EDITORIAL

ORIGINAL ARTICLES
• Gut microbiota and the quest for dietary fibre intake in obesity and type 2 diabetes
• Diabetic Nephropathy: Countdown to Disaster? Part 2: Management
• Early use of DPP-4 Inhibitors in Treating Diabetes
• HIV and Diabetes
• Footwear for people living with diabetes - Part III: Offloading strategies for ulcerated feet
• Hypoglycaemia in type 2 diabetes – what are the real risks?
• From Knowledge to Creativity

CPD ACCREDITED DIABETES TRAINING

The Official Healthcare Professional Journal of the CDE
Your Partner in Diabetes
In this issue, we present the second part of ‘Diabetic Nephropathy - Countdown to disaster?’ the content of Dr Julien Trokis’s ‘Ascending Star’ lecture at the 15th CDE Postgraduate Forum. One of the many salient features apparent within the piece is just how many facets of care are required for people with chronic kidney disease. Some of these go undertreated and others are possibly ignored. It is thus imperative that unless you can provide comprehensive care for advanced chronic kidney disease, you must refer onwards. Fortunately, as Trokis writes, early intervention will delay if not reverse much of the future harm.

I guess that some of these thoughts tie up with the perennial matter of HIV/AIDS, an epidemic our country has had to deal with more than any other has. Excellent rollout of treatments is well under way, making positive inroads into peoples’ lives. However, it now looks like the impending diabetes epidemic might surpass this major problem. Many similarities exist between these two chronic conditions. Raising awareness and education still seem to be at the cornerstone of any successful intervention. Dr Duma Khutsoane shares his thoughts on the practicalities of treating patients with the double burden of HIV infection and diabetes. He offers valuable insights into how to select appropriate anti-retroviral treatment and describes some of the metabolic pitfalls associated with each of the available classes of treatment.

The World Diabetes Congress took place this past December in Melbourne, Australia. Johannesburg-based psychologist Rosemary Flynn captures some of the themes at this busy meeting. One aspect given a lot of coverage at the meeting was that of ‘diabetes distress’, a feature unique to diabetes and quite separate from depression. Numerous scoring systems are available to gauge the degree of distress people with diabetes have. Our own Clinic has just started polling patients with Problem Areas in Diabetes Questionnaire (PAID) so we can attain greater insights into our patients needs beyond merely their blood glucose readings.

It is with great pleasure that we publish an original piece by KZN Family Physician, Dr Russel Kirkby. Dr Kirkby discusses the unexpected success achieved with the addition of vildagliptin to a patient’s treatment regimen. I must emphasize that the agent was used in an ‘off-label’ manner, but he does raise the point of whether a specific DPP4-inhibitor might add benefit beyond glucose lowering.

Finally, we bid a sad and fond farewell to Anette Thompson as she prepares to complete her PhD. Anette firmly anchors her last piece in the pragmatic experience of daily clinical practice. We thank you for your valuable contributions to this Journal and wish you the best of luck going forward Anette!

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**EDITORIAL**

Dr Stan Landau

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**ORIGINAL ARTICLES**

**Gut microbiota and the quest for dietary fibre intake in obesity and type 2 diabetes**

Ria Catsicas

**Diabetic Nephropathy: Countdown to Disaster?**

Part 2: Management

Dr Julien Trokis

**Early use of DPP-4 Inhibitors in Treating Diabetes**

Dr Russel Kirkby

**HIV and Diabetes**

Dr Duma Khutsoane

**Footwear for people living with diabetes - Part III: Offloading strategies for ulcerated feet**

Anette Thompson

**Hypoglycaemia in type 2 diabetes – what are the real risks?**

Dr Louise Johnson-Loots

**From Knowledge to Creativity**

Rosemary Flynn

**CPD Accredited Diabetes Training**

38
Gut microbiota and the quest for dietary fibre intake in obesity and type 2 diabetes

Ria Catsicas
RD (SA) Registered Dietician - Nutritional Solutions

Introduction
We know that many genetic, physiological, socio-economic and psychological factors contribute to the prolonged, impaired energy balance that determines fat gain. However, not all these factors can fully explain the dramatic increase of the prevalence of obesity and the eventual development of type 2 diabetes mellitus (T2DM). Evidence now indicates that the gut microbiota plays a significant role in the development of obesity, obesity-associated inflammation and insulin resistance.

Each individual has a specific gut microbiota composition. Despite variations caused by age, gender, ethnicity and location, most microbial communities in human faeces (80 to 90 %) cluster into two phyla. They are the Bacteroidetes (Bacteroides, Prevotella) and the Firmicutes (Clostridium, Enterococcus, Lactobacillus) followed by Actinobacteria (Bifidobacterium) and the Proteobacteria (Helicobacter, Escherichia).

This paper explores the impact of modern lifestyle on the composition of the gut microbiota, the consequences thereof and the recommended advice health professionals should promote.

Microbiota composition and energy harvesting
Earlier studies on the composition of gut microbiota in humans and mammals have shown differences between lean and obese subjects. Initially, it was thought that the ratio of Bacteroides to Firmicutes might play a role in energy harvesting and storage, but the significance of this ratio is still debatable, and the basis of differences between the studies has not been established. Recent studies have shown that the dysbioses preceding the development of obesity in humans might also involve the participation of less prevalent species such as low numbers of some of the Bifidobacterium species and higher numbers of Staphylococcus aureus.

Studies conducted on mammals have demonstrated the possibility that certain gut microbiota modulate energy harvesting, energy expenditure and storage for the host through various complex mechanisms. These include production of short chain fatty acids (SCFA), gene expression and regulation of pathogen-recognising Toll-like...
receptors such as TLR5, and the enzymes lipoprotein lipase and AMP-activated protein kinase to name a few. Although certain microbiota compositions influence the recovery of energy from dietary residue, this is one of many factors contributing to the complex aetiology of obesity.

**Bacterial metabolites of dietary compounds**

Two main factors that influence gut motility and integrity are the fibre content of the diet and the consequent metabolic products produced by the specific microbial community such as methane and SCFA. Although theoretically the gut transit time may have an important impact on energy recovery from the diet, the production of SCFA provides additional health benefits such as strengthening of the colonic wall and improved immunity.

