

## ABSTRACTS

### 7<sup>th</sup> Annual Workshop on Diabetes Mellitus and its Complications

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#### THE NATURE OF DIABETIC POLYNEUROPATHY

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The commonest form of diabetic neuropathy is a distal length-related symmetric sensory and autonomic polyneuropathy. The emphasis on these two functional modalities indicates that diabetic polyneuropathy can be classified as a neuronal system degeneration in which there is a selective vulnerability of particular sets of neurons to the diabetic state. Proposals have been made that diabetic neuropathy can be the result of an indirect effect via small vessel disease. It is clear that superimposed multifocal lesions in peripheral nerve, possibly vascular in nature, can produce a distal approximately symmetric motor and sensory neuropathy, but pathological studies suggest that diabetic sensory polyneuropathy is a central-peripheral distal axonopathy of dying-back type. Once established, diabetic sensory polyneuropathy is largely irreversible. One explanation for this could be involvement of the centrally directed axons of the primary sensory neurons as axonal regeneration does not occur in the central nervous system. A further reason is that although axonal regeneration in peripheral nerves in diabetic polyneuropathy is initially profuse, it later fails. Recent

experimental studies have suggested that this is partly because of reduced regenerative capacity by the sensory nerve fibres and partly because the microenvironment in the peripheral nerve trunks in diabetic subjects is not favourable for axonal elongation.

#### A2

#### DIABETES AND IMPAIRED GLUCOSE TOLERANCE IN JORDAN: PREVALENCE AND ASSOCIATED RISK FACTORS

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Objectives: To study the prevalence of diabetes mellitus (DM) and impaired glucose tolerance (IGT) and their risk factors in Jordan.

Design: A cross-sectional study in four Jordanian communities was conducted: Sarih in the north, Sikra in the middle of the country, Mazar in the south and Subha- Subheih in the east. Within each community, a systematic sample of households was selected. All subjects  $\geq 25$  years of age within the selected households were invited to participate in the study. A total of 2836 subjects were actually included in the study with an overall response rate of 70.5% (45% in

males and 86% in females). World Health Organisation criteria were adopted for the diagnosis of DM (fasting plasma glucose  $\geq 7.8$  mmol L<sup>-1</sup> or plasma glucose of  $\geq 11.1$  mmol L<sup>-1</sup>, 2h after an oral anhydrous glucose load of 75g) and IGT (fasting plasma glucose  $< 7.8$  mmol L<sup>-1</sup> and plasma glucose between 7.8 mmol L<sup>-1</sup> and 11.1 mmol L<sup>-1</sup>, 2h after an oral glucose load of 75 g).

**Results:** The overall prevalence of DM was 13.4% : 14.9% in males and 12.5% in females. IGT was found in 9.8% of the study population: 9.0% in males and 10.3% in females. Factors independently related to DM using stepwise logistic regression analysis were sex, age, family history of DM, hypertension, hypercholesterolaemia (HC), and hypertriglyceridaemia (HTG).

**Conclusion:** Diabetes mellitus and IGT are common among adult Jordanians. Considering the high prevalence of this sickness makes it imperative to formulate a national plan to face this disease and its complications.

#### A4

### **THE IMPACT OF THE NEW DIAGNOSTIC CRITERIA FOR DIABETES ON THE DIAGNOSIS OF ABNORMAL GLUCOSE TOLERANCE IN A HOSPITAL REFERRED POPULATION**

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The ADA and WHO have recently produced new diagnostic criteria for diabetes. We compared the diagnostic sensitivity of these new criteria and

examined their impact on misclassification of individuals. We reviewed data obtained from oral glucose tolerance tests on 2760 non-pregnant subjects referred with suspected Type 2 or gestational diabetes respectively over a 3 year period to the Royal Preston Hospital. The rates of diabetes among 2759 individuals was 12.2% according to the 1985 WHO, 10.7% according to the 1997 ADA and 14.3% according to 1998 WHO criteria. The 1997 ADA criteria misclassified 33% of subjects as non-diabetic classified as diabetic by 1985 WHO criteria which misclassified 36% diabetic subjects by the 1997 ADA criteria as non-diabetic. Such misclassification was abolished on using the proposed 1998 WHO criteria.

