivered by sectio compared with neonates born spontaneously (p < 0.0001), APGAR scores by maternal diabetes status were controlled for the mode of delivery. Again, rates of low APGAR 5' scores were higher and rates of maximally good scores lower both in offspring from diabetic mothers delivered by sectio and in children born spontaneously compared to offspring from non-diabetic mothers (p < 0.034, p < 0.0001). HbA1c levels at delivery were slightly higher in mothers who gave birth by sectio (5.86%) compared to mothers who delivered spontaneously (5.69%, p < 0.035). Mean APGAR5 scores were also lower in offspring from mothers with elevated HbA1c levels when comparing HbA1c-subgroups defined by an HbA1c >8% vs. 7–8% vs. 6–7% vs. 5–6%, p < 0.007, Kruskal-Wallis). In con-

clusion, offspring of mothers with well controlled T1D may not be at risk of severely compromised vitality at birth, however, they less often score maximum points on the APGAR scale compared to offspring from non-diabetic mothers.

3

**Protein array reveals different protein levels in subcutaneous adipose tissue of patients with growth hormone deficiency in adulthood**

Gasperičková D<sup>1</sup>, Ukropec J<sup>1</sup>, Penesová A<sup>1</sup>, Skopkova M<sup>1</sup>, Vlček M<sup>1</sup>, Radiková Z<sup>1</sup>, Belan V<sup>2</sup>, Pura M<sup>3</sup>, Payer J<sup>4</sup>, Eckel J<sup>5</sup>, Klimes I<sup>1</sup>

<sup>1</sup>Institute of Experimental Endocrinology, Bratislava, Slovakia, <sup>2</sup>Department of Radiology, Faculty Hospital, Bratislava, Slovakia, <sup>3</sup>National Institute for Endocrinology and Diabetes, Lubochna, Slovakia, <sup>4</sup>V. Clinic of Internal Medicine, Faculty Hospital, Bratislava, Slovakia, <sup>5</sup>German Diabetes Center, Dusseldorf, Germany

The role of adipose tissue adipocytokines for development of the growth hormone deficiency (GHD)-related metabolic derangements has not yet been completely understood. Therefore, we screened the protein level of 120 adipokines in subcutaneous adipose tissue (ScAT) of patients with GHD in adulthood. **Subjects and methods:** Sixteen GHD (10 M/6 F) with BMI: 27 ± 1.0 kg/m<sup>2</sup>, age 30 ± 2 yrs and sixteen controls matched for BMI, sex and age were included into the study. ScAT biopsies were performed after an overnight fast. Protein expression of adipokines was determined in tissue lysates using the RayBio® Human Cytokine Antibody Array C Series-1000. **Results:** GHD subjects had higher waist circumference, hsCRP levels and impaired glucose tolerance. From 120 proteins, one showed to have higher (IGFBP-1) and three (BDNF, NT-3, SDF-1) lower levels in ScAT of the GHD subjects in comparison with controls (p < 0.05). Interestingly, multiple regression analysis revealed that some adipocytokines were associated mainly with GHD and independent on obesity (IGFBP1, b-NGF, TIMP-2, Interferon-gamma, MCP-4, IGF-1, p < 0.05). **Conclusions:** Our data provide the first information on specific changes in the ScAT adipokine protein levels in GHD adults. Moreover, they implicate a different regulation of cytokine ScAT levels in a comparable inflammatory setting, i.e. in equally obese subjects who differ in their metabolic status. *Supported by: APVV-51 – 0406/02 and VEGA 2/7110/27.*

4

**Macular edema treatment in patients with diabetes mellitus**

Gavala C, Kyriakopoulos N, Georgantis I, Patiakas S, Tsoukis E, Aggos I, Kambanis I  
 General Hospital of Kos, Greece

**Background-Aims:** Diabetic maculopathy is the major cause of the loss of sight in the progress of diabetic retinopathy. It is usually divided into edematous and ischemic forms. Macular edema (ME) is verified in the 10% of the diabetic patients with an increase of the 25% if the diabetic disease lasts for more than 20 years. The ME can be: "focal" or "diffuse". According to our and EDTRS experience, the presence of ME constitutes an indication to the laser treatment with photocoagulation; the most diffusely methods used are "focal" and "grid" (scattered) techniques. The focal technique appears more indicated in the treatment of localized edema, while the grid one is more useful when the ME is diffused. **Material-Method:** Our study, one-year-long, has valuated 55 eyes of 35 patients with ME diffused and they were all treated with green-Argon laser. **Results:** The follow-up has given good results both in functional and both morphologic points of view. However, a good control of the metabolism, blood pressure and the cardiac and renal dysfunctions must be considered as a complementary measurements to the photocoagulation. **Conclusions:** We have notice that the functional result does not correspond to the anatomic one, valuable from both ophthalmoscopic and fluorescein angiography condition. That is the reason why we observe an improvement of the edema even in the absence of the visual improvement.

5

**Agoraphobic behavior in diabetics – iatrogenic agoraphobia**

Heras P, Kritikos K, Hatzopoulos A, Safarikas M, Mitsibounas D

Hellenic Medical Society for the Study of Psychosomatic Problems, Athens, Greece

The aim of this study was to estimate the prevalence rate of agoraphobic behaviour in diabetics, the mechanism of agoraphobic arousal and the possibilities of the therapeutic intervention. **Patients and Method** Sample consisted from 53 individuals suffering from diabetes mellitus/DM/:

Insulin-dependent DM (E10)	19	35.8%
Non-Insulin-dependent DM (E11)	34	64.2%

Male: 25 (47.2%) Female: 28 (52.8%) Average age (years): 59.13 ± 12.4 Max: 78 years Min: 26 years The psychosomatic team explored the in patients at the Internal Clinic, in the order of the admission, during the course of diagnostic procedures by the referral physician, in the period of 1.1.98.-15.2.98. We used the following scales: BPRS, SCID, (ICD 10 or DSM In anxiety and phobic disorder/agoraphobia/CheckList of Symptoms (ICD 10), ZUNG and HAMA. **Results** A kind of anxiety disorder was found in 60.4% diabetics:

F40	F41	F41.1	F40.0
E10	64.8%	32.9%	31.8%
E11	52.6%	21.1%	31.5%

The cause of agoraphobia's high frequency is in cognitive learnt fear. Therefore the authors suggest naming this entity: IATROGENIC AGORAPHOBIA. Iatrogenic agoraphobia is considered as the outcome of careless advising by physician concerning the restrictions in behavior or inadequately balanced medication (hypoglycemia).

6

**Cholelithiasis in diabetes mellitus**

Heras P, Hatzopoulos A, Kritikos K, Mitsibounas D

Hellenic Medical Society for the Study of Psychosomatic Problems, Athens, Greece

The aim of this study was to elucidate the factors precipitating to the increased prevalence of cholelithiasis in adult subjects with diabetes mellitus (DM). **Patients and Method** 800 subjects (480 males and 320 females) with DM, 35 – 70 years old, consecutively, hospitalized in our Department last 5 years, were prospectively investigated. **Results** Among the 800 patients, Insulin-dependent (IDDM) was present in 160 (20%) subjects and 14 (15%) of them presented cholelithiasis (CL), whereas among the 640 (80%) non-insulin dependent DM (NIDDM) patients, CL was found in 160 (25%). The difference between the 2 CL prevalences is statistically significant ( $p < 0.01$ ). Overall 174 of the DM patients had CL (21,75%). 75 of these patients had gallstones and 99 had a history of previous cholecystectomy. Among the DM patients, 105 (60,3%) were females, 80 (46,7%) had obesity, 120 (68,9%) were over 50 years old and 75 (43,1%) had a duration of DM over 10 years. **Conclusion** In our study, the factors which seem to determine the increased prevalence of CL in DM, are: NIDDM, female sex, obesity, age over 50 years and duration of DM up to 10 years.

7

**Diabetics identification in front of medical power**

Heras P, Hatzopoulos A, Kritikos K

Hellenic Medical Society for the Study of Psychosomatic Problems, Athens, Greece

**Background** IDD of young people is a constraining chronic illness which concerns every day and definitively the whole patient's personality, and needs education and a severe treatment. **The aim** of this work was to evaluate the relative power of a directive physician facing a patient he would like to be active. **Patients and Methods** 31 IDD patients, 15 to 45 years old, diabetics from childhood or adolescence were personally observed and followed at consultation in a prospective hermeneutic work. The patients were submitted to an open questionnaire including data about IDD and its treatment, story and patient's life with diabetes since the onset, in order to evaluate the patient's relationship to himself, to his illness and the physician. **Results** Four major themes were collected from the questionnaires: 1)-an hermeneutic work for patient identification and the problem of temporality. 2) the patient's health feeling as regards the society and the physician's illness idea. 3) the symbol of

medical power and the physician's fragility in front of that identity work, which acts against medical and intrusion power. 4) the ontologic aim, i.e. the patient's behavior evolution towards his diabetes and his physician. This hermeneutic work is a constant exchange and a reciprocal relation of esteem and listening between the patient and the physician. It represents a kind of ethical choice for both of them. It thus restores some power to the patient which limits the medical power and allows a better participation in his health. It allows the physician to play a role as a health agent and define new responsibilities. **In conclusion** we suggest that IDD patients adhere to a therapeutic project only if they get a self-esteem, good enough to accept their diabetes – and their treatment.

8

**Effectiveness of calcium antagonists in early diabetic nephropathy**

Heras P, Kritikos K, Hatzopoulos A

Hellenic Medical Society for the Study of Psychosomatic Problems, Athens, Greece

To examine the effectiveness of calcium channel antagonists in the early primary prevention of diabetic nephropathy we enrolled, for a 23 months study, 38 type II diabetic patients of mean age 55 ± 7 years, normotensive (BP. 132 ± 8/78 ± 8 mm Hg) and without pathological microalbuminuria (MA) (23 ± 6 mg/min), in good metabolic control (HbA1c < 9%). On account of the well-established effectiveness of ACE inhibitors in the preservation of the renal function in diabetics, patients (pts) were randomized into 3 treatment groups: 1) Reduced dietary protein and phosphate intake+placebo; 2) idem+lisinopril 5 mg/die; 3) idem+lacidipina 4 mg/die. Markers of renal function were considered B.P and MA. B.P, MA, and HbA1c were evaluated every 4 months. In spite of not significant differences in HbA1c, at the end of the study resulted a statistically significant elevation of mean diastolic B.P. ( $P < 0,03$ ) and MA ( $p < 0,05$ ) in pts of group 1 (D.B.P.84 ± 6 mm Hg; MA 49 ± 13 mcg/min) vs. pts of both group 2 (D.B.P.78 ± 7 mm Hg; MA 31 ± 11 mcg/min) and 3 (D.B.P.78 ± 8 mm Hg; MA 32 ± 13 mcg/min) while not significant differences in mean B.P. and MA. were established between group 2 and 3. Calcium channel blockers and particularly lacidipina seems to be as usefull as ACE-inhibitors to prevent renal damage in type II diabetic patients since its early stages.

9

**Effects of calcium antagonists on insulin secretion**

Heras P, Hatzopoulos A, Kritikos K, Mitsibounas D

Hellenic Medical Society for the Study of Psychosomatic Problems, Athens, Greece

**Aim** Citolic calcium levels influence glucose-stimulated insulin secretion. In vitro studies have shown that calcium antagonists can inhibit insulin secretion and thus to alter glucose metabolism. **The aim** of our work was to study if long-term calcium-antagonists treatment alters insulin secretion in vivo. **Patients and Methods** Two groups of essential hypertensive patients were studied: one with obesity ( $n = 18$ ) and the other one without obesity ( $n = 8$ ). All of the patients had normoglycose tolerance and no family history of diabetes mellitus. All patients underwent a frequently sampled intravenous glucose tolerance test for 180 minutes (FSIVGTT). The obese group was placed on Diltiazem (360 mg/d) and the group without obesity on Nitrendipine (20 mg/d), for 12 weeks, and the FSIVGTT was repeated. Insulin secretion was calculated as the area under the curve. **Results** Patients placed on Nitrendipine did not show any significant difference neither in fasting insulin (11 ± 5 vs. 9 ± 5, µU/mL) nor in total insulin secretion (3273 ± 1458 vs. 3114 ± 1220, µU/mL.min). The peak of insulin was similar (66 ± 27 vs. 72 ± 22, µU/mL). Patients placed on Diltiazem did not show any significant differences neither in fasting insulin (17 ± 9 vs. 17 ± 9, µU/mL) nor in total insulin secretion (6052 ± 3096 vs. 5698 ± 3319, µU/mL.min). The peak of insulin was also similar (112 ± 99 vs. 118 ± 87, µU/mL). Moreover, both calcium antagonists did not cause delay on insulin secretion, and we did not find any significant difference in C-peptide levels. **Conclusions** Our data suggest that calcium-antagonists do not impair intravenous glucose-stimulated insulin secretion in vivo.

10

### Effects of hyperinsulinemia on left ventricular (lv) structure and function in the elderly

Heras P, Hatzopoulos A, Kritikos K, Mitsibounas D  
Hellenic Medical Society for the Study of Psychosomatic Problems, Athens, Greece

The aim of the present study was to evaluate the effects of hyperinsulinemia on left ventricle in the elderly. **Patients and Method** 37 hypertensives, 17 male/20 female, age range 50–85 yrs were compared with 17 normotensives controls of the same age and obesity. LV mass was evaluated echocardiographically according to the Penn's Convention. A 75 g OGTT was performed after an overnight fasting, and both glycemia and insulinemia were assayed basally and after each 30 min in the first three hours. Comparison between groups was performed by analysis of variance.  $P < 0.05$  was considered statistically significant. **Results** Hyperinsulinemic patient (2hr postloading plasma insulin above the median value) presented an increased LV mass index (+18%,  $p < 0.05$ ) and septal thickness, (+11.5%  $p < 0.05$ ), when compared with subjects with lower insulinemia. In addition, LV systolic function was better in hyperinsulinemic patients (ejection fraction and shortening fraction +14%  $P < 0.0001$  for both parameters). **In conclusion**, hyperinsulinemia is associated with both increased LV mass and contractile performance in the elderly.