The amount and type of carbohydrates in the diet and the microbiota composition of the host determines the production of SCFA. This is due to non-digestible food components (fibre) that act as a food source for fermentation by the anaerobic colonic microbiota. Most dietary fibre contains about one third soluble (pectins, gums, mucilages, and some hemicelluloses) and two-thirds insoluble fibre (lignins, cellulose and some hemicelluloses). SCFA production is fairly constant in a molar ratio of 60:20:20 acetate, propionate and butyrate respectively. Butyrate specifically nourishes the colonic cells, and this contributes to a decrease in gut permeability and consequent reductions in inflammation and improved immunity. Studies have shown that an increased SCFA production in the distal colon plays a protective role with regard to gastrointestinal disease with special reference to colon cancer. Additionally, propionate, a gluconeogenerator, can further inhibit cholesterol synthesis. Connolly et al (2010) studied the microbiota modulation abilities of different sized oat flakes in vitro. They found that the larger and thicker oat flakes resulted in fermentation that produced a significant increase in the Bifidobacteria numbers. It is important to note that the oat flakes, independent of size, produced a propionate rich profile of 72:24:4. Unexpectedly, it was not the β-glucan fibre component, but the arabininoxylan component of the oat flake that contributed significantly to the number of Bifidobacteria produced in the gut. Most whole grain cereals also contain oligosaccharides such as galacto and fructo-oligosaccharides that act as prebiotics and contribute to the proliferation of beneficial microbiota.

The popular high-protein, high-fat, low-carbohydrate diets prescribed to obese individuals have been shown to lower total SCFA production with special reference to butyrate-producing Roseburta relatives and Bifidobacterium spp. A meta-analysis has confirmed that the gut dysbiosis characterized by the increase of opportunistic pathogens, a reduction in the Firmicutes/Bacteroidetes ratio and consequent decrease in SCFA producers, is a hallmark of T2DM. This has also been correlated with glycaemic control. It is thus important to consider carefully both the type and amount of carbohydrate in the diets to which we recommend to obese individuals with T2DM.

**Gut hormones**

Earlier studies in mammals have shown that a high-fibre diet, with the consequent increased production of SCFA and supplementation of prebiotics (oligofructose, fructans), resulted in increased production of the incretin hormone glucagon-like peptide 1 (GLP-1) and the anorexic gut hormone peptide YY (PYY) and a decrease in the orexigenic gut hormone, ghrelin.

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**Most dietary fibre contains about one third soluble (pectins, gums, mucilages, and some hemicelluloses) and two-thirds insoluble fibre (lignins, cellulose and some hemicelluloses)**

Adequate research now supports that high-calorie, high-fat feeding contributes to changes in microbiota composition and numbers, increased gut permeability and ultimately, through the complex processes of metabolic endotoxaemia, to increased inflammation.

It appears that a high-calorie, high-fat diet (HFD) causes an increase in the level of lipopolysaccharide (LPS), a major component of the outer membrane of gram-negative bacteria. A HFD causes a decrease in the Bifidobacteria important to maintain gut permeability and thus the uptake of LPS into the systemic circulation. LPS bind to pathogen sensing Toll-like receptor 4 (TLR4)-CD14 complexes, activating the immune system and the release of pro-inflammatory cytokines, leading to insulin resistance. It is important to note that a poor diet (low-fibre, nutrient-poor, high-fat and sugar), consequent overgrowth of non-beneficial bacteria and increased production of endotoxins in the gut are factors contributing to, rather than a consequence of obesity.

**The Immune response to structural components of bacteria and inflammation**

The cluster of metabolic abnormalities (metabolic syndrome, T2DM, dyslipidaemia, hypertension) resulting from abdominal obesity are all characterized by low-grade inflammation.

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**Nutritional intervention**

*Prescribe a balanced diet*

An observational study comparing children from Italy with children from a rural village in Burkina Faso showed that the...
Italian subjects had a diet high in sugar, fat and animal protein, whereas a high content of complex carbohydrates, fibre and polysaccharides characterized the diet of the village children. These differences resulted in distinct differences in the microbiota populations, including levels of diversity, SCFA production and resident microbes to metabolize fibre.

The American Heart Association (AHA) and European Society for Atherosclerosis (ESA) suggested an intake of 5 to 15 g of soluble fibre as part of the nutrition intervention for treating dyslipidaemia. This translates to a minimum of five portions of fresh fruit and vegetables and three portions of whole grains consumed daily. Whole grains refer to the intact grain or the dehulled, ground, milled, cracked, or flaked grain where the endosperm, germ and bran are present in the same proportions as found in the whole kernel. Whole grains include rolled oats, barley, brown wild rice, stampkoring, crushed wheat, quinoa, bulgur wheat, corn, millet, high-fibre wheat cereals, heavy whole-grain breads and pure rye breads. In a study that compared different grains, rye appeared to induce the highest butyrate production by the faecal microbiota in obese individuals.

The benefits of whole grains extend beyond the fibre content – the synergistic effect of the B vitamins, vitamin E, iron, phosphorus, phytoestrogens and phenolic compounds, together are protective against disease.

In the light of the above, it is evident that advising your overweight patients with T2DM to follow a high-protein, high-fat, low-fibre, very-low-carbohydrate diet may be detrimental in treating obesity, the ‘metabolic syndrome’, T2DM and dyslipidaemia. It is advisable to refer such patients to a registered dietician who is best qualified to provide nutrition education and to calculate a balanced eating plan and menu. These should be based on a moderate and nutritionally balanced distribution of macronutrients (40-45 % CHO, 15-20 % protein and 25-35 % fat – as a percentage of total energy intakes). This will ensure an adequate intake of both soluble and insoluble fibre.

Changing eating habits is a process
The dietician needs to negotiate with the patient the changes required. A move from eating habits characterized by a high intake of red meat, processed meats, sweets, desserts, refined starchy and French fries to an eating pattern that incorporates fish, legumes, whole grains and fresh fruit and vegetables must be facilitated, guided by the patient’s readiness for change. Ultimately, the process guides the patient to explore, enjoy and favour more foods like those in sample Menu 2 at the expense of foods found in Menu 1 (See Table 1).

Including or excluding single nutrients and foods into the patients daily meal plan, seems to be of little benefit. Several dietary practices need concurrent implementation. The change from a high saturated / trans-fat, refined carbohydrate / sugar, nutrient-poor dietary pattern to a moderate unsaturated fat, lean protein, complex carbohydrate, high-fibre, nutrient-dense eating pattern will contribute to a positive outcome. Although a number of patients in my practice often claim to be wheat intolerant, I find that their diets tend to include high intakes of refined carbohydrate (all types of refined flours [including gluten-free] and sugars). Gut dysbiosis, often in combination with stress, inactivity and inadequate sleep, are contributing factors to the bloating and indigestion they attribute to wheat intolerance.