The new 1998 WHO criteria for the diagnosis of diabetes identifies the highest number of diabetic subjects and abolishes misclassification of individuals that results on using the ADA 1997 criteria. We suggest guidelines based on a single fasting plasma glucose concentration in the diagnosis of diabetes require revision.

#### A5

### **CHANGING THE FOCUS IN DIABETES MANAGEMENT: POSTPRANDIAL HYPERGLYCAEMIA**

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The goals for treating diabetes mellitus have changed over time. Initially insulin was given to prevent ketoacidosis and coma. Then the goal was to reduce the classical symptoms of diabetes. i.e., polyuria and weight loss. Multicentre trials like DCCT and UKPDS have taught

us that intensified treatment will prevent or at least delay microvascular and macrovascular complications.

It is now time to move the goalposts again. Macrovascular complications of diabetes, i.e., cardiovascular disease (CVD) including arteriosclerosis, myocardial infarction and stroke are especially important in type 2 diabetes. CVD seems to increase in intensity which is already at relatively low-level hyperglycemia. Thus, it becomes necessary for us not only to focus on fasting hyperglycaemia (FHG) but postprandial hyperglycaemia (PPHG).

What is the evidence that postprandial hyperglycaemia is more important than fasting? The evidence is twofold:

1. HbA1c levels correlate better with PPHG than FHG.
2. PPHG is a stronger risk factor for CVD than FHG.

In a patient in early development of clinical diabetes, fasting glucose levels may or may not be high. However, abnormalities are more clearly seen in the postprandial state, including blood glucose and plasma triglyceride peaks which are higher, come later and remain on a high level for a longer time. These biochemical abnormalities have a clearly negative impact on endothelial function in the blood vessels. This means that the postprandial state does not last only 1-2 hours after a meal but can instead be 4-6-8 hours, i.e., only night time is outside the postprandial period.

Equally important is the fact that we have recently got drugs that are targeted specifically towards the postprandial period, i.e., can reduce the postprandial hyperglycaemia and avoid the late hypoglycaemia which in turns leads to

intake of snacks. These drugs include two short acting insulins (Lispro and aspart) and the new oral beta-cell stimulator repaglinide.

## A7

### **ELECTROPHYSIOLOGIC CHANGES IN SUBCLINICAL NEUROPATHY OF DIABETES**

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To investigate early changes in peripheral nerve conduction in subclinical neuropathy of diabetes, we carried out peripheral nerve conduction studies in 49 asymptomatic patients with negative ankle jerk. To select patients, we collected a questionnaire on numbness and pain in the foot from a total of 2685 patients under the age 65. Of these, 1053 patients had no neuropathic symptoms. Out of these 1053 asymptomatic patients, 341 showed bilaterall negative ankle jerk (subclinical neuropathy)

Motor and sensory nerve conduction studies were carried out in median, tibial and sural nerves of 49 subclinical patients (age 33-65y, mean 56y). Parameters evaluated were: distal latency and amplitude of CMAP, MCV, minimal F-wave latency, amplitude of CSAP, and SCV. Patient data were compared with control data obtained from 50 healthy subjects aged between 30 and 69 (mean 53y).

In 33 out of 49 patients (67%), tibial F-wave latency was out of the normal range ( $>\text{mean} + 2\text{SD}$ ). Sural CSAP amplitudes were abnormally small in 40% of the patients. Only 2 patients had no abnormal parameters.

**A8****DIABETES MELLITUS IN OLDER PERSONS**Abdulla FM

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Diabetes mellitus (DM) affects 20% of the people above the age of 65. In addition, another 20-25% have impaired glucose tolerance, which is associated with at least two-fold increase in the incidence of macrovascular complications.

There are age-related changes in the carbohydrate metabolism in older persons that predispose to the increasing incidence of diabetes with increasing age. Whatever role such intrinsic mechanisms play in the tendency towards diabetes, the major contribution comes from the extrinsic factors. Fortunately these are modifiable and include diet, activity, drugs, chronic illnesses and stress.

The other problem is disease presentation. Older persons may be totally asymptomatic, blood glucose screening is therefore recommended. On the other hand, they may present with a multitude of dramatic features attributed to many organ problems, weight loss and weakness that can mistakenly be attributed to malignancy, or urinary incontinence attributed to bladder problem. Several specific syndromes are described in elderly diabetics, such as the neuropathies, diabetic amyotrophy that typically occurs in older men, and diabetic cachexia. Psychiatric features are more frequent in old diabetics.