11

### Heart rate variability in diabetic patients

Heras P, Hatzopoulos A, Kritikos K  
Hellenic Medical Society for the Study of Psychosomatic Problems, Athens, Greece

**Purpose** Heart rate variability (HRV), i.e. the fluctuations of the heart rate through the average heart rate, is a useful tool to study the autonomic nervous system function and yields important information about the balance between the parasympathetic and sympathetic systems. Abnormalities of HRV have been described in several groups of patients, mainly those with cardiovascular and neurological diseases, and in diabetes mellitus. The aim of the present study is to analyze the HRV in a group of diabetic patients without heart disease and to compare it with a control group. **Patients and Method** The study group comprised 33 diabetic patients (21 men and 12 women) with a mean age of 43,9 years old (range: 18–67). Every patient underwent a thorough clinical examination, blood tests and urinalysis, Doppler – echocardiography and a 24-hour Holter recording. Ischemic and valvular heart disease and left ventricular dysfunction were ruled out. An analysis was performed in the time domain [mean (M), standard deviation (SD) and the number of adjacent cycles  $> 50$  msec apart (ND) and in the frequency domain low (LF), middle (MF) and high (HF)] in the moments of highest and lowest HR during activity and night rest periods. The control group comprised 33 healthy persons watched for age and sex with the study group. **Results** The mean of the R-R intervals did not differ between the diabetic and the control groups. SD was significantly different in both groups during the activity period. ND was significantly different during the activity period and during the time of the highest HR of the night rest period. LF was significantly different during the time of the lowest HR in the night rest period. HF was significantly different in both groups during the activity period. HF was significantly different during the time of the lowest HR in the activity period. **Conclusions** Although the mean heart rate was not different in the diabetic and the control groups, several differences were found in statistic (SD and ND) and spectral (LF, MF, HF) parameters. HRV in diabetics without evidence of heart disease is different to the HRV in healthy persons without diabetes.

12

### Postural instability neuropathic subjects at risk of foot ulceration

Heras P, Hatzopoulos A, Kritikos K  
Hellenic Medical Society for the Study of Psychosomatic Problems, Athens, Greece

Diabetic peripheral neuropathy is believed to cause postural instability due to abnormal proprioception. We therefore assessed body sway in 4 groups of patients matched for age and sex: Group A: normal healthy controls (n=9); B: non-neuropathic diabetic subjects (n=9); C: diabetic neuropathy (n=14) and C: diabetic neuropathy + foot ulcer history (n=11). Postural sway control was assessed on a Kistler force plate using a Romberg test, measuring the standard deviation of the centre of pressure in both sagittal and frontal planes on 2 occasions, with the eyes open and closed. Analysis of variance was used to assess inter-group

difference. Significantly greater instability was observed in the foot ulcer group (D) compared with all other groups in all studies: eq:- frontal plane, eyes open: A 3.4 mm, B 3.3, C 3.8 and D 6.2 ( $p < 0.05$ ). Sagittal plate, eyes closed:- A 5.6 mm, B 5.8, C 6.9 and D 12.6 ( $p < 0.05$ ). These results are strongly indicative of an effect of severe neuropathy, as present in foot ulcer patients, on body sway control, that could result from loss of proprioception and/or motor weakness. Such instability is likely to have clinical significance and may increase the risk of minor trauma and ulceration.

13

### Psychological structure of the patients with diabetic polyneuropathy

Heras P, Hatzopoulos A, Safarikas M, Argyriou A, Mitsibounas D  
Hellenic Medical Society for the Study of Psychosomatic Problems, Athens, Greece

We multidisciplinary investigated 44 patients, who were admitted in the Department of Internal Medicine by the internist, neurologist and psychiatrist. The diagnosis of the polyneuropathy was given on the ground of the neurologists exploration. These patients were divided in two groups, both with 22 patients, experimental group with polyneuropathy and control group without polyneuropathy. The psychological structure of these patients was followed continually by the semistructured interview with 32 items in connection with the origin, course, treatment and psychological acceptance of diabetes. The assessment was also made with Zung Depression Scale, MMPI, and Analog Scale for Measuring Pain. It was found that degree of the neurotic expression on MMPI, Zung scale and interview were in the direct proportion with the degree of the pain experience in the experimental and control group. Pain experience was found in 32% of the control group without polyneuropathy. Specially high scores were found on the depression, paranoid and social introversion scales. The objective assessment of polyneuropathy which was checked by the EMG methods, is not in the same ratio with the degree of the neurotic scores and pain experience, what was in total contrast to our expectations.

14

### Die nichtalkoholische Fettlebererkrankung (NAFLD) ist mit einer qualitativen Änderung der HDL Lipoproteine und deren Fettsäuremuster assoziiert

Kantartzis K, Rittig K, Alexander C, Thamer C, Machann J, Balletshofer B, Fritsche A, Schleicher E  
Universitätsklinikum Tübingen, Abteilung Innere Medizin IV

**Einleitung:** Die nichtalkoholische Fettlebererkrankung (nonalcoholic fatty liver disease, NAFLD) und die Atherosklerose sind eng miteinander assoziiert. Als mögliche Erklärung dafür gelten u.a. eine quantitative Änderung der Serumlipide, z.B. erniedrigtes HDL-Cholesterin (HDL-c) und erhöhte Triglyzeride, und ein erhöhter Anteil kleiner, dichter LDL-Partikel. Ob eine qualitative Änderung der Serumlipide ebenfalls eine Rolle spielt, ist nicht bekannt. Da vor allem ein hoher HDL2-c Spiegel im Serum vor Atherosklerose schützt und die Anteile der HDL2-c und HDL3-c Spiegel im Serum von der Leber bestimmt werden, untersuchen wir, ob NAFLD mit einer Änderung der HDL-Subfraktionen und deren Fettsäuremuster vergesellschaftet ist. **Methoden:** In 37 gut phänotypisierten Probanden wurde das Leberfett mittels  $^1\text{H}$ -Kernspinspektroskopie und die HDL2-c und HDL3-c Spiegel nach der Trennung mit Ultrazentrifugation gemessen. Das Fettsäuremuster in den Subfraktionen wurde mittels Dünnschicht- und Gas-Chromatographie bestimmt. NAFLD ist als Leberfettgehalt  $\geq 5,5\%$  definiert. **Ergebnisse:** Menschen mit NAFLD haben erniedrigte HDL2-c Spiegel und einen erniedrigten HDL2-c:HDL3-c Quotienten im Serum ( $p=0,001$  bzw.  $p=0,0001$ ) im Vergleich zu gesunden Kontrollen. Wie erwartet, war das Leberfett negativ mit dem gesamt - HDL-c assoziiert ( $r=-0,47$ ,  $p=0,003$ ). Stärker jedoch war die Assoziation mit HDL2-c ( $r=-0,56$ ,  $p=0,0003$ ) und mit dem HDL2-c:HDL3-c Quotienten ( $r=-0,61$ ,  $p < 0,0001$ ). Adjustiert für Geschlecht, Alter und Körperfett, korrelierte das Leberfett weniger stark mit dem gesamt - HDL-c ( $r=-0,40$ ,  $p=0,02$ ), aber weiterhin sehr stark mit dem HDL2-c:HDL3-c Quotienten ( $r=-0,54$ ,  $p=0,001$ ). Außerdem war der Gehalt an ungesättigten Fettsäuren in der HDL2 Fraktion höher als in der HDL3 Fraktion ( $p < 0,0001$ ) und Probanden mit NAFLD haben somit einen verminderten Anteil an ungesättigten Fettsäuren in den HDL Partikeln. **Schlussfolgerung:** NAFLD hängt nicht nur mit einer quantitativen Verminderung, sondern auch mit einer qualitativen Änderung der HDL Lipoproteine und deren Fettsäuremuster zusammen. Das

deutet auf einen neuen pathophysiologischen Link zwischen NAFLD und Atherosklerose hin.

15

### Können wir der Knöcheldruckmessung bei Diabetikern vertrauen?

Kasalova jr Z, Kasalova Z, Krupicka J  
Tschechische Republik

Die Knöcheldruckmessung und anschließende Berechnung des Knöchel-Arm-Druckindex ist eine einfache, nichtinvasive, routinemäßig vielfach eingesetzte Methode zur Beurteilung der Schwere der peripheren arteriellen Verschlusskrankheit (pAVK). Bei Diabetikern ist die Inzidenz der pAVK hoch. Gerade bei diesen kann jedoch die Genauigkeit der Knöcheldruckmessung durch die Anwesenheit der Mediakalkinose beträchtlich verzerrt werden. Die Ergebnisse können im Falle extrem hoher Druckwerte an den rigiden Arterien völlig unplausibel sein, bei manchen Patienten können sogar im Gegenteil falsch normale Ergebnisse bei schwerwiegend verengten Gefäßen vorkommen. Unsere Arbeit stellt die Ergebnisse der Knöchel- und Zehendrücke bei Diabetikern gegenüber. **Patienten und Methodik:** 58 Extremitäten von 29 Diabetespatienten im Durchschnittsalter von 64 J. wurden untersucht. Gleichzeitig wurden bei Allen die Zehendrücke plethysmographisch und Knöcheldrücke mittels Dopplersonde gemessen. **Ergebnisse:** Bei Untersuchung von 13 Extremitäten waren die Knöcheldrücke extrem hoch, d. h. unplausibel, wegen der Mediakalkinose. In 24 Fällen wurden hochgradige Verengungen mit beiden Methoden nachgewiesen. In 10 Fällen wurden normale Knöcheldruckwerte bei gleichzeitig bedeutsam herabgesetztem Zehendruck gefunden, was auf eine hochgradige arterielle Verengung hindeutet. Lediglich in 3 Fällen wurden extrem hohe, auf Mediakalkinose hinweisende Druckwerte mit beiden Methoden gefunden. **Folgerung:** Aus unseren Ergebnissen kann abgeleitet werden, dass die Anwesenheit der Mediakalkinose bei pAVK bei Diabetikern zur unplausiblen Knöcheldruckwerten führen kann. Es ist daher von Vorteil, den Zehendruck zu messen, weil die Zehenarterien nur selten von Mediokalkinose betroffen werden.

16

### Die Steifigkeit der arteriellen Gefäßwände weist eine Korrelation mit oxidierten kleinen und dichten LDL (ox-LDL)-Molekülen bei Patienten mit Typ-2 Diabetes auf

Walu-Miarka M, Katra B, Fedak D, Czarnecka D, Idzior-Walu B, Sieradzki J  
Department of Metabolic Diseases Jagellonian University Cracow, Poland

Die erhöhte Steifigkeit der arteriellen Gefäßwände wird häufig bei Patienten mit Typ-2 Diabetes (DM2) festgestellt. Es wurde gezeigt, dass diese Gefäßveränderung einen Risikofaktor der Krankheiten des Herz- und Kreislaufsystems darstellt. Das Ziel der Arbeit war die Bestimmung der Zusammenhänge zwischen der Steifigkeit der arteriellen Gefäßwände und Typ-2 Diabetes. **Material und Methode:** Die Studie umfasste 55 Patienten mit Typ-2 Diabetes. Die Untersuchung wurde ambulant durchgeführt. Die Nachgiebigkeit der Schlagadern wurde anhand der Messungen der Pulswellengeschwindigkeit (PWV = pulse wave velocity) in den Oberschenkel- und Halsschlagadern (Mittelwert aus 20 Messungen) bewertet. Die Messungen wurden mithilfe des automatischen Fühlers (Fukuda) und eines Nachgiebigkeitssystems durchgeführt. Die Gesamtmenge des Fettgewebes sowie der Prozentsatz des viszeralen Fettgewebes wurden mithilfe der DEXA-Technik bestimmt. Die Serumfettwerte wurden mit der enzymatischen Methode bestimmt; Homocystein, P-Selektin und TGF $\beta$ -1 mit der ELISA-Methode, ox-LDL mit der ELISA-Methode unter Verwendung der Mercodia-Reagenzien. **Ergebnisse:** Das mittlere Alter der Studienpatienten betrug: 59 +/- 9 Jahre, Diabetesdauer: 9 +/- 6,8 Jahre, HbA1c-Niveau 7,3 +/- 1,6%. Das mittlere Cholesteroll-Niveau LDL: 2,9 +/- 1,4 mmol/l, HDL-Cholesteroll: 1,2 +/- 0,4 mmol/l. Das mittlere Niveau von ox-LDL: 52,9 +/- 16,8 mU/L. Mittelwert von PWV betrug: 11,5 +/- 2,3 m/sek. Es wurde gefunden, wie es zu erwarten war, dass eine Korrelation zwischen der Pulswellengeschwindigkeit und dem Alter der Patienten ( $r=0,52$ ,  $p<0,0007$ ) sowie dem systolischen Blutdruck ( $r=0,49$ ,  $p<0,003$ ) besteht. Unter den untersuchten Risikofaktoren wurde eine Korrelation zwischen dem PVW-Wert und dem LDL-Cholesteroll-Niveau ( $r=0,41$ ,  $p<0,05$ ), ox-LDL ( $r=0,40$ ,  $p=0,009$ ) sowie der Gesamtmenge des Fettgewebes ( $r=0,39$ ,  $p=0,032$ ) festgestellt. Es wurde kein Zusammenhang zwischen der PVW, der metabolischen Kompensation (HbA1c), anderen biochemischen Parametern, oder dem Prozentsatz des viszeralen Fettgewebes nachgewiesen. Die erzielten Er-

gebnisse weisen darauf hin, dass die Steifigkeit der arteriellen Gefäßwände bei Patienten mit Typ-2 Diabetes eine Korrelation mit atherogenen LDL-Cholesteroll-Molekülen, ox-LDL und mit der Gesamtmenge des Fettgewebes im Organismus aufweist. Diese Ergebnisse bestätigen, wie wichtig das Anstreben einer Verminderung des LDL-Cholesteroll-Niveaus in dieser Patientengruppe ist. Die Verminderung des ox-LDL-Niveaus sowie die Reduktion der Menge des Fettgewebes können auch eine wichtige Rolle bei der Prävention der Steifigkeit der arteriellen Gefäßwände bei Patienten mit Typ-2 Diabetes spielen.