Supplementation
Although the benefits of deliberately changing the host microbiota by supplementation are debatable, increasing the levels of Bifidobacterium and Lactobacillus has positive health outcomes, especially in patients with compromised gut function. Supplementation can be significantly useful for stabilising bacterial communities disturbed by the use of medications, antibiotics and anaesthesia. Although colonization is not simply a mixture of microbes but rather a cohesive, interrelated ecosystem, supplementation, a nutritionally balanced, calorie-controlled eating plan and physical activity should be considered as interventions for the obese patient.

Conclusion
The composition of the ideal microbiota in the gut is still to be defined. Further studies in humans are needed to identify microbiota that correlate with improvements in health symptom outcomes. Such changes are likely to be dose- and strain-specific and may lead to the identification of microbes that are causal or correlative biomarkers for beneficial health outcomes.

REFERENCES AVAILABLE ON REQUEST
Diabetic Nephropathy: Countdown to Disaster? Part 2: Management

Abstract

In diabetic kidney disease (DKD), an intensive and multifactorial management approach is needed to target all risk determinants simultaneously. Although glycaemic control is important, blood pressure control remains a modifiable risk factor even in overt DKD. The benefits of lipid control with statins are limited to early DKD. Whilst lifestyle changes, such as smoking cessation, weight loss, and dietary changes, are recommended, the data supporting these interventions are less robust.

Not only is proteinuria a risk factor for kidney failure, it has been demonstrated that halving proteinuria is associated with a halving of kidney risk. For this reason, it may be asked whether proteinuria itself should be seen as a modifiable risk factor. In incipient DKD, both hypertension and hyperglycaemia are modifiable risk factors. In overt DKD, only hypertension remains a modifiable risk factor.

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Various landmark studies have demonstrated the renal benefits of glycaemic control in the patient with diabetes. In the Diabetes Control and Complications (DCCT) study, long-term risk of impaired glomerular filtration rate (GFR) decreased by 50% in the patients in the intensively controlled group. This effect was not evident, however, until 10 years after randomization. In the United Kingdom Prospective Diabetes Study (UKPDS), intensive glycaemic control was associated with a 24% reduction in risk of development of microalbuminuria (MAU), and a 33% reduction in risk of developing proteinuria. Furthermore, each 1% reduction in HbA1c was associated with a 37% reduction in microvascular risk. Intensive glycaemic control in the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) trial showed a reduction in both new DKD and worsened DKD. In the Veterans Affairs Diabetes Trial (VADT), the intensive glycaemic control group showed a reduction in progression from normoalbuminuria to microalbuminuria and then macroalbuminuria, compared to the control group.
Hypertension is a key pathogenic factor in kidney deterioration and treatment of hypertension is probably the most important intervention in the management of patients with DKD. Blood pressure control delays the development and progression of DKD. Hypertension develops in more than 75% of patients with CKD and in fact may be present at the time of diagnosis of diabetes in about one-third of patients with type 2 diabetes. The UKPDS showed that tighter blood pressure control had a beneficial effect on kidney function, and that each 10 mmHg reduction in systolic blood pressure resulted in a 13% reduction in cardiovascular (CV) risk. Whilst no benefit was shown on risk of proteinuria, fatal or non-fatal renal failure, or doubling of serum creatinine, the mean blood pressure in the UKPDS was 144/82 (a 9/3 reduction compared to the control group), a reading which would not be considered at target in many current guidelines. In type 1 diabetes, hypertension is usually caused by underlying diabetic nephropathy and typically manifests about the time that patients develop microalbuminuria.

Although the ADVANCE trial demonstrated a reduction in DKD with a blood pressure below 140/80 mmHg (HR 0.79), the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial failed to show benefit of a systolic blood pressure below 120 mmHg. Whilst these studies show that reducing systolic blood pressure reduces risk in patients with high CV risk, too tight control of blood pressure may be harmful.

Lowering systolic blood pressure reduces cardiovascular risk in patients who have diabetes, but it is uncertain as to what extent it should be lowered. In patients with diabetes, no data exists from large studies to compare the effects of commencing therapy with a systolic blood pressure of 130-139 mmHg, versus systolic blood pressures of 140 mmHg or more. Thus, a blood pressure target of less than 130/80 mmHg cannot be supported by data from prospective studies. The suggestion is that current blood pressure targets are based on consensus recommendation, rather than hard data. An exception, however, may be patients with advanced proteinuric kidney disease, who have an eGFR less than 50 ml/min with proteinuria in excess of 500 mg per day.

Whilst different guidelines may offer different blood pressure targets, in South Africa, the Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) has adopted the same blood pressure target as that recommended by the American Diabetes Association (ADA), namely a goal of ≤ 140/80 mmHg in both type 1 and type 2 diabetes. The ADA further suggests that a target of ≤ 130/80 mmHg may be appropriate in otherwise young and healthy patients. SEMDSA also cautions the clinician to not lower the blood pressure below 120/70 mmHg, due to the J-shaped relationship between blood pressure and cardiovascular outcomes. The INternational VErapamil SR Trandolapril Study (INVEST) illustrated this relationship, with an increase in primary end-point seen in patients with diastolic blood pressures below 70 mmHg.

In elderly patients, targets may need to be individualized based on age, co-morbidities, and adverse effects associated with treatment, such as electrolyte disturbances, orthostatic hypotension, and acute deterioration in kidney function.

The mainstay of blood pressure reduction is via the use of renin-angiotensin system (RAS) inhibition. Landmark studies such as HOPE (Heart Outcomes
Prevention Evaluation), RENAAL (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan) and IDNT (Irbesartan Diabetic Nephropathy Trial), showed that treatment with angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) reduce proteinuria and slow nephropathy progression.

In hypertensive, normo-albuminuric patients with type 2 diabetes, RAS inhibition delays the onset of MAU. In addition, ARB’s have been shown to reduce the rate of progression from micro- to macro-albuminuria and end stage renal disease (ESRD) in patients with type 2 diabetes. However, ARB’s do not prevent the onset of MAU in normotensive patients with type 1 or 2 diabetes. No benefit of RAS inhibition has been demonstrated in normotensive, normo-albuminuric patients, with either type 1 or type 2 diabetes. If the patient’s initial blood pressure is more than 20/10 above goal, then combination therapy should be initiated. When initiating an ACE-inhibitor or ARB, it is important to monitor serum creatinine and potassium.

In considering treatment with a diuretic, some are more favourable in patients with CKD. Thiazide diuretics are thought to decrease GFR, and have a lower efficacy in renally impaired patients. Loop diuretics more readily increase diuresis at lower GFR’s, and are thus specifically recommended in patients with a lower level of renal function or ESRD. One study has suggested that torasemide reduces myocardial fibrosis in patients with CKD. The most orally bioavailable diuretic is torasemide, although furosemide is the drug with the least hepatic elimination when intravenously.