The treatment of old adults with diabetes requires careful consideration of the effects of advancing age and changes in health status on the benefits and risks of

therapeutic interventions. Although tight glycaemic control is not always appropriate, many old people with diabetes are undertreated and could benefit from a better glycaemic control and more aggressive treatment of risk factors. Old persons are a large group of people that more awareness will benefit, putting in mind the increasing life expectancy with the passage of time and the obligatory need for more care to this large sector of the community.

**A9****DO STZ-DIABETIC RATS HAVE AN AUTONOMIC NEUROPATHY?**Morrison JFB<sup>1</sup>, Sheen S<sup>2</sup>, Qureshi MA<sup>1</sup>, Stephen S<sup>2</sup>, Howarth FC<sup>1</sup><sup>1</sup>Depts. of Physiology, <sup>2</sup>Pharmacology, Faculty of Medicine & Health Sciences, UAE University, Al Ain, UAE

Samples from the bladder and penis of STZ-diabetic rats were analysed for concentrations of noradrenaline and adrenaline, to investigate changes in autonomic function following the induction of diabetes. There were no significant changes in the concentration of these amines in the bladder but there was a highly significant increase in penile concentration of the vasoconstrictor amine noradrenaline, which was 235% of the control value ( $p < 0.00001$ ). This change may be significant in that noradrenaline could potentially antagonize the relaxation of vascular smooth muscle in the corpus cavernosum during penile erection, and be one causative factor in erectile dysfunction.

**A11**

## **DO STEROID HORMONES AFFECT THE METABOLIC PROFILES OF DIABETIC RATS?**

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Steroid hormones are used daily by more than 200 million people worldwide as a contraceptive or hormone replacement therapy. These drugs are not restricted only to non-diabetics but are prescribed to diabetic patients as well. This study examined the effect of 0.05 mg Norgestrel + 0.01 ethinyl estradiol (NEE) Kg body wt<sup>-1</sup> on some metabolic parameters of diabetic rats (body weight, random blood glucose, glycosylated haemoglobin and plasma insulin levels). NEE was administered orally for a five-week period. Weight loss was greater in NEE-treated diabetic rats when compared to that of untreated diabetics. Random blood glucose and GHbA<sub>1c</sub> values were higher in the NEE-treated when compared to those of untreated diabetic rats. Plasma insulin level in NEE-treated rat was slightly but not significantly lower than that of untreated diabetic rats. In conclusion, NEE caused a greater weight loss, higher GHbA<sub>1c</sub> and blood glucose levels and decreased insulin level in rats with established diabetes compared to untreated diabetics. It thus appeared that NEE might worsen the symptoms of diabetes mellitus.

**A12**

## **TREATMENT OF CRITICAL LIMB ISCHEMIA IN DIABETIC PATIENTS**

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With the improvement of diagnostic and surgical techniques distal bypasses, even to foot arteries, are performed more often for diabetic patients with critical limb ischemia. 32 diabetic patients operated with distal bypasses were followed for at least one year. Primary patency rate after 30 days was 90%, after 1 year 68%, secondary patency 75%. Very distal bypasses to foot arteries had even slightly better patency rate than bypasses to distal leg arteries. All patients with combination of diabetes and end-stage renal failure were amputated or dead after 1 year.

To conclude:

- 1) Results of distal bypasses in diabetic patients are not worse than in non-diabetics.
- 2) The combination of diabetes and end-stage renal failure predict very bad prognosis for the critically ischemic limb.

**A13**

## **DIABETIC NEPHROPATHY: POSSIBILITIES OF PREVENTION**

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Recent studies, including our own investigations, have demonstrated that preventive use of metabolic intervention and/or antihypertensive agents can effectively modify the course of diabetic

nephropathy. In patients with normoalbuminuria, a strict metabolic control is essential for the preventive effect. In those with microalbuminuria, we have demonstrated that, besides near-

normoglycaemia obtained by insulin pump treatment, a complementary use of antihypertensive treatment is needed. Finally, in patients with macroalbuminuria, angiotensin-converting enzyme inhibitors are most effective in reducing the decline of renal function although an optimal metabolic control can exhibit some limited beneficial influence.