17

### Assessing the correlation between diabetes mellitus cardiovascular risk factors and coronary disease

Akritopoulos P, Akritopoulou K, Fotiadis E, Patiakas S, Kontogiannis I, Kiriakopoulos N, Aggos I, Tsoukis E  
Department of experimental pharmacology, Medical school of Aristotle's University of Thessaloniki, Greece

**Aim** Of this study was to investigate if cardiovascular risk factor (smoking, obesity, pathological values of blood lipids, hypertension) are predispositional factors of morbidity of Diabetes Mellitus (D.M.) and if there is a correlation between D.M. and coronary disease. **Material-Method** We examined a representative sample of greek adults who attended the General Hospital of Goumenissa. A questionnaire containing epidemiologic data, such as smoking habits, pathological values of blood lipids, hypertension, was used. Measurement of the height, waist perimeter, blood glucose and blood lipids (Total Cholesterol, LDL, HDL) was made after a recommendation of an all night fasting in these patients. These values were assessed according to the National Cholesterol Education Program Third Adult Treatment Panel (NCEP ATP III). 1906 participants took part in our study from 17 until 92 years old, mean age 59,67, st.deviation 15,33. 480 (25%) of them (168 men/312 women) had D.M. **Results** From 1906 patients 389 were smokers 136 (60 men/76 women) had D.M., 1025 were obese 322 (76/256) were diabetic patients, 428 had pathological value of TChol 178 (50/128) had D.M., 884 had pathological value of HDL 222 (84/138) had D.M., 339 had pathological value of LDL 124 (38/86) had D.M., 777 had pathological value of TG 210 (76/134) had D.M. Finally 177 patients suffered from angina pectoris 88 (28/68) had D.M. **Conclusions** In this study we observed that the obesity and the coronary disease are developed mainly among women with pathologic values of blood lipids. This is probably due to the lack of exercise and their dietary habits.

18

### Assessing the time relevance of morbidity of diabetes mellitus towards morbidity of target organs

Akritopoulos P, Akritopoulou K, Fotiadis E, Patiakas S, Kontogiannis I, Kiriakopoulos N, Aggos I, Tsoukis E  
Department of experimental pharmacology, Medical school of Aristotle's University of Thessaloniki, Greece

**Aim** Of this study was to investigate the correlation between the duration of morbidity of Diabetes Mellitus and the morbidity of target organs such as the kidney and retina. **Material-Method** We examined the medical files of a representative sample of diabetic greek adults who attended the General Hospital of Goumenissa. Patients were from 42 till 78 years old (Mean Age: 68, S.D.:16). Mean duration of morbidity of Diabetes Mellitus was 6 years (S.D.: 3,6). It must be noticed that diseases of the kidney found among diabetic patients were diabetic nephropathy, polycystic kidneys, chronic glomerulonephritis and nephrolithiasis. **Results** From 480 diabetic patients (168 men/312 women), only 24 (5%) (10men/14women) of the patients showed retinopathy mean duration of diabetic morbidity was 9 years. 38 (8%) (16men/22women) patients mean duration of Diabetes Mellitus 12,5 years demonstrated a nephropathy of some kind. In particular 28 patients (10men/18women) had diabetic nephropathy mean duration of D.M. was 15 years, 4 patients (0,8%) (2men/2 women) had polycystic kidneys mean duration of D.M. was 2 years, 2 male patients revealed chronic glomerulonephritis with mean duration of D.M. 7,75 years and 4 patients (0,8%) (2men/2women) suffered from nephrolithiasis. **Conclusions** In this study we observed that retinopathy is a rare morbidity, but it is developed much earlier than diabetic nephropathy. Diabetic nephropathy is much more usual among diabetic patients but it is developed a much longer duration of morbidity of D.M.



19

### Can firstly diagnosed diabetes mellitus be combined with systolic arterial hypertension

Akritopoulos P, Fotiadis E, Akritopoulou K, Patiakas S, Kontogiannis I, Kiriakopoulos N, Aggos I, Tsoukis E  
Department of experimental pharmacology, Medical school of Aristotles University of Thessaloniki, Greece

**Aim** Of this study was to estimate the combination between firstly diagnosed Diabetes Mellitus and the existence of fostered, asymptomatic, Systolic Arterial Hypertension (SAH). **Methods** We examined 1666 patients, which were randomly selected (mean age 58,42). 803 of these patients (mean age 49,67) had no medical history of neither hypertension, nor of diabetes mellitus. All these patients were fully clinically examined. The examination included the measurement of arterial pressure 3 times after relaxing in a sitting position for at least 15 minutes. Measurement of the blood glucose was made after a recommendation of an all night fasting in these patients. These values were assessed according to the National Cholesterol Education Program Third Adult Treatment Panel (NCEP ATP III). **Results** Diabetes mellitus was firstly met in 252 (25,48%) patients (mean age 56,45). These patients were slightly more aged than other patients (mean age 51,61). SAH was significantly higher  $p < 0,001$  according to the ANOVA test  $F_{10, df 1}$  in firstly diagnosed patients with diabetes mellitus in comparison with the rest, while diastolic arterial pressure was almost the same in both groups. **Conclusion** There seems to be a connection between patients with firstly diagnosed Diabetes Mellitus and asymptomatic Systolic Arterial Hypertension (SAH). This finding is important for the choice of the appropriate medical treatment in hipertensive diabetic patients.

20

### Demonstration and assessment of the treatment of diabetic patients in the rural area of Paionia

Akritopoulou K, Fotiadis E, Akritopoulos P, Patiakas S, Kontogiannis I, Kiriakopoulos N, Aggos I, Tsoukis E  
Department of experimental pharmacology, Medical school of Aristotles University of Thessaloniki, Greece

**Aim** The aim of this study is to demonstrate the medical treatment of Diabetes Mellitus (D.M.) under which the diabetic population of Paionia is treated and the compliance of the patients in the treatment. **Material-Method** We examined the medical files of a representative sample of diabetic greek adults who attended the General Hospital of Goumenissa. Patients were from 42 till 78 years old (Mean Age: 68, S.D.:16). From 480 diabetic patients (168 men/312 women) 108 (22,5%) had family history of D.M. **Results** Concerning the treatment of diabetic patients 46 (10men/36women) were treated conservatively 36 received treatment only for after-lunch hyperglycemia 28 (6men/22women) with repaglinide and 8 female patients were treated with rosiglitason. 72 (30men/42women) received diguanide, 136 (62men/74women) sulfonylurea, 66 (24men/42women) received a combination of diguanide and sulfonylurea and 98 (32men/66women) received insulin. We must add that 10 patients (2/8) received a combination of diguanide and repaglinide, 2 female patients a combination of diguanide and rosiglitason, 8 patients (2/6) a combination of sulfonylurea and repaglinide, 2 female patients received a combination of insulin and repaglinide and 2 female patients a combination of insulin and rosiglitason. Among these patients 306 had optimum glucose control and 174 had unbalanced glucose levels. **Conclusion** This study demonstrated a sub-optimal follow-up. The prevalence of D.M. is much higher among women. In women treatment of D.M. is harder due to the lack of exercise, the daily stress, the denial on complying with our dietary instructions while a crucial role is displayed by the neglect of elder patients from their family.

21

### Epidemiologic study of the appearance of diabetes mellitus in correlation with the patient's socioeconomic status

Akritopoulou K, Fotiadis E, Akritopoulos P, Patiakas S, Kontogiannis I, Kiriakopoulos N, Aggos I, Tsoukis E  
Department of experimental pharmacology, Medical school of Aristotles University of Thessaloniki, Greece

**Aim:** The assessment of the correlation of Diabetes Mellitus (D.M.) with the socio-economic status, their kind of job of the patients and the achievement of successful regulation of D.M. **Material-Method** Recording of the diabetic patients of the rural area of Goumenissa was done. We used a questionnaire which contained retrospective data concerning

blood glucose values, their level of education, the kind of job they conduct and their family history of D.M. **Results** From 1906 patients 480 (25,2%) had D.M. (168 men/312 women). From these patients 108 (22,5%) had a family history of D.M., 56 of them (18men/38 women) were illiterate, 374 patients (78%) (124men/250women) had elementary level of education, 38 patients (8%) (16 men/22women) had intermediate level of education, while only 12 patients (2,5%) (11men/1 woman) had a higher level of education. On the other side 144 (30%) patients (144women) were housewives, 82 (17%) patients (54men/28women) were farmers, 12 (2,5%) patients (8men/4women) were private employees, 14 (3%) patients (6men/8women) were state employees, 12 (2,5%) patients (11men/1woman) were businessmen/women, none of the freelancers had D.M., 208 (43,5%) (85 men, 123 women) were pensioners while 8 (1,5%) (5men/3women) stated another kind of job. **Conclusion** From this data we can see that there is a mild correlation of appearance of D.M. with the level of education with a higher frequency with its absence and with the elementary level of education  $p < 0,001$ . Furthermore at a closer look, the percentage of patients, in which their occupation has a lot of physical activity, have a lower percentage of D.M.  $p < 0,001$ .

22

### Investigating the lipidemic profile of patients with diabetes mellitus

Akritopoulou K, Fotiadis E, Akritopoulos P, Patiakas S, Kontogiannis I, Kiriakopoulos N, Aggos I, Tsoukis E  
Department of experimental pharmacology, Medical school of Aristotles University of Thessaloniki, Greece

**Aim** Of this study was to investigate the lipidemic profile of patients with Diabetes Mellitus in the rural area of Goumenissa-Kilkis. **Material-Method** We examined the medical files of a representative sample of diabetic greek adults who attended the General Hospital of Goumenissa. Measurement of the blood glucose and blood lipids (Total Cholesterol, LDL, HDL) was made after a recommendation of an all night fasting in these patients. These values were assessed according to the National Cholesterol Education Program Third Adult Treatment Panel (NCEP ATP III). Patients were from 42 till 78 years old (Mean Age: 68, S.D.:16). Mean duration of morbidity of Diabetes Mellitus was 6 years (S.D.: 3,6) **Results** From 480 diabetic patients (168 men/312 women), 132 (27,5%) had non-pathological values of blood lipids, 164 (34%) showed pathological value in 1 of the blood lipids, 152 (31%) had 2 pathological lipid values and 32 (7,5%) had all the examined lipids over normal values. In particular, 164 (34%) patients (26 men/138 women) had pathologic HDL, 222 (46,25%) patients had pathologic Total Cholesterol and 178 (37%) had pathologic LDL. **Conclusions** In this study we observed that the percentage pathologic blood lipids in the general population (patients with Diabetes Mellitus) is very high (72,5%) which is probably related to their dietary habits and the absence of physical activities. Moreover the lack of symptoms leads to insufficient compliance to instructions.

23

### Investigating the risk factors of patients who suffered a brain stroke

Akritopoulos P, Akritopoulou K, Fotiadis E, Patiakas S, Kontogiannis I, Kiriakopoulos N, Aggos I, Tsoukis E  
Department of experimental pharmacology, Medical school of Aristotles University of Thessaloniki, Greece

**Aim** Of this study was to investigate the risk factors of patients who suffered a brain stroke in the rural area of Goumenissa-Kilkis. **Material-Method** We examined the medical files of a sample of greek patients who suffered from a brain stroke and attended the General Hospital of Goumenissa for treatment during the period from 2004 - 2006. Risk factors of brain strokes were defined and detected such as Diabetes Mellitus (DM), Arterial Hypertension (AH), Atrial Fibrillation (AF), Coronary Disease (CD) and Hyperlipidemia. **Results** From 62 patients who suffered a brain stroke (35 men/27 women Mean Age 71,2 st 9,6), 51 (82%) had hypertension, 30 (48%) showed pathological values blood lipids, 24 (39%) had Diabetes Mellitus, 18 (29%) had Atrial Fibrillation and 14 (22,5%) had Coronary Disease. In particular, from the 30 patients who showed pathologic values blood lipids all 30 had pathologic Tchol, 20 had pathologic of HdL, 8 had pathologic LdL and 13 had pathologic TG. **Conclusions** In this study we observed that AH is the most frequent risk factor of a brain stroke. While among the most frequent risk factors are hyperlipidemia, DM. Relatively low percentages of the traditionally most frequent risk factor, Atrial Fibrillation, can be explained if we take under consideration that the other morbidities are asymptomatic.

24

**Verminderte Glyoxalase-1 Aktivität bei Patienten mit schmerzhafter diabetischer Neuropathie**Konrade I, Skapare E, Dambrova M, Lejniaks A, Liepins E, Stoyanov S, Haag GM, Humpert PM  
Medizinische Klinik, Universität Riga, Lettland

**Ziele:** Die Akkumulation von Advanced Glycation Endproducts (AGEs) im Gewebe von Patienten mit Diabetes mellitus (DM) gilt als eine Ursache für die Entstehung diabetischer Spätschäden. Da ein wesentlicher Teil von AGEs intrazellulär aus Methylglyoxal entsteht, stellt das intrazelluläre Glyoxalasesystem, das Methylglyoxal und andere  $\alpha$ -Oxoaldehyde detoxifizieren kann, einen wichtigen Abwehrmechanismus dar. In Vorarbeiten konnten wir nachweisen, dass Hyperglykämie und AGE-Bindung an den Oberflächenrezeptor RAGE GO-1-Expression und Transkription mindert. Diese Daten legen nahe, dass das eine verminderte GO-1 Expression und die damit verbundene Akkumulation von AGEs zur Entstehung diabetischer Spätkomplikationen, insbesondere zur diabetischen Neuropathie, bei Patienten mit Diabetes mellitus beitragen könnte. **Material und Methoden:** In Patienten mit Typ 2- DM (n=48, 27 Frauen, Alter 48,10,7, HbA1c: 8,261,6, Nichtraucher) und Typ 1- DM (n=41, Frauen 23, Alter 31,9, HbA1c: 8,91,6, Nichtraucher) mit bestätigter sensomotorischer Polyneuropathie (klinisch-neurologisch und elektrophysiologisch) wurde das Ausmaß der Schmerzempfindung (visuelle Analogskala 0–10 Punkte), die GO-1-Aktivität im Blut (spektrophotometrischer Enzym-Assay) sowie metabolische Parameter bestimmt. Ab 4 Punkten in der Schmerzskala wurde eine mäßige schmerzhaft Neuropathie angenommen. **Ergebnisse:** In den Subgruppen der Typ 1- und Typ 2- DM-Patienten mit schmerzhafter Polyneuropathie (n=24 und n=23 respektiv) wurde eine deutlich verminderte GO-1 Aktivität beobachtet: Median 6,551,01 vs. 7,781,04 mmol/min/ml; p=0,0006 bei Typ 1-Diabetikern und 6,61 1,16 mmol/min/ml vs. 7,87 1,16mmol/min/ml; p=0,0008 bei Typ 2-Diabetikern). Die GO-1 Aktivität der Typ 1-DM-Patienten korreliert ( $R^2=0,34$ ) mit aktuellen Nüchternblutglukosewerten, aber nicht mit dem HbA1c-Wert ( $R^2=0,13$ ), der Diabetes-Dauer, dem BMI oder dem Lipidstatus. **Zusammenfassung:** Patienten mit schmerzhafter Polyneuropathie weisen eine gegenüber Kontrollpersonen und Diabetikern ohne schmerzhaft Neuropathie erniedrigte Aktivität des detoxifizierenden Enzyms GO-1 auf.