Spironolactone may be used to assist in blood pressure control, but potassium levels must be carefully monitored due to a significant risk of hyperkalaemia. Spironolactone augments the reno- and cardiovascular protective effects when added to an ACE-inhibitor or ARB, by reducing albuminuria and blood pressure in patients with type 2 diabetes and nephropathy.

Whilst the combination of an ACE-inhibitor and ARB has shown a greater reduction in proteinuria than achieved individually, this combination demonstrated worsened renal and cardiovascular outcomes in the Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial (ONTARGET).

Clinical studies suggest that dyslipidaemia contributes to the progression of CKD, especially hypertriglyceridaemia and reductions in HDL levels. In the Study of Heart and Renal Protection (SHARP), lowering of low-density lipoprotein (LDL) cholesterol was associated with a slowing in the progression of nephropathy, and a reduction in cardiovascular events. In patients with CVD, statins have been shown to stabilize kidney function, and to reduce the risk of major CV events. There is evidence that statins can significantly improve GFR or delay GFR reduction in patients with type 2 diabetes. However, statins have little effect in patients with type 2 diabetes and advanced renal impairment, and therefore need to be used early.

It has been demonstrated that atorvastatin suppresses aldosterone production induced by glucose, angiotensin II, and LDL cholesterol in human renal mesangial cells (aldosterone plays a role in the development of DKD via local effects on the mesangial cells). Rosuvastatin reverses the angiotensin II-induced pro-fibrotic response in the mesangium. The ADA guidelines recommend statin use in patients over the age of 40 years who have at least one additional CV risk factor (including albuminuria).

Although fibrates have been shown to reduce CV events in patients with CKD, as well as reduce albuminuria, they reversibly increase creatinine levels, and their effects on kidney outcomes remains unknown. It should be noted that the risk of rhabdomyolysis with a statin-fibrate combination is greater in patients with CKD. This risk is thought to be lower with fenofibrate than with gemfibrocil. A fibrate-statin combination should thus not be used in patients with renal impairment.

Fibrates are recommended as primary therapy in patients with triglyceride levels greater than 4.5 mmol/l, with the caveat that they should be used as monotherapy, at low doses, and only in patients with mild renal impairment. Nonetheless they should be used cautiously.

The National Kidney Foundation recommends reducing the fenofibrate dose by 50 % in patients with a GFR of 60-90 ml/min, by 75 % in patients with a GFR of 15-59 ml/min, and stopping fenofibrate if the GFR is less than 15 ml/min or if the patient is on dialysis.

There remains a question of whether fenofibrate may be nephrotoxic, and some authors suggest that fenofibrate-associated nephrotoxicity may be an under-recognized adverse drug reaction. Literature reports are,
however, conflicting on this issue. Whilst a rise in serum creatinine in response to fenofibrate is well documented, it has been suggested that this does not reflect true renal injury or an actual fall in GFR. In the ACCORD lipid study, patients who experienced raised serum creatinine on fenofibrate demonstrated a return to normal creatinine levels by a mean of 51 days after stopping the fribrate. As far as fibrates are concerned, however, the evidence supporting their use remains moderate.

The US National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI)™ guidelines recommend statins or a statin/ezetimibe combination to reduce CV risk in patients with CKD.

Lipid goals remain the same as those recommended for the diabetes patient without kidney disease. The ADA guidelines recommend an LDL cholesterol target of less than 2.6 mmol/l or 1.8 mmol/l depending on the presence of other CV risk factors. Since DKD is a CV risk factor, the lower target would seem appropriate. HDL cholesterol levels >1.0 mmol/l for men, and > 1.3 mmol/l for women are advised. No formal goal is set for triglycerides, but a level < 1.7 mmol/l is considered optimal. Ezetimibe is an alternative for statin-intolerant patients.

In terms of lifestyle management, smoking cessation is vital, as smoking is known to promote both the onset and progression of DKD. In fact, the combination of diabetes and smoking increases the prevalence of microalbuminuria, macroalbuminuria, and GFR decline. Smoking cessation also reduces CV risk, which is so important in this high CV risk patient population.

Higher body mass index is associated with an increased incidence and rate of progression of CKD. Weight loss reduces proteinuria and microalbuminuria, and stabilises kidney function. The benefits of weight loss may be gained indirectly via blood pressure reduction. Nevertheless, weight loss also assists in glycaemic control and reduces CV risk.

Whilst the data on the benefits of dietary modifications is by no means robust, there is some evidence to suggest that protein restriction may slow the progression of albuminuria, GFR decline, and the development of ESRD.

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A benefit on blood pressure. Dietary changes may also improve dyslipidaemia.

In animal models, exercise attenuates the progression of early DKD, reduce albuminuria, and maintain podocyte numbers in the Bowman’s capsules of the kidneys. Benefits of exercise may be exerted via effects on blood pressure, triglyceride, HDL cholesterol, insulin resistance, and glycaemic control. In ESRD, exercise was demonstrated to improve arterial stiffness, blood pressure, and cardiorespiratory function.

Aspirin may offer a moderate reduction in CV risk, and its use may be guided as per ADA recommendations in patients with type 2 diabetes.

At this stage, there is insufficient evidence to support the use of uric acid lowering agents or thiamine replacement in DKD.

Approximately 20% of patients with diabetes and stage 3 CKD develop anaemia, the severity of which worsens with advancing CKD. Low haemoglobin (Hb) is a risk factor for left ventricular hypertrophy, heart failure, and CV mortality, as well as being a risk multiplier for all-cause mortality. However, whilst raising the Hb level improves the quality of life of patients, it has not been shown to reduce their CV risk.

Whilst the use of erythropoietin stimulating agents slows the progression of CKD in non-diabetic patients, their effect in DKD remains unknown. Furthermore, their use may be associated with significant adverse effects, such as myocardial infarction, stroke, thrombosis, heart failure, and death. Cautious targets for Hb have therefore been set by the National Kidney Foundation (Hb target 11-12 g/dl) and the United States Food and Drug Administration (FDA - Hb target 10-12 g/dl). Patients should be screened for anaemia annually if the GFR is 30-59 ml/min and bi-annually if the GFR is < 30 min/min.