#### A14

### **SURVIVAL OF PATIENTS WITH TYPE 2 DIABETES IN UAE**

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Background: Diabetes patients show increased morbidity and mortality, primarily from cardiovascular and renal disorders. Furthermore, diabetes type 2 (DM2) is linked to hypertension which further accentuates the dismal prognosis of macrovascular disease. The prevalence of DM2 in UAE is among the highest in the world. This is also reflected in the high percentage of diabetics among inpatients and the marked increase in the occurrence of myocardial infarction, stroke and cardiac failure (Siitonen et al 1998). Both for inpatient and outpatient populations in UAE the prevalence of diabetes is decreasing after age 65, which may be explained by overmorbidity among DM2 patients (Siitonen et al 1998, Glasgow et al 1997).

Aim of study: Estimate the maximum duration of disease of Emirati DM2 patients.

Material and Method: During a 30-day period 365 Emirati patients with diabetes were given a questionnaire (all inpatients, all diabetes clinic patients and 100 primary health care patients). Data from 331 DM2 patients were evaluated (after exclusion of patients on insulin with a debut <30 years of age).

Results: Among patients <50 years the duration of disease (calculated as 50<sup>th</sup> and 95<sup>th</sup> percentiles) increased with age. However, after 60 years of age this increase of maximum duration (95<sup>th</sup> pc.) leveled off at barely 20 years duration, and the median duration even decreased.

Conclusion: The maximum lifespan after diagnosis of DM2 in UAE is limited to 20 years.

#### A15

### **THE ONGOING CARE OF DIABETIC PATIENTS-STRATEGIES TO IMPROVE COMPLIANCE**

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The Al Ain Military Medical Centre looks after about 200 diabetics every month comprising mainly active and retired armed forces personnel of different nationalities and their families. These patients consisting of old and new cases are seen as outpatients and inpatients for management.

Over the past years the health system in UAE has improved tremendously and is now very efficient. Despite that, in all disciplines, there are always some patients who present difficulties in management of their diabetes. There are many reasons for

that and we shall be trying to look into the following aspects:

- Type of non-compliance
- Reasons for non-compliance
- Remedies/Suggestions to improve compliance.

We will discuss different strategies and cooperation among various doctors and establishments dealing with these diabetic patients so that they could be reviewed at a place to achieve better control and less complications among these patients.

#### **A16**

### **A DIABETIC CLINIC IN A GENERAL PRACTICE SETTING-IS IT APPROPRIATE?**

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Given the high prevalence (>25% in urban UAE nationals over the age of 30) of Type 2 diabetes in the UAE, and the serious nature of the disease, comprehensive and effective health care delivery systems need to be developed and supported. Al Jahili clinic has taken an innovative approach in setting up a 'special interest' diabetes clinic in a general practice setting. The clinic utilizes locally developed IT management systems, with a diabetic patient register, computer assisted medical records and decision support software.

There are more than 1400 patients on the diabetic register with greater than half under active management. The general practice setting allows for rapid referral to our clinic, frequent review and opportunistic care, as records are fully integrated with the general clinic.

The in-house designed database allows for comprehensive regular clinical audit in an efficient manner, acts as a quality control tool and helps guide clinic management strategies. The clinic has set process target based on internationally accepted guidelines. The goals relating to the measurement of various parameters such as Hb A1c, lipids, renal function and ophthalmologic assessment are being achieved.

Most new patients to the clinic have long-standing diabetes (average 7years) and have been under management elsewhere. Various parameters were analyzed by comparing values at first presentation, to the most recent value measured. The average time between these readings was 18 months. Average HbA1c fell from 8.53 to 7.50 (p<0.001). Average total cholesterol fell from 5.89 to 5.25 (p<0.001).

Tertiary diabetic centers are incapable of handling the vast number of diabetic patients in the UAE. Increased resources need to be targeted at the primary care arena to further develop and evaluate effective models of diabetic care.