25

**Alterations of vaginocervical epithelium of women with diabetes mellitus tracing with pap-test**Kyriakopoulos N, Gavalas C, Georgantis I, Patiakas S, Tsoukis E, Tsitlakidou S, Kotsidas I, Kambanis I  
General Hospital of Kos, Greece

**Background-Aims:** To study the vaginocervical epithelium of women with DM and correlate the altered epithelium with the disease by using Pap-test. **MATERIAL- Methods:** The thesis includes 68 vaginocervical smears of diabetic patients 22–70 years of age. They all were under medical treatment. **Results:** We found: 32 smears with pathological alteration, 13 identified as vaginitis, 5 identified as cervicitis, 5 showed atrophical degeneration, 2 ASCUS and 1 LG-SIL. These findings and the epithelium growth are compatible with the patients' age. **Conclusions:** Vaginocervical epithelium of diabetic patients develops inflammatory alterations more often, while epithelium maturation results the same in the whole population.

26

**Diabetes mellitus type I and perinatal result**Kyriakopoulos N, Gavalas C, Georgantis I, Patiakas S, Tsitlakidou S, Aggos I, Kotsidas I, Kambanis I  
General Hospital of Kos, Greece

**Background-Aims:** The study of the perinatal results, occurring during pregnancy complicated by diabetes mellitus type I. **Material-Method:** we studied all diabetes mellitus type I complicated pregnancies hospitalized in the Department of Obstetrics and Gynecology of Kos General Hospital during the period 2005–2006. All women were under instructions of a nutritionist. **Results:** 50 pregnant women with diabetes mellitus type I were hospitalized. In the mean time, 52 infants were born, 2 of which were twins. The average weight was 2050–4200gr. The average of long bodied embryos was 20% (10 infants), IUGR 4% (2 infants), the effect of premature labor was 10% (5 infants), while the percentage of performing Caesarian Section was 85% (43 infants). **Conclusion:** The perinatal result was satisfactory, due to well regulated serum glucose level during pregnancy and the strict surveillance of the pregnant wo-

men by a diabetes mellitus specialist. Therefore, thanks to the enforcement of adequate pregnant women surveillance programs, perinatal mortality and the hazards of complications have been significantly well regulated and reduced.

27

**The effect of diabetes mellitus in the progress of pregnancy**Kyriakopoulos N, Gavalas C, Georgantis I, Tsitlakidou S, Tsoukis E, Aggos I, Kotsidas I, Kambanis I  
General Hospital of Kos, Greece

**Background-Aims:** The presentation of the evolution of pregnant women that are about to give birth with GESTATIONAL DIABETES MELLITUS, who were examined in Department of Obstetrics and Gynecology of the General Hospital of Kos Island during the period 01–01–2000 to 31–12–2006. **Material-Method:** We observed and hospitalized 140 pregnant women during their pregnancy in the Department of Obstetrics and Gynecology of the General Hospital of Kos Island during the period of 2000–2006. **Results:** The average age of the pregnant women of this thesis was 20 to 48 years old. 60% (84 women) of the cases concerned gestational diabetes mellitus and 40% (56 women) diabetes mellitus type I. 41% of them were giving birth for the first time while 3 of these cases were carrying twins. The main indication for hospitalization was the regulation of the serum glucose levels. The average duration of hospitalization, in cases concerning gestational diabetes mellitus was 2 days while those with diabetes mellitus type I was 3 days. In these cases the frequency of performing a Caesarian Section was 84%. **Conclusions:** Diabetes mellitus is the most common complication during pregnancy and has many consequences on its progress. It's often needed for the pregnant women to be hospitalized in order to regulate the serum glucose level. It's also confirmed that Caesarian Section is a chosen method for labor.

28

**Zusammenhang zwischen TCF7L2 Gen und diabetischer Nephropathie**Moczulski D, Remiszewska B, Grzeszczak W  
Department of Internal Medicine, Nephrology and Dialysis, Medical University in Lodz, Poland

**Hintergrund und Fragestellung:** Die diabetische Nephropathie ist die häufigste Ursache für eine terminale Niereninsuffizienz. Jeder dritte Patient, bei dem eine Dialysetherapie begonnen werden muss, ist ein Diabetiker. Die Ursachen für die diabetische Nephropathie sind multifaktoriell. Neben der glykämischen Kontrolle und der Hypertonie spielt eine genetische Prädisposition eine wichtige Rolle. Durch die Analyse von Patienten aus Island wurden mehrere genetische Varianten des TCF7L2-Gens identifiziert, die das Risiko für Typ 2 Diabetes mellitus erhöhen. Die Variante rs7903146 birgt danach das höchste Risiko, an Typ 2 Diabetes mellitus zu erkranken. Der Zusammenhang zwischen der rs7903146 Variante des TCF7L2-Gens und Typ 2 Diabetes mellitus wurde auch in der polnischen Population nachgewiesen. Die Frequenz des TT Genotyps bei den Typ-2-Diabetes Patienten was signifikant erhöht. Ziel war es nun, den Zusammenhang zwischen der rs7903146 Variante des TCF7L2-Gens und der diabetischen Nephropathie zu analysieren. **Patienten und Methodik:** DNA wurde aus dem peripheren Blut von 290 Typ-2-Diabetes- Patienten ohne Proteinurie und 118 Typ-2-Diabetes-Patienten mit Proteinurie extrahiert. Zur Genotypisierung der rs7903146 Variante des TCF7L2-Gens wurde ein PCR (Polymerasekettenreaktion)-RFLP (Restriktionsfragmentlängenpolymorphismus) -Verfahren ausgearbeitet. Die Genotypfrequenz wurde in beiden Gruppen bestimmt. **Ergebnisse:** In der Kontrollgruppe ohne Proteinurie wurde der TT Genotyp bei 13% Personen nachgewiesen. In der Gruppe mit Proteinurie war der TT Genotyp bei 6% Personen nachweisbar. Damit war die Frequenz des TT Genotyps bei den Patienten mit Proteinurie signifikant erniedrigt (p=0,044). **Schlussfolgerung:** Unsere Studie weist darauf hin, dass der TT Genotyp des TCF7L2-Gens, der das Risiko für Typ- 2- Diabetes mellitus erhöht, mit einem schützenden Effekt gegen die Entwicklung der diabetischen Nephropathie assoziiert ist.

29

### The differences and similarities of newborns with diabetes mellitus – analysis of two cases from the Pomeranian region (Poland)

Myliwiec M, Balcerska A, Zorena K, Myliwska J  
Diabetological Department Clinic of Pediatrics, Hematology,  
Oncology and Endocrinology Medical University of Gdańsk,  
Poland

Neonatal diabetes mellitus is an extremely rare disease, with estimated incidence of 1: 400 000 – 500 000 life births. Regardless epidemiologic data in the last two years in the Pomeranian region of Poland two new cases of neonatal diabetes mellitus were diagnosed. The treatment of diabetes mellitus in newborn and infancy period is particularly difficult due to scarce fat tissue and necessity of delivery of very low doses of insulin. The aim of this work is to present diagnostic and therapeutic success achieved in two cases of children diagnosed with persistent neonatal diabetes mellitus after introduction of continuous subcutaneous insulin infusion (Novo Rapid; Novo Nordisk, DK) delivered using insulin pump Paradigm712, Medtronic USA. This case report present two children diagnosed with diabetes mellitus in the first day of life. Both children had no auto antibodies against antigens of the pancreatic islets detected: analysis comprised glutamate decarboxylase antibody (GAD), insulin auto antibody (IAA) and islet cell antibody (ICA). The C-peptide level both in fasting state and after glucagone stimulation was < 0.5 ng/ml. The HbA1c in the case 1 was 6.3%, in the case 2 – 8.3%. Both of the children had no mutation in the KCNJ1 gene detected. In the two presented cases the introduction of the insulin therapy delivered using individual insulin pump appeared to be safe and efficient treatment approach which enabled correct psychomotor development of the patients.

30

### Prevalence of anti-GAD65 in Greek population with type II diabetes mellitus

Panagiotidou M<sup>1</sup>, Tsiotra P<sup>2</sup>, Economopoulos T<sup>1</sup>, Raptis SA<sup>2</sup>, Hatzigelaki E<sup>1</sup>  
<sup>1</sup>2<sup>nd</sup> Dept of Internal Medicine, Diabetes Center and  
Research Institute „ATTIKO“ University Hospital – Athens,  
Greece; <sup>2</sup>Hellenic National Diabetes Center

**Background and aims:** Autoimmune destruction of pancreatic  $\beta$ -cells is the main cause of insulin deficiency in type I diabetes mellitus and in a number of patients with type II diabetes. The presence of markers such as GAD65 or IA2, before the development of overt disease, can identify patients at risk. The aim of this retrospective study was to evaluate the prevalence of GAD65 in the Greek type II diabetic population. **Materials and methods:** We examined 1225 diabetic patients divided in two groups depending on their GAD65 reactivity. Both groups (GADAb+ and GADAb-) were further subdivided according to their BMI (lean: BMI < 25, overweight: BMI  $\geq$  25). Serum GAD65 antibodies were detected by a commercial available RIA kit (Medipan Diagnostica). Fasting plasma c-peptide levels were also available. **Results:** In a cohort of 1225 diabetic patients, 358 were GADAb+ (29,22%) (age: 36,21  $\pm$  0,76 years, BMI: 24,64  $\pm$  0,24) and 867 GADAb- (70,78%) (age: 40,23  $\pm$  0,57, BMI: 25,41  $\pm$  0,52). Duration of diabetes was significantly lower ( $p < 0.01$ ) in GADAb+ patients compared to GADAb- (4,9  $\pm$  0,35years, 7,38  $\pm$  0,30years respectively). As far as transition time, from drug to insulin therapy, is concerned, was significantly lower in GADAb+ (lean or overweight), compared to GADAb- (lean or overweight) group (Table). Fasting c-peptide levels were significantly lower in GADAb+ compared to GADAb- patients (Table). Interestingly, GAD65 titers were similar in GADAb+ patients, regardless of their BMI. Furthermore, fasting c-peptide levels were similar in GADAb+ (lean or overweight) patients and correlated reversely with GAD65 titers ( $p < 0.006$ ,  $r = -0,192$ ).

		AGE (years)	C-PEPTIDE (ng/ml)	BMI (Kgr/cm <sup>2</sup> )	GAD titre (U/ml)	DURATION DISK- INS (years)
GADAb <sup>+</sup> n = 358	LEAN	36,15 $\pm$ 1,58	0,77 $\pm$ 0,06	21,45 $\pm$ 0,25	21,68 $\pm$ 2,32	3,2 $\pm$ 2,20
	OVERWEIGHT	36,27 $\pm$ 2,26	0,77 $\pm$ 0,14	27,82 $\pm$ 0,84*	17,77 $\pm$ 5,50*	2,58 $\pm$ 0,90
GADAb <sup>-</sup> n = 867	LEAN	38,45 $\pm$ 2,54	2 $\pm$ 0,20*§	21,87 $\pm$ 0,26§	0,79 $\pm$ 0,013- *§	10,77 $\pm$ 5,8- 0
	OVERWEIGHT	42 $\pm$ 1,99*§	2,4 $\pm$ 0,23* §#	28,95 $\pm$ 0,50- *#	0,770,016* §	10,12 $\pm$ 1,8- 0*§

\*  $p < 0,05$  vs. GADAb<sup>-</sup> -lean, §  $p < 0,05$  vs. GADAb<sup>-</sup> -overweight, #  $p < 0,003$  vs. GADAb<sup>-</sup> -lean

**Conclusions:** According to our results, measurement of GAD65 antibodies is highly recommended in all diabetic patients regardless of their BMI.

31

### Correlation of $\gamma$ -GT in obese individuals with insulin resistance

Patiakas S, Xaralampous X, Kyriakopoulos N, Gavala C, Pelegri E, Tsoukis E, Akritopoulou K  
General Hospital of Kos, Greece

**AIM:** To investigate the relationship of  $\gamma$ -GT with insulin resistance markers in overweight-obese individuals, taking into consideration that in literature there are epidemiological studies that support this, probably due to the increases of the oxide processes that takes place. **Material-Method:** Retrospectively 482 overweight individuals were chosen for studying, 195 men and 287 women, average age 49,7  $\pm$  11,2 and 44,6  $\pm$  12,1 respectively and BMI 35,5  $\pm$  6,3 and 34,8  $\pm$  6,5. From them 186, 97 men and 89 women had diagnosed sacharoid diabetes history (HbA1C > 6,2 and fasting diabetes > 110 mg/dl). All the pre-chosen sample individuals showed normal function of the thyroid gland, did not consume alcohol quantity greater than 30 and 20 gr per day (men and women respectively) and their hepatic function was good, since they showed no values greater than the third of the normal. All were further checked with human metric calculations and a full check, while the markers for insulin resistance (HOMA) and insulin sensitivity (QUICKI) were calculated. **Results:** From the statistical analysis of the results with the partial co-efficient, that in men the strongest with the normal  $\gamma$ -GT was recorded by insulin ( $R^2 = 0,7$   $F = 10,27$   $si = 0,002$   $Beta = 0,231$   $p = 0,002$ ), in the other hand in women the insulin resistance HOMA ( $R^2 = 18,2$   $F = 32,41$   $sig = 0,000$ ). Age and BMI were not shown to be an important factor in our study. **Conclusions:** It was proven that there is close correlation between the  $\gamma$ -GT level and the insulin resistance of overweight and obesity individuals, independently of age, BMI and the presence or not of diabetes. As a result its measurement shows interest in those individuals that due to the increased body fat and its distribution, are showing higher insulin resistance in the first place.