The clinician also needs to be cognisant of possible abnormalities in mineral metabolism. CKD may result in hyperphosphataemia and hypocalcaemia. The global Kidney Disease Improving Global Outcomes (KDIGO) and the United Kingdom National Institute for Health and Care Excellence (NICE) guidelines recommend checking calcium, phosphate, PTH, ALP, and vitamin D levels in stage 4-5 CKD (routine testing of these are not recommended in CKD stages 1-3). Normal phosphate levels should be maintained if the GFR is < 45 ml/min.
Routine testing of bone mineral density is not recommended when the GFR is below 45 ml/min, as information from bone mineral density tests at these lower levels of GFR may be misleading. Bisphosphonates should not be given at GFR levels below 30 ml/min without strong clinical rationale, as their safety and efficacy at these low GFR levels has not been validated. Vitamin D supplementation is not recommended in the absence of a documented vitamin D deficiency, as there is little evidence of the impact of supplementation in the absence of such deficiency.

Whilst the list of drugs known to be nephrotoxic may extend from the common culprits such as nonsteroidal anti-inflammatory drugs to those like digoxin, lithium, and possibly fibrates, drugs that are usually beneficial in CKD (such as RAS inhibitors and diuretics) may become nephrotoxic at times of acute kidney injury. For this reason, one may need to consider stopping an ACE-inhibitor or ARB during acute febrile illness or diarrhoea especially where there is contraction of the intravascular volume. Oral bowel preparation medications that contain phosphate should be avoided in patients with CKD.

Patients with DKD should be offered vaccination against influenza, as well as pneumococcus. Patients at high risk of kidney disease progression, and with GFR < 30 ml/min, should also be vaccinated against Hepatitis B.

The clinician should bear in mind that altered insulin pharmacokinetics in DKD place these patients at higher risk for hypoglycaemia.

Whilst previous guidelines recommended stopping metformin therapy when creatinine levels rose above 132 μmol (men) and 123 μmol (women), guidelines that are more recent recommend continuing metformin above GFR levels of 45, reviewing metformin treatment if the GFR is 30-45, and stopping metformin when GFR falls below 30. Amongst sulphonylureas, the second generation agents such as gliclazide are preferred, with dose adjustments necessary in CKD.

Meglitinides (repaglinide, nateglinide, mitiglinide), as well as thiazolidinediones, do not require dose adjustment in CKD. Acarbose is not recommended in advanced CKD, whilst the use of dipeptidyl peptidase-4 (DPP-4) inhibitors in CKD would require dose adjustment. When using glucagon-like peptide-1 (GLP-1) agonists, caution with exenatide is advised at GFR levels of 30-50, and it should be avoided at GFR levels below 30. No dose adjustment is necessary for liraglutide in CKD.

An important aspect of the management of patients with CKD is that the condition may make the interpretation of some tests difficult. For instance, cancer biomarkers may be altered in patients with proteinuria, with or without diabetes. CA125, CA15-3, CA19-9 have been found to be increased, and TPSA, FPSA, AFP, and CEA have found to be decreased in these patients.

One needs to be cautious in interpreting pro-BNP in DKD patients with respect to the diagnosis of heart failure and assessment of volume status, as pro-BNP is less reliable at lower levels of GFR. Likewise, caution needs to be exercised when interpreting serum troponins with respect to the diagnosis of acute coronary syndrome, as these biomarkers are renally excreted, and may be chronically elevated in renal impairment.

Pulmonary function is known to be impaired in DKD, with greater impairment of pulmonary function as DKD progresses. This is particularly relevant for those clinicians involved in critical care patients.

Nephrology referral should be considered where the aetiology of CKD is uncertain, with resistant hypertension, when the albumin-creatinine ratio persists above 60 mg/ mmol, in patients intolerant of ACE-inhibitors or ARBs due to elevated potassium or creatinine and in the context of anaemia, hyperparathyroidism, metabolic bone disease or electrolyte disturbance.

In summary, an intensive and multifactorial management approach is needed to target all risk determinants simultaneously. Whilst glycaemic control is important in the management of patients with DKD, strict blood pressure control is critical. Although statins stabilize kidney function and reduce cardiovascular risk, they have little effect in advanced kidney impairment. Recommendations in evidence-based guidelines should be adhered to in this high-risk patient population. Medications used in the treatment of diabetes and DKD may be nephrotoxic at times, and increase the risk of acute kidney injury if not withdrawn when appropriate. Timeous nephrology referral reduces mortality as well as the risks of hospitalization.

**Medications used in the treatment of diabetes and DKD may be nephrotoxic at times, and increase the risk of acute kidney injury if not withdrawn when appropriate. Timeous nephrology referral reduces mortality as well as the risks of hospitalization.**

**REFERENCES AVAILABLE ON REQUEST**
Mrs. L H, a 45-year-old Caucasian lady, presented for a routine medical check-up. She was feeling stressed and expressed that much of this was related to her career as a police officer dealing with child abuse cases. Her additional history included well-controlled hypertension.

On examination, her weight and height were 98.4 kg and 164 cm respectively. The calculated BMI was 36.5 kg/m². Her waist circumference was 115 cm, blood pressure 190/100 mmHg and her pulse rate was 110 beats per minute. Her blood glucose was 19.3 mmol/l (finger-prick).

Additional biochemical testing revealed a fasting plasma glucose of 17.9 mmol/l, an HbA1c of 11.4 % and positive antibodies against islet cell antigen (IA-2). The latter results were unavailable until after I had initiated therapy.

A diagnosis of diabetes was thus confirmed.

In light of the above glycaemic parameters, and in keeping with current 2012 Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) Guideline for the Management of Type 2 Diabetes, I recommended that she immediately commence insulin. The patient felt strongly against this option. Our National Diabetes Guideline also makes mention of needing to individualize treatments for our patients. These guidelines encourage patient empowerment and education. In this vein, the patient and I negotiated what treatment to initiate and, failing any improvement in her glycaemic control thereafter, we agreed to commence insulin. Thus, initially she embarked on prudent lifestyle and dietary changes together with structured exercise. I commenced metformin and I titrated the daily dose up to 2500 mg.

I had read articles by both Bosi and Siddiqui asking whether it was time for testing incretin-therapies early on in the diagnosis of diabetes, but this was in 2011 and these molecules were still unfamiliar to me. Nonetheless, I added the DPP-4 inhibitor, vildagliptin (Galvus®) 50 mg twice daily. I did inform Mrs LH that this was not a labelled indication for the drug. In keeping with the openness of our consultation, she consented to follow my recommendation. Liver function tests initially, and subsequent to the commencement of vildagliptin, were normal. The glycaemic outcomes achieved by Mrs. L H are shown in Table 1 and Figure 1 below.