#### **P3**

### **RECURRENCE OF MYOCARDIAL INFARCTION IN TYPE 2 DIABETICS: AN ASSOCIATION WITH HIGHER PAI-1 ACTIVITY AND PLASMA INSULIN LEVELS**

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This study was aimed to compare plasminogen activator inhibitor (PAI-1) activity and plasma insulin levels between type 2 diabetics with recurrent myocardial

infarction (MI) (group A; N=31) and those with a single MI (group B; N=49). We found that both PAI-1 and insulin levels were higher in group A than in group B (PAI: A: 6.9+/-0.3U/ml, B: 5.8+/-0.4U/ml; insulin: A:30.6+/-3.9; B:21.6+/-2.7; (p<0.05) with a significant correlation between the two marker(r=0.693, p<0.05).

Our results signify that increased PAI-1 activity, together with increased insulinemia, represent strong determinants of recurrence of myocardial infarction in type 2 diabetics.

#### **P4**

#### **FASTING PLASMA GLUCOSE AS A SCREENING TEST FOR GESTATIONAL DIABETES IN A HIGH RISK POPULATION**

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Aims: We investigated the value of fasting plasma glucose (FPG) as an alternative to the more cumbersome screening tests for gestational diabetes mellitus (GDM).

Methods: 1470 pregnant women in our multiethnic, high-risk population were evaluated by the FPG, with GDM diagnosis being confirmed by the oral glucose tolerance test.

Results: At optimal cut-off values (from ROC curves), a sensitivity of 94.8% and a specificity of 92.6% were achieved.

Conclusions: FPG has been a neglected test for screening of GDM in our population. It would have eliminated need for the OGTT in 52.7% of pregnant women. It offers a simple approach to screen for GDM by being cost effective and patient friendly.

#### **P5**

#### **TIME-DEPENDENT EFFECTS OF STREPTOZOTOCIN (STZ)-INDUCED DIABETES ON THE ULTRASTRUCTURE OF RAT CARDIAC MUSCLE**

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We investigated the effects of STZ-induced diabetes on the ultrastructure of ventricle and papillary muscle. Diabetes was induced in male Wistar rats (250-300g) with a single i.p. injection of STZ (60 mg/kg). STZ and control animals were sacrificed after 4 and 8 months of treatment. Hearts were perfused with Ca-free saline followed by a formaldehyde based fixative (McDowell & Trump). After further processing samples of ventricle and papillary muscle were examined using the transmission electron microscope (Philips, CM-1). Sarcomere lengths were measured using SIS imaging analysis software. We observed no qualitative differences in the ultrastructure and no significant differences in sarcomere length in either ventricle or papillary muscle after 4 or 8 months of STZ-treatment. These findings suggest that the contractile dysfunctions, which have been reported in STZ-diabetic heart cannot be attributed to structural changes in cardiac muscle.

#### **P6**

#### **NATURAL HISTORY OF EXTREME INSULIN RESISTANCE CAUSED BY INSULIN RECEPTOR MUTATION**

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In a consanguineous family, five of nine siblings were identified as having Ile 119> Met mutation in the insulin receptor gene (Hone et al, 1994), causing a congenital syndrome with extreme insulin resistance, hyperglycemia, and paradoxical hypoglycaemia. We studied the seven years outcome of these siblings with respect to glucose tolerance and serum insulin.

After seven years observation the mean age of the siblings was 12.8 yrs (range 8-19), the mean weight 32.0 kg (range 18.3-52.05), the mean height 140.2 cm (range 114-174) and the mean HbA1c

7.5%. Blood glucose during OGTT at baseline and after seven years is given in table 1 and insulin in table 2.

**Table 1**  
Blood glucose in 2 hour OGTT

	Baseline			After seven years		
	0	60	120 min	0	60	120 min
1)	3.6	13.0	15.0	9.8	23.0	23.2
2)	2.6	14.4	13.2	6.2	26.9	2.0
3)	2.6	6.1	9.0	6.3	23.3	16.1
4)	1.5	6.0	9.4	4.1	16.0	16.1
5)	2.6	5.4	9.8	5.1	10.4	13.0

**Table 2**  
Serum insulin in 2 hour OGTT

	Baseline			After seven years		
	0	60	120 min	0	60	120 min
44		656	1590	121	283	234
48		227	495	75	134	75
21		129	656	102	330	198
63		372	640	17	1386	1155
55		240	268	29	539	1056

Conclusion: The early childhood phase is characterised by fasting hypoglycemia and postprandial hyperglycemia and extreme hyperinsulinemia. In adolescence insulin secretion is exhausted leading to fasting normoglycemia or even hyperglycemia, i.e., development of diabetes.