32

### Effect of antiplatelet treatment on lipid levels and glycosilated hemoglobine in diabetic patients

Patiakas S, Kiriakopoulos N, Gavala C, Xaralampous X, Pelegri E, Georgantis H, Akritopoulou K, Xiropoulou E  
General Hospital of Kos, Greece

**Objective:** To define the possible effect of antiplatelet treatment on HbA1C and lipid levels in diabetic individuals. **Material-Method:** 167 diabetic patients were studied, 92 men and 75 women, with average age 61,3  $\pm$  11,4 and 56  $\pm$  12,3 years respectively, all of which were under hypoglycaemic treatment (metmorphine), as well as hypolipidemic (atorvastatine). From those 73 received in addition antiplatelates treatment (aspirin) either for primary prevention (7 individuals) or for secondary level, due to head stroke, coronary angiopathy, etc. All were submitted to cholesterol, LDL cholesterol, triglycerides and HbA1C examinations. **Results:** The average numbers and their standard deviation:

Examination (n = 167)	Under antiplatelates treatment ((n = 73)	Without antiplatelates treatment ((n = 94)
HbA1C (%)	7,4 ( $\pm$ 1,7)	7,9 ( $\pm$ 1,9)
Total Cholesterol (mg/dl)	216 ( $\pm$ 32,6)	238 ( $\pm$ 30,2)
LDL Cholesterol (mg/dl)	98 ( $\pm$ 20,6)	113 ( $\pm$ 17,6)
Triglycerides (mg/dl)	140 ( $\pm$ 28,7)	144 ( $\pm$ 34,8)

**Conclusions:** 1) Diabetic patients under antiplatelet treatment show better levels, as far as the therapeutic aims were concerned. The values of HbA1C, total cholesterol and LDL cholesterol between the two groups showed an significant difference ( $p < 0,01$ ). 2) the levels of triglycerides doesn't seem to be effected by the simultaneous administration of antiplatelet drugs ( $p > 0,01$ ). 3) Besides secondary level prevention, it gets obvious that antiplatelates treatment in diabetic patients should be administrated also in primary level, even in higher percentage.

33

### Prevalence of diabetes mellitus in Paionia county, according to previous and recent W.H.O. criteria

Patiakas S, Gavala C, Kiriakopoulos N, Akritopoulou K, Akritopoulos P, Aggos I, Xiropoulou E, Georgantis H  
General Hospital of Kos, Greece

**Purpose:** To evaluate: 1) the frequency of diabetes mellitus (D.M.) in the population of Paionia, 2) the impact of the new W.H.O. criteria for diagnosis of D.M. in the incidence determined. **Materials – methods:** A random sample of 4727 individuals, aged 30 to 85 (were examined) for D.M. in our Microbiology Laboratory in the year's 2005 – 2006. Fasting serum glucose levels were determined with the hexokinase method, using the TARGA 3000 biochemical analyzer (Menarini Diagnostics). According to recent W.H.O. guidelines, to diagnose D.M., fasting serum glucose levels should be above 126 mg%. previous W.H.O. guidelines had suggested diagnostic levels above 140 mg%. **Results:** The results are summarised in the following table.

Samples with serum glucose > 126 mg%	Samples with serum glucose > 140 mg%
N = 465	n = 360
9.8%	7.6%

89 patients (1.9% of samples) had intermediate levels. This implies that the recent W.H.O. criteria have lead to an almost 2% increase in the estimated frequency of diabetes mellitus in the general population. Moreover, implementation of the recent criteria allow for an increase in the sensitivity of D.M. screening by means of serum glucose determination by 20.4%. **Conclusions:** The following conclusions can be made: 1) There is a significant disproportion between the prevalence of diabetes mellitus in the population of Paionia (7.2 – 9%) and the prevalence mentioned in the international literature (2 – 4%). Genetic and/or environmental factors (notably nutrition) may be responsible for this. Future research should further clarify the reasons for this increased levels. 2) Almost 2% of the population have intermediate serum glucose levels (between 126 and 140 mg%). Implementation of the recent diagnostic criteria increased the sensitivity of serum glucose screening by approximately 20%. Earlier diagnosis consequently allows more patients to follow earlier treatment, thus favorably affecting the course and prognosis of the disease. 3) These data strongly emphasize the serious social and financial consequences of diabetes mellitus and the need for regular screening of the general population.

34

### The effect of thiazolidinediones on leucocytes in type II diabetic patients

Patiakas S, Xaralampous X, Gavala C, Kiriakopoulos N, Tsoukis E  
General Hospital of Kos, Greece

**Objective:** To investigate the effect of thiazolidinediones, which are peroxisome proliferator-activated receptor gamma (PPARgamma) ligands used to treat diabetes mellitus. In particular our study is interested in the effect of rosiglitazone in the number of leucocytes knowing that it causes reduction of haemoglobin and haematocrit mainly due to water retention. **Materials – methods:** In 25 patients, 12 men and 13 women, already under insufficient hypoglycaemic control (mainly under glibenclamide) 4 mg/die of rosiglitazone were added. 5 of them had positive hypertensive anamnesis and in 8 hypertension was newly diagnosed. No one was under pharmacologic control. Plasma leucocytes were counted in every patient at the beginning of our study and after 6 months. A control group of 25 more diabetic patients under their usual therapy was included in the study. **Results:** Average leucocytes number at the beginning of the study was  $7216 \pm 452 \times 10^6/L$ , while 6 month later was reduced to  $6480 \pm 352 \times 10^6/L$ , ( $p < 0,05$ ). The control group did not show significant variation. Corresponding leucocytes level was of  $7186 \pm 442 \times 10^6/L$  initially and  $7212 \pm 456 \times 10^6/L$  after 6 months. It is remarkable that not any patient developed abnormally low leucocytes level nor showed correlated symptoms while patients under rosiglitazone recorded significant weight increase (from  $76,8 \pm 2,2$  initially to  $78,7 \pm 2,5$  Kgr 6 months after). Bioreactor analysis recorded total body water increase from  $39,5 \pm 1,4$  to  $41,3 \pm 1,6$  L. **Conclusions:** It has been concluded that additional rosiglitazone in type II diabetic and hypertensive patients is connected to leucocytes decrease. Although water retention can be taken as a fact, further effect of thiazolidinediones on leucocytes must be deeply investigated.

35

### The lipid profile of patients with diabetes mellitus in Paionia county

Patiakas S, Kiriakopoulos N, Gavala C, Aggos I, Akritopoulou K, Akritopoulos P, Xiropoulou E  
General Hospital of Kos, Greece

**Purpose:** To identify the lipid profile of the inhabitants with diabetes mellitus. **Materials – methods:** 12-hour fasting specimens from 432 diabetic patients (203 men and 229 women), aged from 35 to 82 years old, presented at the Microbiology Laboratory of the General Hospital of Goumenissa in the year's 2005 – 2006. Blood cholesterol and triglyceride levels were measured with enzyme chromatometric methods, using the TARGA 3000 biochemical analyzer (Menarini). Blood cholesterol values higher than 200 mg% and triglyceride levels higher than 150 mg% were considered abnormal. **Results:** Among the 203 males the following results were obtained:

1. High blood cholesterol with normal triglyceride values were found in 34 males (16,7%).
2. High triglycerides with normal cholesterol levels were found only in 2 males (1%).
3. Mixed hyperlipidemia (high cholesterol and high triglyceride levels) was diagnosed in 31 male individuals (15,3%).
4. 67% of the examined male samples (136 individuals) were normal.

Among the 229 females the measurements included:

1. High blood cholesterol with normal triglyceride values were observed in 62 females (27%).
2. Only in 2 females (0,9%) were observed high triglycerides and normal cholesterol levels.
3. Mixed hyperlipidemia was diagnosed in 38 females (16,6%).
4. 55,5% of the examined female samples (127 individuals) were normal.

#### Conclusions:

1. The frequency of hyperlipidemia is much higher in patients with diabetes mellitus than in nondiabetic individuals.
2. Of all three lipidemic types studied occult hypercholesterolemia was the most frequent and the occult hypertriglyceridemia is the least frequent.
3. There is not important statistically difference between males and females in  $\alpha\mu\gamma\eta$  hypertriglyceridemia and mixed hyperlipidemia. ( $p < 1$ ).

36

### Burning mouth syndrome in diabetic patient: an update on treatment methods

Piagou M, Piagos G, Nikolakis G, Mazarakis A  
Department of Anatomy, Medical School, University of Athens, Greece

**Backgrounds/Aim** Burning mouth syndrome is a chronic pain syndrome that mainly affects middle-aged/old women with hormonal changes or psychological disorders. The aim of this review is to emphasize in the multifactorial origin often idiopathic, and its prognosis and treatment especially in diabetic patients. **Methods** International literature is reviewed and a variety of chronic oral symptoms are described. Clinical features include pain, dysgeusia, xerostomia, sensory anomalies, oral findings, mood changes and alterations in personality. **Results-conclusion** The correlation between diabetes mellitus and BMS is still controversial. It has been suggested that type II diabetes mellitus plays a role in BMS development and a link between the type of insulin used for the diabetes treatment and BMS has also been proposed. In contrast, other studies report a lack of association between these two conditions. A possible explanation for this controversy may be that these diabetic patients were erroneously classified as BMS. In fact, at the time of the above studies, a lack of strict criteria for BMS diagnosis could have affected the selection of the patients. For instance, burning oral complaints in diabetic subjects, who are more prone to oral infections, are probably caused by oral candidiasis. Owing to the large variety of associated factors, the protocol for BMS management is complex. An effective approach for these patients should be based on a strict collaboration among different oral medicine specialists. Patient management involves a differential diagnosis for BMS and the discrimination between "Primary" and "Secondary BMS" based on the identification of possible etiologic factors for the syndrome. Although a large variety of drugs, medications, and miscellaneous treatments has been proposed in BMS, the treatment management of this syndrome is still not satisfactory, and there is no definitive cure. BMS patients have shown a good response to long-term therapy with systemic regimens of anti-depressants and anxiolytics.

37

### Rhinocerebral mucormycosis: a rare but life-threatening opportunistic infection in diabetic patients

Piagou M, Makri A, Piagos G, Douvetzemis S, Nikolakis G  
Department of Anatomy, Medical School, University of Athens, Greece

**Background/Aim** Mucormycosis is an uncommon necrotizing infection caused by fungi within the class Zygomycetes and the order Mucorales. It mainly occurs in immunocompromised states, including diabetes, with the rhinocerebral disease being the most common type of mucormycosis seen in patients with diabetes. The aim of this study is to document the pathogenesis and clinical presentation of rhinocerebral mucormycosis as well as to emphasize the need of early recognition and aggressive treatment of the disease, as it is the only chance to increase the survival rate. **Methods** From the review of the international literature, it is obvious that the disease originates in the nasal/sinus mucosa after inhalation of fungal spores and takes rapidly progressive course extending to neighboring tissues, including the orbit and sometimes the brain. The pathogenesis of the disease includes the reduced iron-binding capacity to transferrin, due to the acidic milieu (in case of diabetic ketoacidosis), that results in increased free iron and therefore promotes the growth of the fungus. Patients typically present with malaise, retro-orbital headache, fever, dark blood-tinged rhinorrhea and a characteristic black eschar in the oral and nasal cavity. In the diagnostic work-up, the histologic section reveals wide, non-septate hyphae with right-angled branching. Sinus and blood cultures are less important, however they should not be omitted. Imaging studies (CT, MRI) are important in order to evaluate the extent of the disease. **Results-conclusion** Treatment of rhinocerebral mucormycosis should consist of prompt control of hyperglycemia and ketoacidosis, aggressive surgical debridement of involved tissue and administration of parenteral amphotericin B. A high index of suspicion is needed, in appropriate clinical settings, to diagnose and aggressively treat this infection in view of the high mortality rate for susceptible patients.

38

### Nocturnal hypoglycemic episodes detected with the CGMS in adolescent patients with type 1 diabetes mellitus

Piekarski R, Azab Y, Bury A, Szweczyk L  
Medical Academy of Lublin, Department of Pediatric Endocrinology and Neurology, Poland

The recent availability of a continuous glucose monitor in pediatric patients offers the opportunity to improve the monitoring in diabetes care. **Material and methods:** 62 adolescent patients (13–18 years old) with poor controlled type 1 diabetes (av. HbA<sub>1c</sub> – 10.74%, fructosamine – 471 μmol/l) were monitored using the Minimed continuous glucose monitoring system (CGMS). **Results:** A wide range in daily glucose level measurements was observed. There was a considerable increase of glycemia (>250 mg%) at the forenoon hours; most episodes occurred between 9 and 10 AM. The more frequent incidences of hypoglycemia (<40 mg%) were registered at night between 22 PM and 4 AM, in 33% of patients were at 3–4 AM. **Conclusions:** 1. The largest insulin requirement in adolescent with poor controlled diabetes mellitus considered forenoon hours. 2. The greater tendency to hypoglycemia episodes at the late hours at the night required nocturnal glycemic profiles to determine. 3. The CGMS is useful tool in monitoring of diabetes care.

39

### Key role of postprandial hyperglycemia for the presence and extent of coronary atherosclerosis

Saely CH, Drexel H, Sourij H, Aczel S, Jahnel H, Zweiker R, Marte T, Hoefle G  
VIVIT Institute, Feldkirch, Austria, Academic Teaching Hospital Feldkirch, Feldkirch, Austria

**Background/Aims:** The coronary angiographic state of patients with abnormal glucose tolerance is unclear. **Methods:** We enrolled 1040 consecutive patients undergoing coronary angiography for the evaluation of coronary artery disease (CAD). An oral glucose tolerance test was performed in patients without established diabetes. **Results:** From our patients, 394 had normal glucose tolerance (NGT), 190 impaired glucose tolerance (IGT), 90 isolated postprandial diabetes (postprandial glucose ≥200 mg/dl), and 366 type 2 diabetes previously established or newly diagnosed on the basis of fasting glucose (conventional diabetes). Angiographically detectable CAD was more frequent in patients with IGT,

isolated postprandial diabetes, or conventional diabetes when compared to NGT subjects (87.9%, 95.6%, 89.1% vs. 80.7%;  $p=0.030$ ,  $0.001$ ,  $0.043$ , respectively). The prevalence of significant coronary stenoses ≥50%, compared to NGT subjects (57.4%), was similar in IGT patients (59.5%;  $p=0.628$ ), but significantly higher in patients with isolated postprandial diabetes (77.8%;  $p=0.001$ ) or conventional diabetes (68.0%;  $p=0.002$ ). Also the number of significant stenoses compared to NGT subjects was similar in IGT patients, but significantly higher in those with isolated postprandial or conventional diabetes. As a continuous variable postprandial glucose proved independently associated with CAD (standardized adjusted odds ratio (OR) 1.624 [95% CI 1.163–2.269];  $p=0.004$ ) and with significant stenoses (OR 1.345 [1.061–1.704];  $p=0.014$ ). **Conclusions:** Postprandial hyperglycemia is strongly and independently associated with angiographically characterized CAD. In IGT, non-significant CAD is more frequent than in NGT; the prevalence and number of significant stenoses increases when postprandial diabetes evolves.