This patient, who initially presented more in keeping as a person with typical type 2 diabetes, has had a durable and most satisfactory clinical and biochemical response. The combination of lifestyle changes, (albeit resulting in minimal weight loss) and the addition of dual pharmacological therapy yielded a good outcome.

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Specific autoantibodies to islet cells, insulin, and glutamic acid decarboxylase help identify patients with autoimmune type 1 diabetes. Judicious use of the available antibody assays (anti-GAD and anti IA-2) can help in discriminating the precise type of diabetes in the atypical situation. Selective use of C-peptide measurement may also aid in determining if endogenous insulin production is still present. Nearly one in seven adults presenting with diabetes mellitus as a new diagnosis are insulin deficient.

The above case study presents as an enigma. Mrs L H presented a problem often seen at the first presentation. What type of diabetes does she have? What is the most appropriate therapy? How can I fulfil her wishes and needs? My experience is that few at the outset are ever keen on insulin. They look for another option or even the possibility of a cure.

I did initially assume that Mrs L H had type 2 diabetes. I did not, and have not subsequently performed all of the tests that might have helped me confirm the diagnosis. This is a problem of rationalising of tests in a funder-contained environment coupled with what the patient can afford or is prepared to pay. Might she now be in the honeymoon period of type 1 diabetes? Her initial glucotoxicity was reduced without using insulin. Much has been written about this concept and recently Kramer et al discussed the amelioration of glucose toxicity subsequent to early insulin therapy. Remission of diabetes of up to two years has been well described following this approach.

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Finally, to what extent did the vildagliptin add value in terms of beta-cell rejuvenation? Bosi postulated it was a good idea and this unusual case presentation would support his contention. I do know I have a contented patient who avoided insulin and is still enjoying good glycaemic control.

So, is there a role for using incretin therapies in type 1 diabetes? Perhaps this case study raises more questions than it does provide answers.

REFERENCES AVAILABLE ON REQUEST
HIV and Diabetes

Introduction
South Africa, with a population of just over 51 million people, has the highest prevalence of human immunodeficiency virus (HIV) infection globally - approximately 11% of the population. South Africa has the largest government-sponsored anti-HIV rollout programme with approximately 1.4 million people on highly active antiretroviral therapy (HAART) in the state/public sector. This has led to a dramatic decline in the acute manifestation of the disease as well as a reduction in the mortality. The consequent increase in longevity has enabled HIV to be labelled as a chronic condition with subsequent increases in chronic complications not previously seen before in HIV-positive patients. These conditions include osteoporosis, dyslipidaemia, and cardiovascular disease including myocardial infarctions, coagulation disorders, insulin resistance and type 2 diabetes. These latter conditions impose further challenges on both the patient, who now has to deal with a ‘double burden’ of diseases, and on the treating physician, in terms of timeous diagnosis, monitoring, drug selection, and offering appropriate psychological support.

Data collection on adverse events of anti-HIV therapy (The DAD study) demonstrated that the adjusted risk of having elevated total cholesterol increased by 24% per two-fold increase in the CD4 cell count and that the risk of myocardial infarction is more than doubled among HIV-infected patients with diabetes. Type 2 diabetes is four fold more common in HIV positive patients on HAART than in someone who is HIV negative.

This article seeks to review management strategies of patient with both diabetes mellitus (DM) and HIV on HAART.

Classification of HIV and DM
1. Patients with pre-existing diabetes mellitus who contract HIV
2. Patients who have both diabetes mellitus and HIV at diagnosis
3. Patients who develop diabetes subsequent to the initiation of HAART

The major significance of this classification is that it aids in terms of drug selection. In those cases when both conditions co-exist, you do not necessarily have to follow national guidelines when making a drug selection. A salient example might be a patient with pre-existing diabetes complicated by nephropathy who then contracts HIV. In this case, tenofovir would not be regarded as an ideal first-line treatment. A second scenario might be a patient with HIV-related enteropathy who subsequently develops diabetes. Here the use of metformin would not be a suitable drug choice given its potential gastrointestinal side effects. Careful consideration of drug selection is of the utmost importance to prevent exacerbation of any pre-existing conditions.

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Risk factors for the development of diabetes
Many factors predispose HIV-positive patients to developing diabetes. The same factors that apply to HIV-negative people are still pertinent here as illustrated in Table 1.

Table 1: Risk factors for the development of diabetes in the HIV-positive patient

<table>
<thead>
<tr>
<th>DM TRADITIONAL RISK FACTORS</th>
<th>HIV Specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Family history</td>
<td>• HIV virus itself (Viral load, CD4 count, duration of disease)</td>
</tr>
<tr>
<td>• Ethnicity</td>
<td>• Co-infection with Hepatitis C virus</td>
</tr>
<tr>
<td>• Overweight and obesity</td>
<td>• Return to health phenomena</td>
</tr>
<tr>
<td>• Physical inactivity</td>
<td>• Iatrogenic (drug related)</td>
</tr>
<tr>
<td>• Previous gestational diabetes</td>
<td></td>
</tr>
<tr>
<td>• Cardiovascular disease</td>
<td></td>
</tr>
<tr>
<td>• Low birth weight</td>
<td></td>
</tr>
<tr>
<td>• Polycystic ovary syndrome</td>
<td></td>
</tr>
<tr>
<td>• Dyslipidaemia</td>
<td></td>
</tr>
<tr>
<td>• Age &gt; 45 years</td>
<td></td>
</tr>
</tbody>
</table>

Aetiopathogenesis
The HIV virus itself, and especially fluctuating levels of the virus, induces a chronic inflammatory state, which in turn results in an increase in the levels of various cytokines including IL-1, IL-6, TNF-α, CRP and a reduction in adiponectin. These processes induce a state of insulin resistance. Most cases of HIV-associated diabetes can be considered type 2, but a Japanese study by Takarabe demonstrated in the population studied that autoimmune (type 1) diabetes mellitus occurred after immune restoration via the use HAART. This can occur especially if the CD4 cell count increases rapidly and there is development of either or both the glutamic acid decarboxylase (GAD) antibody (anti-GADab) and insulinoma-associated antigen-2 antibody (IA2-ab). In these cases, glycaemic control may rapidly deteriorate and mandate the commencement of insulin.

Co-infection with hepatitis C (HCV) causes dysglycaemia by increasing intrahepatic tumour necrosis factor and by causing hepatic steatosis. HCV-positive HIV patients above the age of 40 years are 3 times more likely to develop diabetes than are those who are HCV negative.

Return to health phenomenon: As patient’s general health improves, a rapid increase of visceral fat with wasting of the subcutaneous fat occurs (as opposed to lean muscle mass which they typically lose during the catabolic phase of HIV). This weight gain can overwhelm the secretory capacity of pancreatic beta cells resulting in beta-cell failure and insulinopaenia.