40

### Low HDL cholesterol, high triglycerides, and small LDL particles are the main lipid risk factors in statin treated coronary patients with type 2 diabetes

Drexel H, Aczel S, Schmid F, Koch L, Marte T, Langer P, Rein P, Hoefle G  
VIVIT Institute, Feldkirch, Austria, Academic Teaching Hospital Feldkirch, Feldkirch, Austria

**Background/Aims:** Current guidelines recommend statin treatment in patients with the combination of type 2 diabetes (T2DM) and coronary artery disease (CAD), but vascular risk in these patients remains high. We aimed at investigating which lipid parameters most strongly predict vascular risk in diabetic coronary patients receiving statins.

**Methods:** We prospectively recorded over 6 years vascular events in 432 consecutive patients with angiographically proven CAD who were on statin treatment. At baseline, lipids and lipoproteins were measured from fasting serum samples.

**Results:** From our patients, 142 had a normal fasting glucose <100 mg/dl, 184 had an impaired fasting glucose ≥100 mg/dl, and 106 had T2DM. The incidence of vascular events significantly ( $p < 0.001$ ) increased from the group of patients with normal fasting glucose (17.6%) over the group of patients with impaired fasting glucose (25.0%) to the group of patients with T2DM (39.6%). Among patients with T2DM, triglycerides (standardized adjusted hazard ratio (HR)=1.234 [1.050–1.450];  $p=0.011$ ), and, inversely, HDL cholesterol (HR=0.623 [0.414–0.938];  $p=0.023$ ) as well as the LDL peak particle diameter (HR=0.690 [0.488–0.976];  $p=0.036$ ), but not total cholesterol (1.179 [0.876–1.586];  $p=0.278$ ), LDL cholesterol (0.960 [0.718–1.285];  $p=0.785$ ), or apolipoprotein B (1.190 [0.880–1.609];  $p=0.259$ ) significantly predicted vascular events after adjustment for age, gender, smoking, hypertension, and BMI.

**Conclusions:** We conclude that high triglycerides, low HDL cholesterol, and small LDL particles are the main lipid risk factors for the incidence of vascular events in type 2 diabetic coronary patients who receive LDL lowering statin treatment.

41

### Low serum adiponectin is independently associated with both the metabolic syndrome and angiographically determined coronary atherosclerosis

Saely CH, Risch L, Hoefle G, Rein P, Marte T, Aczel S, Langer P, Drexel H  
VIVIT Institute, Feldkirch, Austria, Academic Teaching Hospital Feldkirch, Feldkirch, Austria

**Background/Aims:** The metabolic syndrome (MetS) and coronary artery disease (CAD) frequently, but not necessarily coincide. We aimed at investigating serum adiponectin in patients with the MetS, in patients with angiographically diagnosed CAD, and in patients who had both, the MetS and CAD.

**Methods:** We enrolled 687 consecutive patients undergoing coronary angiography for the evaluation of CAD.

**Results:** From our patients, 178 had neither the MetS (Adult Treatment Panel III definition) nor significant CAD (MetS-/CAD-), 91 had the MetS, but not significant CAD (MetS+/CAD-), 251 did not have the MetS but had significant CAD (MetS-/CAD+), and 167 had both, the MetS and significant CAD (MetS+/CAD+). Serum adiponectin was highest ( $12.1 \pm 8.3 \mu\text{g/ml}$ ) in MetS-/CAD- subjects. It was significantly lower in MetS+/CAD-

( $9.5 \pm 7.3 \mu\text{g/ml}$ ;  $p = 0.001$ ) and in MetS-/CAD+ patients ( $9.2 \pm 5.3 \mu\text{g/ml}$ ;  $p < 0.001$ ) and lowest in MetS+/CAD+ patients ( $6.7 \pm 3.8 \mu\text{g/ml}$ ) in whom it was significantly lower than in MetS-/CAD-, MetS+/CAD-, and MetS-/CAD+ patients ( $p < 0.001$  for all comparisons). In analysis of covariance the MetS and significant CAD proved associated with serum adiponectin in a mutually independent manner ( $p < 0.001$  for both). Analysis of covariance adjusting for age, gender, smoking, LDL cholesterol and for the presence of significant stenoses confirmed the associations between serum adiponectin levels and the MetS traits high waist circumference ( $p < 0.001$ ), high fasting glucose ( $p = 0.011$ ), high triglycerides ( $p < 0.001$ ), and low HDL cholesterol ( $p < 0.001$ ). When all MetS traits were entered simultaneously into the model, the waist criterion ( $p = 0.009$ ), the high triglycerides criterion ( $p = 0.001$ ) and the low HDL cholesterol criterion ( $p = 0.012$ ) were independently associated with low serum levels of adiponectin.

**Conclusions:** Low serum adiponectin is independently associated with both the metabolic syndrome and coronary atherosclerosis.

42

### Significant impact of the presence of type 2 diabetes on the cardiovascular risk conferred by the plasminogen activator inhibitor-1 – 675 5G/4G polymorphism

Muendlein A, Saely CH, Marte T, Koch L, Schmid F, Rein P, Aczel S, Langer P  
VIVIT Institute, Feldkirch, Austria, Academic Teaching Hospital Feldkirch, Feldkirch, Austria

**Background/Aims:** The -675 5G/4G polymorphism of the plasminogen activator inhibitor-1 (PAI-1) gene has been associated with increased plasma levels of PAI-1 and, in some studies, with increased vascular risk. Hardly any data on the vascular risk conferred by this polymorphism are available for patients with type 2 diabetes (T2DM). We therefore aimed at investigating i) the association of this polymorphism with angiographically diagnosed coronary artery disease (CAD) and ii) its impact on future vascular events in patients with T2DM and in nondiabetic individuals.

**Methods:** Genotyping was performed in 672 consecutive Caucasian patients (463 men and 209 women, mean age  $62 \pm 10$  years) undergoing coronary angiography for the evaluation of stable CAD. Prospectively, we recorded vascular events over 4 years. **Results:** The prevalence rates of the 5G/5G, the 5G/4G, and the 4G/4G genotypes were 17.6%, 52.7%, and 29.7% in patients with T2DM ( $n = 148$ ) and 23.5%, 48.3%, and 28.2% in non-diabetic subjects ( $n = 524$ ). In non-diabetic subjects the homozygote PAI-1 4G4G genotype after adjustment for age, gender, hypertension, smoking, BMI, LDL cholesterol, and HDL cholesterol was significantly associated with significant stenoses (adjusted odds ratio (OR) 1.77 [95% CI 1.13 – 2.78],  $p = 0.013$ ), whereas no such association was observed in patients with T2DM (OR 0.81 [0.34 – 1.93];  $p = 0.635$ ). An interaction term T2DM x 4G4G genotype was significant ( $p = 0.026$ ), indicating that the association of the polymorphism with CAD was significantly stronger in non-diabetic subjects than in patients with T2DM. Also prospectively, the 4G4G genotype conferred an increased risk of vascular events in non-diabetic subjects but not in T2DM patients, with hazard ratios of 1.66 [1.05 – 2.64],  $p = 0.031$  and 0.72 [0.33 – 1.60],  $p = 0.423$ , respectively (adjusted for age, gender, hypertension, smoking, BMI, LDL cholesterol, and HDL cholesterol). Again, an interaction term T2DM x 4G4G genotype was significant ( $p = 0.042$ ). **Conclusions:** We conclude that presence of T2DM significantly modulates the vascular risk conferred by the PAI-1 – 675 5G/4G polymorphism.

43

### Type 2 diabetes and the coronary angiographic state are mutually independent predictors of future vascular events among angiographed coronary patients

Saely CH, Rein P, Schmid F, Koch L, Aczel S, Benzer W, Hoefle G, Marte T  
VIVIT Institute, Feldkirch, Austria, Academic Teaching Hospital Feldkirch, Feldkirch, Austria

**Background/Aims:** Type 2 diabetes (T2DM) in cross-sectional studies is associated with coronary artery disease (CAD) and prospectively confers a strongly increased risk of vascular events. It is not certain to what extent the baseline CAD state accounts for the increased vascular risk of diabetic patients in prospective studies because angiography usually is not performed. **Methods:** We therefore enrolled 750 consecutive patients undergoing coronary angiography for the evaluation of estab-

lished or suspected stable CAD. At angiography, CAD was diagnosed in the presence of any irregularities of the vessel wall. Stenoses  $\geq 50\%$  were considered significant, and the extent of CAD was defined as the number of significant stenoses in a patient. Vascular events were recorded over 4 years. **Results:** The prevalence of CAD (87.8% vs. 80.4%;  $p = 0.029$ ) and of significant stenoses (69.5% vs. 58.4%;  $p = 0.010$ ) as well as the extent of CAD ( $1.7 \pm 1.5$  vs.  $1.4 \pm 1.5$ ;  $p = 0.014$ ) were significantly higher in patients with T2DM ( $n = 164$ ) than in nondiabetic subjects ( $n = 586$ ). Prospectively, T2DM after multivariate adjustment strongly predicted vascular events (adjusted hazard ratio (HR) = 1.66 [1.15 – 2.39];  $p = 0.006$ ). Also, the presence of CAD (HR = 2.78 [1.39 – 5.57];  $p = 0.004$ ), the presence of significant stenoses (HR = 3.67 [2.30 – 5.85];  $p < 0.001$ ) and the extent of CAD (standardized adjusted HR = 1.62 [1.41 – 1.87];  $p < 0.001$ ) significantly predicted vascular events. These angiographic characteristics still predicted vascular events after additional adjustment for T2DM (HR = 2.66 [1.33 – 5.34];  $p = 0.006$ , 3.57 [2.24 – 5.70];  $p < 0.001$ , and 1.60 [1.34 – 1.84];  $p < 0.001$ , respectively). Conversely, T2DM remained strongly and significantly predictive of future vascular events after adjustment for the presence and extent of CAD (HR = 1.50 [1.04 – 2.15];  $p = 0.029$ ). **Conclusions:** Among angiographed coronary patients, the presence and the extent of CAD are higher in patients with T2DM than in nondiabetic individuals. Prospectively, T2DM and the baseline CAD state are mutually independent predictors of future vascular events.

44

### Role of Interleukin-6 in hepatic glucose production

Immel L, Runge H, Lehmann R, Häring HU, Weigert C, Schleicher E  
Department of Internal Medicine University of Tübingen, Germany

**Aims:** Besides its function in inflammatory processes IL-6 is a potent player in metabolism. It is known to regulate insulin action and to stimulate lipolysis. The aim of our work is to elucidate the function of IL-6 in gluconeogenesis in hepatocytes. **Methods:** All experiments were conducted in Fao rat hepatoma cells (Fao). Cells were starved overnight in a serum and glucose free medium containing 2 mM lactate. On the following day cells were stimulated with various substances in a glucose- and serum-free medium containing 5 or 10 mM lactate. After indicated timepoints supernatant, protein and RNA was collected for subsequent analyses. **Results:** Fao cells produced glucose when lactate as substrate was provided. Increasing insulin concentrations (0.1 – 100 nM) reduced the glucose production gradually, while the rate of glucose production was increased by 67% and 40% under stimulation with dexamethasone and IL-6, respectively. Furthermore we found that IL-6 counteracts the insulin action on gluconeogenesis. After the overnight starvation in glucose-free medium no glucose production derived from glycogenolysis was detectable. Studying the putative underlying mechanism, we observed that IL-6 did slightly reduce insulin-induced Foxo-1 phosphorylation with no inhibitory effect on phosphorylation of Ser-473 of Akt. However, IL-6 did not abolish the inhibitory action of insulin on the expression of the gluconeogenic enzymes PEPCK and Glucose-6-phosphatase. **Conclusions:** IL-6 is able to induce glucose production in Fao cells and to counteract the inhibitory action of insulin. This effect is not mediated by altered expression of gluconeogenic enzymes.

45

### Does alfalcidol prevent pancreatic beta cells from further destruction in children at the onset of diabetes mellitus type 1?

Szewczyk L, Azab Y, Bury A, Piekarski R  
Medical Academy of Lublin, Department of Pediatric Endocrinology and Neurology, Poland

In recent years studies focused on prevention of type 1 diabetes mellitus (DM) and possibility of beta-cell protection at the clinical diagnosis of DM. Some recent studies have demonstrated beneficial role of vit. D3 analogue in human beta-cell activity maintenance at the early stages of DM. **Material and methods:** The study was performed in 63 children and adolescents (32 female and 31 male) aged 4 – 16 years who received insulin and vit D3 analogue (alfalcidol – 1alpha-OH-vitamin D3) in daily dose 0.25  $\mu\text{g}$ . 37 peers (17 female and 20 male) with type 1 DM who received only insulin therapy without vit. D3 administration were the control group. After one year therapy we compared the level of HbA1c, body mass, daily insulin dose in both groups. **Results:** There are no differences in mean body mass and in metabolic control of dia-

betes reported by mean HbA1c level at the onset of the DM and after one year observation of these patients among studied groups. However, daily insulin dose in group of patients who received vit. D3 therapy after one year observation were at the similar level compared to the early stage of DM (0.36 u/kg – 0.37 u/kg). On the contrary, insulin requirement in the group of patients without vit. D3 treatment significantly increased after one year observation (from 0.37 u/kg to 0.63 u/kg). **Conclusions:** In group of children treated alfalcidol insulin requirement after one year therapy with vit. D3 analogue sustained at the level found at the early stage of DM. Children without vit. D3 administration had twofold increase of insulin requirement after one year observation from clinical diagnosis. Our observations suggest, that alfalcidol could play a role in prevention of further beta-cells destruction.

46

#### Prevalence of hypercholesterolemia in diabetic patients and in population who do not suffer from diabetes in the island of Kos

*Tsoukis E, Patiakas S, Aggos I, Kiriakopoulos N, Gavala C, Pelegri E, Koutouzi G, Akritopoulou K  
General Hospital of Kos, Greece*

**Purpose:** The comparison of prevalence of hypercholesterolemia among diabetic patients and population who don't suffer from diabetes in the island of Kos. **Material-Method:** The material was composed by 7774 non diabetic people (3732 men – 4042 women) and 750 diabetic patients (338 men – 412 women). Both groups came to the Microbiological Lab of Kos General Hospital during 2005 – 2006. The concentration of cholesterol was counted with enzyme chromometric method at the biochemical analyzer Architect (Abbott). Cholesterol rates > 200 mg/dl were considered to be pathologic. **Results:** Cholesterol concentrations was of: „200 mg/dl in diabetic patients (62,5%) “200 mg/dl in diabetic patients (37,5%) „200 mg/dl in non-diabetic patients (78,7%) “200 mg/dl in diabetic patients (21,3%) **Conclusions:** 1) The frequency of hypercholesterolemia in both population groups is quite high. 2) The prevalence of hypercholesterolemia in diabetic patients (37,5%) is by 76% higher than the corresponding prevalence to the rest of the population (21,3%). This remark is related to the metabolic syndrome which appears to overweight people with hyperlipidemia and diabetes. 3) The high frequency of hypercholesterolemia in diabetics, has as a consequence

47

#### Prevalence of hypertriglyceridemia in diabetic patients and in population who do not suffer from diabetes in the island of Kos

*Tsoukis E, Aggos I, Patiakas S, Gavala C, Kiriakopoulos N, Pelegri E, Xaralampous X, Akritopoulos P  
General Hospital of Kos, Greece*

**Purpose:** The comparison of prevalence of hypertriglyceridemia among diabetic patients and population who don't suffer from diabetes in the island of Kos. **Material-Method:** The material was composed by 7774 non diabetic people (3732 men – 4042 women) and 750 diabetic patients (338 men – 412 women). Both groups came to the Microbiological Lab of Kos General Hospital during 2005 – 2006. The concentration of triglyceride was counted with enzyme chromometric method at the biochemical analyzer Architect (Abbott). Triglyceride rates > 150 mg/dl were considered to be pathologic. **Results:** Trygiceride concentrations were of: „150 mg/dl in diabetic patients (80,5%) “150 mg/dl in diabetic patients (19,5%) „150 mg/dl in non-diabetic patients (90%) “ 150 mg/dl in diabetic patients (9,8%) **Conclusions:** 1) The frequency of hypertriglyceridemia of the population group who don't suffer from diabetes is relatively low (9,8%). 2) The frequency of hypertriglyceridemia of diabetic patients is relatively high (19,5%). 3) The prevalence of hypertriglyceridemia among diabetic patients is 99% higher than the respective prevalence to the rest of the population. This has as a consequence greater risk of coronary disease in diabetic patients than the rest of the population.

48

#### Evaluating the clinical outcomes associated with insulin aspart versus human insulin as the bolus component of a basal bolus regimen for type 2 diabetes over patient lifetimes

*Valentine W, Goodall G, Townsend C, Nielsen S, Kotchie R, Erny-Albrecht K  
IMS Health Economics and Outcomes Research, Basel, Switzerland*

**Aim:** To evaluate the long-term clinical implications of using insulin aspart (NovoRapid®) versus human insulin (HI) as the bolus component of basal-bolus therapy in type 2 diabetes patients in Germany. **Material and Methods:** A published computer simulation model of diabetes, previously validated against real-life data, was used to project long-term clinical outcomes. Three-month data for patients in the German cohort (n = 920) receiving insulin aspart or HI, both in combination with insulin detemir, from the PREDICTIVE observational study was used as the basis of the analysis (mean age 63 years, duration of diabetes 13 years, HbA1c 8.17%, BMI 30.3 kg.m<sup>-2</sup>). The model was used to predict life expectancy, time to onset and cumulative incidence (CI) of diabetes-related complications over patient lifetimes. **Results:** Treatment with insulin aspart was projected to improve undiscounted life expectancy by 0.23 years versus HI (12.79 ± 0.13 versus 12.56 ± 0.12 years). Mean time to onset of first complication was delayed by 0.29 years with insulin aspart (3.66 years) versus HI (3.37 years). Insulin aspart was associated with a reduced CI of most complications. For proliferative diabetic retinopathy, the CI was decreased by 10% with insulin aspart (2.11%) versus HI (1.90%). Similarly, the CI of end-stage renal disease, one of the costliest complications, was decreased by 13% (5.41% versus 4.72%). The CI of most cardiovascular complications was also reduced in the insulin aspart arm with the exception of stroke, where an increase of 3.5% was projected. This was most likely due to the survival paradox, whereby patients living longer on insulin aspart were exposed to the risk of stroke for longer than those on HI. **Conclusion:** Insulin aspart, as the bolus component of basal-bolus therapy, was projected to improve life expectancy, delay the onset and reduce the incidence of most diabetes-related complications compared to HI in German type 2 diabetes patients.

49

#### Long-term complications costs for type 1 diabetes patients on detemir versus NPH-based basal-bolus therapy in a German setting. A modelling evaluation based on results from a meta-analysis of three clinical trials

*Kotchie R, Aagren M, Valentine W, Goodall G  
IMS Health Economics and Outcomes Research, Basel, Switzerland*

**Aim:** To evaluate lifetime costs associated with complications in type 1 diabetes patients treated with either insulin detemir (IDet) or human insulin (NPH) based basal-bolus therapy in a German setting. **Methods:** A published and validated computer simulation model was used to project the long-term progression of diabetes-related complications based on probabilities from landmark clinical and epidemiological studies and account associated costs. Clinical effects of treatment were obtained from a meta-analysis of three clinical trials demonstrating reductions in HbA<sub>1c</sub> (-0.13%), body mass index (BMI) (0.21 kg.m<sup>-2</sup>) for IDet versus NPH. Baseline simulated cohort characteristics (mean age 40.3 years, duration of diabetes 16.3 years, HbA<sub>1c</sub> 8.3%, BMI 25.2 kg.m<sup>-2</sup>) were taken from the meta-analysis. Complication treatment costs were obtained from published sources and total lifetime costs were accounted from a German Health Service perspective and discounted at 5% annually. **Results:** Over patient lifetimes IDet was associated with reduced complications costs versus NPH of € 229 (€ 66,063 versus € 66,292) primarily driven by lower treatment costs for nephropathy of € 414 (€ 20,363 versus € 20,777) and savings due to reductions in retinopathy complications of € 174 (€ 17,666 versus € 17,840). Cardiovascular complication costs were comparable between arms (€ 7,379 versus € 7,411) as were the costs of treating diabetic foot complications (€ 12,475 versus € 12,582). Results were shown to be stable under reasonable variation in a range of assumptions. **Conclusions:** The use of IDet versus NPH leads to reduced complication costs over patient lifetimes, particularly for nephropathy and retinopathy, due to improvements in glycaemic control. This is despite the survival paradox whereby IDet patients live longer than those receiving NPH and are therefore at a greater risk of complications.

50

**Long-term cost-effectiveness of insulin detemir versus NPH in type 2 diabetes patient: An evaluation in the German setting**Valentine W, Aagren M, Kotchie R, Goodall G  
IMS Health Economics and Outcomes Research, Basel, Switzerland

**Aims:** To evaluate the long-term clinical and economic outcomes associated with therapy conversion to insulin detemir (Levemir, Novo Nordisk) from human insulin (NPH) in type 2 diabetes patients in the German setting. **Material and Methods:** A validated computer simulation model of type 2 diabetes was used to make long-term projections of clinical and cost outcomes based on patient characteristics and treatment effects from the German cohort of the PREDICTIVE observational study. The trial indicated that therapy conversion from NPH to insulin detemir was associated with a significant improvement in glycemic control (HbA1c -0.6%) as well as reduced weight gain (-0.382 kg/m<sup>2</sup>). Based on these clinical findings the model was used to evaluate life-expectancy, quality-adjusted life expectancy and direct medical costs for the detemir and NPH treatment arms. Future costs and clinical benefits were discounted at 5% *per annum*. **Results:** Treatment with insulin detemir was projected to improve life expectancy by approximately 0.13 years compared to NPH (7.14±0.12 versus 7.01±0.13 years). Quality-adjusted life expectancy was 0.28 quality-adjusted life years (QALYs) higher in the detemir arm than in the NPH arm (4.54±0.08 versus 4.26±0.08 QALYs). Direct medical costs over patient lifetimes were comparable in the detemir (€59,585±1,594) and NPH (€59,216±1,778) arms (difference €369). This led an incremental cost-effectiveness ratio of approximately €1,314 per QALY gained for insulin detemir versus NPH, which represents very good value for money by commonly reported standards in Germany. Acceptability curve analysis indicated that there was a 99% likelihood that insulin detemir would be considered good value for money at a willingness to pay threshold of €30,000 per QALY gained. **Conclusion:** This health economic evaluation, based on the findings of PREDICTIVE, indicates that treatment with insulin detemir is likely to be highly cost-effective versus NPH in type 2 diabetes patients in Germany.

51

**Reducing the incidence of complications over patient lifetimes: A modeling analysis of insulin detemir versus NPH in German type 2 diabetes patients**Valentine W, Aagren M, Kotchie R, Goodall G  
IMS Health Economics and Outcomes Research, Basel, Switzerland

**Aims:** To evaluate the time to onset and long-term cumulative incidence of diabetes-related complications in type 2 diabetes patients receiving either insulin detemir (Levemir, Novo Nordisk) or NPH in the German setting based on the findings of a recent observational study. **Material and Methods:** A validated computer simulation model of type 2 diabetes was used to make long-term projections of clinical outcomes based on patient characteristics and treatment effects from the German cohort of the PREDICTIVE observational study. The trial demonstrated that therapy conversion from NPH to insulin detemir was associated with a significant improvement in glycemic control (HbA1c -0.6%) as well as reduced weight gain (-0.382 kg/m<sup>2</sup>). The model brings together data from a number of landmark clinical and epidemiological studies to make long-term projections of diabetes progression and related complications, using Markov modeling techniques and second order Monte Carlo simulation. Its accuracy has been validated against real-life clinical and epidemiological studies. **Results:** Insulin detemir was projected to improve undiscounted life expectancy by approximately 0.27 years compared to NPH (10.24±0.12 versus 9.97±0.13 years). The mean time to onset of any diabetes-related complication was delayed by 0.11 years in the detemir arm (0.76 versus 0.65 years). The cumulative incidence (CI) of diabetes related complications was notably lower in the insulin detemir arm over patient lifetimes. For example, the CI of myocardial infarction was 1.2% lower (20.3% versus 21.5%) with detemir versus NPH and, similarly, benefits were projected for severe vision loss (0.9% lower, 6.3% versus 7.2%), neuropathy (3.9% lower, 49.0% versus 52.9%) and end-stage-renal disease (1.4% lower, 5.4% versus 6.8%). **Conclusion:** Using data from the German cohort of PREDICTIVE, our modeling analysis suggests that insulin detemir is likely to improve life expectancy, delay the onset of and reduce the cumulative incidence of diabetes-related complications in type 2 diabetes patients.

52

**Dehydroepiandrosterone sulfate and common carotid intima-media thickness in patients with type 2 diabetes mellitus**Vasiliadis M, Papaioakim M, Heliopoulos I, Gioka T, Tsiligris A, Toromanidou M, Nikelli M, Pagalos E  
General Hospital "Papageorgiou", Thessaloniki, Greece

**Backgrounds/Aims:** Cardiovascular disease (CVD) is the primary cause of mortality in patients with diabetes mellitus (DM). Studies have shown an inverse relationship between plasma levels of dehydroepiandrosterone sulfate (DHEA-S) and coronary artery disease. It has been reported that DHEA-S levels are negatively correlated with common carotid intima-media thickness (CCIMT) with type 2 DM but only in men. We examined the association between endogenous DHEA-S and CCIMT, in patients of both sexes with type 2 DM. **Methods:** Serum DHEA-S concentration was measured in 169 participants with type 2 DM (102 females and 67 males). High-resolution real-time ultrasonography was used to measure the left and right CCIMT. Along with demographic data and anthropometric variables, traditional CVD risk factors, alcohol and tobacco use were also assessed. **Results:** DHEA-S concentration was negatively correlated with age ( $r = -0.287$ ,  $p < 0.001$ ) and CCIMT ( $r = -0.236$ ,  $p = 0.002$ ). A positive correlation was found between mean CCIMT and age ( $r = 0.325$ ,  $p < 0.001$ ), and duration of DM ( $r = 0.17$ ,  $p = 0.03$ ). Multiple regression analysis showed that DHEA-S concentration remained negatively associated with CCIMT after adjustment for age, smoke use and hypertension ( $b = -0.21$ , 95% CI: 0.259 – 1.414,  $p = 0.005$ ). Sex, BMI, waist-hip ratio (WHR), lipid profile chemistries, GHb, and alcohol habits did not show significant association with CCIMT when included in the model. **Conclusion:** The decline of DHEA-S is negatively associated with CCIMT in both sexes, implicating a possible atheroprotective role of DHEA-S in patients with type 2 DM.