HAART
The benefits of HAART, including suppression of the viral load, improvement of CD4 cell counts, reduction of opportunistic infections and malignancies and a reduction in mortality from HIV, have come at the expense of an increase in cardio-metabolic sequelae. More recently, prospective studies report that 10 % of HIV patients treated with HAART develops diabetes during 4 years of follow up. Compared with the 3 % of HIV-seronegative men who develop diabetes, this represents a greater than four-fold increase in the relative risk of developing diabetes (after adjusting for age and body mass index (BMI)).

Drug Classes
Currently, six different classes of anti HIV drugs are available in South Africa

1. NRTI’s (nucleoside reverse transcriptase inhibitors): stavudine (d4T), lamivudine (3TC), zidovudine (AZT), didanosine (ddl), abacavir (ABC), Truvada (tenofovir/emtricitabine)
2. NNRTI’s (non-nucleoside reverse transcriptase inhibitors): efavirenz, nevirapine, etravirine
3. PI’s (protease inhibitors): (indinavir, ritonavir, saquinavir), Aluvia (lopinavir and ritonavir), darunavir, atazanavir

New Classes
• Entry inhibitors (enfurvirtide)
• Integrase inhibitors (raltegravir)
• CCR5-receptor inhibitors (maraviroc)

We do not fully understand the precise manner by which these drugs cause insulin resistance, but some of the presumed mechanisms are listed below.

1. NRTI’s
A. Mitochondrial toxicity: Mitochondrial dysfunction is responsible for the lactic acidosis for which these drugs are notoriously remembered. However, this toxicity is also implicated in diabetogenesis by decreasing the mRNA concentration of the adipogenic differentiation factors. This leads to increased apoptosis of peripheral adipocytes with subsequent lipoatrophy and therefore reduced uptake of triglyceride and glucose in affected tissues. Stavudine has the highest onset of DM relative risk per year of exposure of 1.19 (95% CI 1.15-1.24) p = 0.0001, followed by zidovudine and didanosine.

B. Lipoatrophy: I will address this at length in relation to protease inhibitors.

C. Pancreatitis: The exact mechanism by which these drugs cause pancreatitis is not known, other than indirectly via resultant hypertriglyceridaemia and possibly direct β-cell toxicity with resultant reduction in the β-cell’s secretory capacity.
**NRTI’s with the most metabolic risk associations**
- d4T
- ddl
- AZT

**Metabolically neutral NRTI’s**
- Abacavir
- Tenofovir
- Emtricitabine
- Lamivudine

2. NNRTI’s
These are not directly implicated in the pathogenesis of diabetes. They might however induce dyslipidaemia in the form of raised triglycerides.

**PROTEASE INHIBITORS** – these are the biggest culprit as far as the onset of diabetes is concerned. They induce hyperglycaemia by different mechanisms, which include but are not limited to:
1. Reduction of insulin production by between 25-50 %
2. Impairment of Glut4 translocation to the surface of the cell membrane which prevents entry of glucose into cells
3. Inhibition of PPAR-γ receptors and thus limitation of adipocyte differentiation with resultant release of free fatty acids
4. Induction of lipodystrophy - the exact mechanism/s remain unknown, with theories suggesting:
   a. mitochondrial dysfunction with an increase in fat cell apoptosis or
   b. inhibition of the sterol regulatory element-binding protein (SREBP-1) activation of the RXR-PPARγ heterodimers in adipocytes

In multivariate modelling, Meininger et al. demonstrated a 1 % increase in fasting insulin levels for each 1 % increase in visceral fat and an independent 1 % increase in fasting insulin levels for each 1 % increase in abdominal subcutaneous fat. These data suggest that increased visceral fat and reduced subcutaneous fat contribute independently to hyperinsulinaemia and insulin resistance in HIV infected patients.

3. **Protease Inhibitors**

<table>
<thead>
<tr>
<th>Metabolically Unsafe</th>
<th>Metabolically Neutral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indinavir (Crixivan)</td>
<td>Darunavir (Prezista)</td>
</tr>
<tr>
<td>Ritonavir (Norvir)</td>
<td>Atazanavir (Reyataz)</td>
</tr>
<tr>
<td>Saquinavir (Invirase)</td>
<td></td>
</tr>
<tr>
<td>Aluvia (Lopinavir and Ritonavir)</td>
<td></td>
</tr>
</tbody>
</table>

Finally, the drugs listed under new classes have not yet been implicated in any cardio metabolic disorders.

**Screening, Diagnosis and Monitoring**
Screening all HIV-positive patients for traditional diabetes risk factors is the same as in non HIV-positive patients. Those HIV-positive patients who have HIV-associated features such as lipodystrophy, or who are on PIs, should be screened every 6 months. This might be done at their general health reviews when the CD4 count and viral load testing is undertaken.

The same diagnostic criteria for diabetes apply as in non-HIV-positive patients. One exception being that the HbA1c test is not advocated for diagnosis because haemoglobin can be affected by the HIV virus itself, opportunistic infections affecting the bone marrow (e.g. tuberculosis [TB]) or by consumption of some drugs (e.g. Bactrim or AZT). The fasting plasma glucose or, where resources allow, the oral glucose tolerance test, remain established diagnostic tools for the diagnosis of diabetes.

The HbA1c does however remain the gold standard for assessing ongoing glycaemic control and glycaemic targets should continue to be individualised based on the patient’s general health.

**Treatment of diabetes in HIV-positive individuals**

**General measures**
1. Aggressive searches for concomitant infections especially TB, sexually transmitted infections, urinary tract infections and hepatitis B and C.
2. Lifestyle modification, which includes dietary advice and physical activity, must be individualised.
3. Smoking cessation is essential.
4. Very cautious use of and surveillance for so-called “immune boosters” and traditional medicines. My personal experience is to recommend complete abstinence from their use.
5. Psychosocial support is sometimes very helpful as many patients have to deal with the double stress and duress of coping with two chronic conditions, each with its own potentially life threatening complications. Use of the family and community resources is advisable.
6. Treatment of other cardiovascular risk factors
   A. Dyslipidaemia - general measures and targets apply; the only major exception is simvastatin is contraindicated in patients using Protease Inhibitors as it competes for the same cytochrome P450 isoenzyme. Fluvastatin and pravastatin are known to be safe.
   B. Hypertension - angiotensin-converting-enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) which typically form the backbone for treatment of hypertension in people with diabetes, should be used with caution. For example, in one study, captopril was associated with new-onset Kaposi’s sarcoma and
enalapril with myaligia and diarrhoea. ARB’s may compete with other drugs that are metabolised by the cytochrome P450 isoenzymes.