53

**Involvement of vascular endothelial growth factor and tumor necrosis factor-alpha in the process of neovascularization in children with type 1 diabetes mellitus**Zorena K, Myliwska J, Myliwiec M, Balcerska A  
Diabetological Department Clinic of Pediatrics, Hematology, Oncology and Endocrinology Medical University of Gdańsk, Poland

**Backgrounds/Aims:** Neovascularization is a complex process, in which crucial role seems to be played by vascular endothelial growth factor (VEGF) and tumor necrosis factor (TNF-alpha). TNF-alpha may exhibit both stimulating and inhibiting effect on angiogenesis. Therefore it appeared to be worth of analysis to investigate the relation between TNF-alpha and VEGF and the clinical course of the disease in children with Diabetes Mellitus type 1 (DM 1). **Material and methods:** 163 children aged 13.6±3.5 years diagnosed with DM 1 from the Department of Paediatrics, Haematology, Oncology and Endocrinology at the Medical University of Gdańsk were enrolled in the study along with 60 healthy children (as the control). All the children had their daily urine albumin secretion, HbA1c, C-peptide measured; 24hrs blood pressure monitoring and ophthalmologic examination. Additionally, all of them had serum VEGF and TNF-alpha measured using highly-sensitive ELISA tests. **Results:** In accordance to the daily albumin urine secretion and ophthalmologic examination, the children were divided into groups: Group A without complications, Group B with retinopathy, Group C with nephropathy and Group D with both retino- and nephropathy. Between the groups statistically significant differences in age, duration of the disease, HbA1c serum level, daily albumin urine secretion and the systolic and diastolic blood pressure were found. Besides, statistically significant differences in the VEGF level and TNF-alpha were measured. Moreover, in the group D statistically significant correlation between VEGF and TNF-alpha levels was observed.

54

**Komplexe Untersuchungen bei Nachkommen von Patienten mit Typ 2 Diabetes**Szykowna I, Wasikowa R  
Wrocław, Polen

In den letzten Jahren wird auf der ganzen Welt, ebenso wie in Polen, ein konstanter Zuwachs der Inzidenz des Diabetes, vor allem des Typ-2-Diabetes beobachtet. Es wird angenommen, dass im Jahre 2030 die Anzahl der Diabetiker über 300 Millionen betragen wird. Man spricht von einer Epidemie des 21. Jahrhunderts. Ziel der Untersuchungen: Bis jetzt gibt



es keine Marker, die eine ganz sichere Diagnose des Diabetes Typ-2 vor der klinischen Manifestation ermöglichen. Es gibt aber eine Reihe von Risikofaktoren. Festgestellt wurde ein familiär gehäuftes Auftreten des Typ-2-Diabetes. Wegen schwerer Komplikationen, die bei zu spät oder nicht diagnostiziertem Diabetes auftreten können, fanden wir es wichtig, komplexe Untersuchungen bei erwachsenen Kindern von Patienten mit Typ -2 -Diabetes durchzuführen. Die Untersuchungen umfassten 197 Personen im Alter von 18 bis 71 Jahren, Frauen und Männer. Bei 74 hatte der Vater Diabetes, bei 121 die Mutter, bei einer Person waren es beide Eltern. Bei allen Patienten wurden folgende Untersuchungen durchgeführt: Glykämie, Cholesterin, HDL, LDL, Insulinämie, C-Peptid, HbA1c, BMI. **Resultate:** Bei 48% der 197 Probanden wurde Diabetes Typ -2 festgestellt, in 25% bei Nachkommen von Vätern mit Typ -2 -Diabetes und in 23% mit diabetischen Müttern. Prädiabetes wurde bei 33% der Untersuchten diagnostiziert. 58% hatten Übergewicht oder Adipositas, 75% im Alter über 44 Jahren. Bei über 50% waren Cholesterin und HbA1c erhöht, vor allem bei Männern über 44 Jahren. Das abnormale Niveau von Insulin, C-Peptid, HbA1c und BMI zeigte eine Korrelation mit dem männlichen Geschlecht und dem Alter über 44 Jahre. **Schlussfolgerungen:** Bei Kindern von Patienten mit Typ-2-Diabetes treten Störungen des Kohlenhydratmetabolismus und unbekannter Diabetes in höherem Prozentsatz auf. Es existieren auch signifikante Störungen im Lipidstoffwechsel und Hypertonie. Kinder von Patienten mit Typ -2 -Diabetes sind eine Gruppe mit sehr hohem Risiko für Typ-2 -Diabetes. Ein frühes Entdecken der festgestellten Störungen ermöglicht ein Vorbeugen der Entwicklung von mit Typ -2-Diabetes verbundenen Spät-komplikationen. Man sollte bei allen Nachkommen von Patienten mit Typ-2-Diabetes ein wiederholtes Screening durchführen und die Parameter des Glukose- und Lipidstoffwechsels sowie auch den Blutdruck untersuchen.

55

#### The relation of thyroid hormone levels and reduced insulin sensitivity to survival of patients with septic shock

Halvatsiotis PC<sup>1</sup>, Stefanopoulou S<sup>1</sup>, Kotanidou A<sup>2</sup>, Orfanos S<sup>2</sup>, Martinos C<sup>2</sup>, Roussos C<sup>2</sup>, Economopoulos T<sup>1</sup>, Raptis SA<sup>1,3</sup>  
<sup>1</sup>2<sup>nd</sup> Dept of Int. Med. Propaedeutic, Athens University Medical School; <sup>2</sup>1<sup>st</sup> Dept. of Critical Care, Athens University Medical School; <sup>3</sup>Hellenic National Diabetes Center

Muscular weakness frequently develops in the intensive care unit patients and it is associated with higher mortality rate. Oxidative phosphorylation produces energy and hypothyroidism produces a hypometabolic state. Studies have showed reductions of thyroid hormone levels in critical illness. We aimed to measure thyroid hormone levels in septic patients and investigate the relationship of these hormones with survival and inhibition of mitochondrial respiration. We determined representative mitochondrial enzyme gene transcript levels in vastus lateralis needle biopsy samples, using a real-time QPCR technique for citrate synthase (SC), Cytochrome C oxidase I & III, NADH, and UCPs 2 & 3. We measured the TSH, FT3, FT4 hormones levels with biochemical methods. We studied 7 critically ill patients under irreversible septic shock (52 ± 7 y) who died within 30 days (SS) and 8 age and gender matched septic patients (46 ± 7 y) (p=0,51) who survived (SSV). All patients were non diabetic and SS group demonstrated lower insulin sensitivity than SSV using the HOMA test (11,56 ± 3,5 vs. 48,59 ± 11,4) (p=0,011). There was no difference in the enzyme activity of all mitochondrial enzymes between the 2 groups. The gene transcript of CS was significantly higher in SSV than SS (2,62 ± 0,3 vs. 1,29 ± 0,6 AU) (p=0,011) while there was no difference in the transcripts of the other mitochondrial enzymes. There was no difference in TSH levels between the 2 groups. The levels of FT3 hormone were significantly higher in SSV than SS (1,481 ± 0,07 vs. 1,123 ± 0,06 pg/ml) (p=0,002) and FT4 were also significantly higher in SSV than SS (1,07 ± 0,1 vs. 0,77 ± 0,06 ng/dl) (p=0,032). In conclusion, in septic patients, we found an association of the severity of sepsis with the development of insulin resistance and mitochondrial dysfunction while lack of thyroid hormones, major ubiquitous regulators of mitochondrial activity, may contribute to the muscular energy production abnormalities.

56

#### Peripheral mononuclear TNF- $\alpha$ , visfatin, and resistin mRNA expression in overweight women with type 2 diabetes

Tsiotra P<sup>1</sup>, Tsigos C<sup>1</sup>, Yfanti E<sup>1</sup>, Anastasiou E<sup>2</sup>, Raptis SA<sup>1,3</sup>  
<sup>1</sup>Hellenic National Diabetes Center; <sup>2</sup>First Endocrine Section and Diabetes Centre, Alexandra Hospital; <sup>3</sup>2<sup>nd</sup> Dept. of Internal Medicine, Research Institute and Diabetes Center, ATTIKO Hospital, University of Athens, Athens, Greece

**Background and Aims:** Adipocytokines, like TNF- $\alpha$ , visfatin and resistin, have been suggested to be important regulators of insulin resistance, and may provide the molecular links between visceral obesity, type 2 diabetes and atherosclerosis. We examined whether TNF- $\alpha$ , visfatin and resistin mRNA expression from human peripheral mononuclear cells is altered in type 2 diabetes and whether it is related to indices of obesity and insulin resistance. **Materials and Methods:** We studied 16 overweight women (BMI > 26) with type 2 diabetes (DM2) and 26 healthy women with normal glucose tolerance (14 with BMI > 26 (NGT-overw), and 12 with BMI < 26 (NGT-lean), all premenopausal. We measured relative visfatin, TNF- $\alpha$ , and resistin mRNA levels in peripheral monocyte-enriched mononuclear cells using a real-time quantitative RT-PCR assay (LightCycler, Roche). Fasting and 2 hour post-OGTT plasma glucose and insulin (RIA) levels, were also measured. **Results:** Relative visfatin and TNF- $\alpha$ , but not resistin, mRNA levels were several-fold higher in DM2 compared to NGT-lean or NGT-overw controls (Table) and correlated significantly with each other (p < 0.001, r = 0.605). Furthermore, visfatin mRNA levels correlated significantly overall with BMI, waist circumference and the HOMA-IR index (p < 0.05, r = 0.326), while TNF- $\alpha$  mRNA levels correlated significantly with the waist to hip ratio (p = 0.04, r = 0.392).

	BMI kg/m <sup>2</sup>	HOMA-IR	Visfatin mRNA	TNF $\alpha$ mRNA	Resistin mRNA
NGT-lean	22.4 ± 0.7	1.4 ± 0.1	0.59 ± 0.27	0.03 ± 0.008	0.39 ± 0.09
NGT-overw	33.1 ± 1.5*	3.0 ± 0.5*	0.68 ± 0.25	0.03 ± 0.01	0.43 ± 0.16
DM2	35.1 ± 1.1*	5.6 ± 0.9* <sup>§</sup>	2.28 ± 0.64* <sup>§</sup>	0.31 ± 0.17* <sup>§</sup>	0.49 ± 0.07

\*, p < 0.02 vs. NGT-lean; §, p < 0.05 vs. NGT-obese

**Conclusions:** Peripheral mononuclear visfatin and TNF- $\alpha$  mRNA expression, is elevated in type 2 diabetic subjects, suggesting that these monocyte-derived adipokines may contribute to the insulin resistance, the atherogenic risk, and the visceral fat accumulation that characterizes type 2 diabetes.

## Namenverzeichnis der Abstractautoren

## A

Aagren M A14, A15  
 Aczel S A12, A13  
 Aggos I A4, A7, A8, A9, A11, A14  
 Akritopoulos P A7, A8, A11, A14  
 Akritopoulou K A7, A8, A10, A11, A14  
 Alexander C A6  
 Anastasiou E A16  
 Argyriou A A6  
 Azab Y A12, A13

## B

Balcerska A A10, A15  
 Balletshofer B A6  
 Belan V A4  
 Benzer W A13  
 Bonifacio E A4  
 Brix J A4  
 Bury A A12, A13

## C

Czarnecka D A7

## D

Dambrova M A9  
 Douvetzemis S A12  
 Drexel H A12

## E

Eckel J A4  
 Economopoulos T A10, A16  
 Erny-Albrecht K A14

## F

Fedak D A7  
 Feder A A4  
 Fotiadis E A7, A8  
 Fritsche A A6  
 Füchtenbusch M A4

## G

Gasperikova D A4  
 Gavala C A4, A9, A10, A11, A14  
 Georgantis H A10, A11  
 Georgantis I A4, A9  
 Gioka T A15  
 Goodall G A14, A15  
 Grzeszczak W A9

## H

Haag GM A9  
 Halvatsiotis PG A16  
 Häring HU A13  
 Hatzigelaki E A10  
 Hatzopoulos A A5, A6  
 Heliopoulos I A15  
 Heras P A5, A6  
 Hoefle G A12, A13  
 Hummel M A4  
 Humpert PM A9

## I

Idzior-Walu B A7  
 Immel L A13

## J

Jahnel H A12

## K

Kambanis I A4, A9  
 Kantartzis K A6  
 Kasalova Z A7  
 Kasalova jr Z A7  
 Katra B A7  
 Kiriakopoulos N A7, A8, A10, A11, A14  
 Klimes I A4  
 Knopff A A4  
 Koch L A12, A13  
 Konrade I A9  
 Kontogiannis I A7, A8  
 Kotanidou A A16  
 Kotchie R A14, A15  
 Kotsidas I A9  
 Koutouzi G A14  
 Kritikos K A5, A6  
 Krupicka J A7  
 Krzyzanowska K A4  
 Kyriakopoulos N A4, A9, A10

## L

Langer P A12, A13  
 Lehmann R A13  
 Lejniaks A A9  
 Liepins E A9

## M

Machann J A6  
 Makri A A12  
 Marte T A12, A13  
 Martinos C A16  
 Mazarakis A A11  
 Mitsibounas D A5, A6  
 Mittermayer F A4  
 Moczulski D A9  
 Muendlein A A13  
 Myliwiec M A10, A15  
 Myliwska J A10, A15

## N

Nielsen S A14  
 Nikelli M A15  
 Nikolakis G A11, A12

## O

Orfanos S A16

## P

Pagalos E A15  
 Panagiotidou M A10  
 Papaioakim M A15  
 Patiakas S A4, A7, A8, A9, A10, A11, A14  
 Payer J A4  
 Pelegri E A10, A14  
 Penesova A A4  
 Piagos G A11, A12  
 Piagou M A11, A12  
 Piekarski R A12, A13  
 Pura M A4

## R

Radikova Z A4  
 Raptis SA A10, A16  
 Rein P A12, A13  
 Remiszewska B A9  
 Risch L A12  
 Rittig K A6  
 Roussos C A16  
 Runge H A13

## S

Saely CH A12, A13  
 Safarikas M A5, A6  
 Schernthaner G A4  
 Schleicher E A6, A13  
 Schmid F A12, A13  
 Sieradzki J A7  
 Skapare E A9  
 Skopkova M A4  
 Sourij H A12  
 Stefanopoulou S A16  
 Stoyanov S A9  
 Szewczyk L A12, A13  
 Szykowna I A15

## T

Thamer C A6  
 Toromanidou M A15  
 Townsend C A14  
 Tsigos C A16  
 Tsiligiris A A15  
 Tsiotra P A10, A16  
 Tsitlakidou S A9  
 Tsoukis E A4, A7, A8, A9, A10, A11, A14

## U

Ukropec J A4

## V

Valentine W A14, A15  
 Vasiliadis M A15  
 Vlcek M A4

## W

Walu-Miarka M A7  
 Wasikowa R A15  
 Weigert C A13  
 Wentzel A A4

## X

Xaralampous X A10, A11, A14  
 Xiropoulou E A10, A11  
 Xiropoulou E A11

## Y

Yfanti E A16

## Z

Ziegler A A4  
 Zorena K A10, A15  
 Zweiker R A12