**Treatment of hyperglycaemia**

**Oral anti diabetic drugs**

**A. Insulin sensitizers**

1. Metformin remains the initial drug of choice on confirmation of the diagnosis of diabetes.

   Most studies have showed good tolerance and an improvement in insulin sensitivity, a reduction in abdominal adiposity with reduction in waist circumference and a reduction in diastolic blood pressure and triglyceride levels.

   Caution has to be exercised in patients with HIV-enteropathy. In these cases, the gastrointestinal side effects of metformin might be exaggerated. In keeping with the package insert, the starting dose of metformin should be low and gradually escalated, using modified release forms of the drug where available. Metformin must never be used in conjunction with thymidine based NRTIs ( stavudine, didanosine). The risk of lactic acidosis is greatly enhanced due to mitochondrial toxicity. It is further equally contraindicated in patients with HIV-associated nephropathy (HIVAN), cachexia, heart failure and disseminated TB.

2. Thiazolidinediones (TZDs) - Conflicting results pertain to the effects of these drugs when used in patients presenting with lipoatrophy. The TZD’s should offer a favourable outcome considering that they redistribute fat from the abdominal viscera to subcutaneous regions. They work by improving insulin sensitivity. Gelato et al showed that patients treated with rosiglitazone for 6-12 weeks had a 59 % increase in insulin sensitivity, a 23 % increase in subcutaneous fat and a 21 % decrease in visceral adiposity. This class of drugs has been discontinued from many national guidelines and our own Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) Guidelines make mention of using pioglitazone only under very specific indications. Side effects, including fractures and fluid retention with an exacerbation of heart failure, are well described.

**B. Insulin Secretagogues**

1. Sulphonylureas – This class of drugs are considered safe and should be used according to the current national diabetes guidelines. Caution should however be exercised in patients with cachexia who might have depleted hepatic glycogen stores. In these patients, the risk of hypoglycaemia is greatly increased.

   2. Glinides – Because of their short-acting mode of action, the risk of hypoglycaemia is minimal. Since they address the defect in 1st phase insulin secretion, they are an appropriate drug of choice in patients on PIs.

Currently no data exists about the use of the newer classes of incretin mimetics (DPP-IV inhibitors and the GLP-1 receptor analogues) in people who are HIV positive.

**Insulin**

Insulin remains the drug of choice for patients with HIV. It has anabolic effects, reduces inflammatory markers, does not interact with antiretroviral drugs and does not have any contraindications

**Amending the HAART regimen**

Controversy still exists as to whether HAART should be changed, and to what it should be changed. Unfortunately, the safer, metabolically-neutral drugs are still very expensive. However, the following general rules are advised:

1. HIV positive patients who already have established risk factors for diabetes should be given metabolically-neutral drugs from onset.

2. Patients on thymidine-based NRTI’s developing lipodystrophy should be switched to safer NRTI’s (e.g. abacavir).

3. Patients on older generation PIs with appearance of lipodystrophy or dysglycaemia should be switched to metabolically safer PIs.

**Conclusion**

As more and more HIV-positive patients are placed onto HAART and therefore live longer, it is vital for the treating physician to screen those patients for diabetes timeously. Appropriate treatment can then be introduced and a plan of action established going forward.

We hope that as novel safer metabolically neutral drugs become more widely available at a reduced cost, it should spell an end to the treatment-related abnormalities such as diabetes and the disfiguring condition of lipodystrophy.

**REFERENCES AVAILABLE ON REQUEST**
"The proper application of medical devices to reduce pressure on wounds, improve gait, warn patients of time spent on delicate tissues, and monitor activity goes far beyond simple insoles and footware modification" (McGuire J, 2012).

This third article on footwear discusses offloading strategies, temporary and therapeutic footwear for diabetic ulcerated feet. The “6W” concept and supporting material has been reprinted with permission from Dr James McGuire, Associate Professor and Wound Center Director of the Temple University School of Podiatric Medicine, Philadelphia, USA. I discussed footwear characteristics for low, medium and high-risk feet in 2013 Issues of SAJD.

The ulcerated foot
A basic approach to healing a diabetic ulcer rests on three legs of a ‘tripod’:
1. Offload the pressures and forces on the ulcer to enable new cells to grow and move into place
2. Control blood glucose tightly and
3. Encourage the best wound environment by means of
   a. adequate perfusion,
   b. debridement of non-viable tissue,
   c. moisture and infection control,
   d. cellular tissue support (E.g. growth factors / substrates and correction of dietary inadequacies).

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Podiatry Association of South Africa Footwear Committee Chairperson

Figure 1: Three basic points supporting the ‘tripod’ of healing a diabetic ulcer (WHASA 2013). Healing is substantially delayed if any one ‘leg’ of the ‘tripod’ is lacking.
Offloading is necessary to redistribute plantar pressure, as well as to reduce the shock and shear forces that contribute to further tissue breakdown. It is also necessary to protect delicate, recently healed tissues from further breakdown during healing maturation. Important is that what is necessary for offloading at ulcer presentation may not be the same needed as healing progresses.

Most wound care practitioners unfortunately often attempt to heal wounds with a single offloading device during the entire healing process.

**Transitional Offloading**

Normal tissue healing will progress from one phase to another, involving specific cell types, growth factors and various signalling molecules. Since the transition of the wound produces a wound that is different in each of these stages, it is reasonable to assume that these changes need the use of various transitional offloading devices.

Dr. James McGuire, of Temple University in Philadelphia, developed the “6W” approach to help practitioners improve their assessment of biomechanical foot risk while choosing appropriate offloading interventions from TCC (total contact casts) to shoes. The 6 W’s are: who the patient is; what the patient wears; when the patient walks; where the patient walks; why the patient walks; and the ‘way’ the patient walks.

This approach includes the intrinsic factors of the patient’s inherent biomechanics, the extent of the effects of diabetes on the foot, the degree of neuropathy and the patient’s basic physiologic status. The 6W assessment also provides information on the patient’s footwear choices, temporal issues associated with walking, walking surfaces and potential obstacles, the conditions the foot experiences, the motivational factors associated with the activity of walking and the specific gait patterns exhibited by the patient.

Dr. McGuire composed each of these variables into a grid and assigned a relative numerical weight to arrive at the “6W Biomechanical Risk Assessment” score for that patient. The higher the relative score, the greater the risk of tissue damage and the more aggressive the offloading approach should be (Table 1).

**WHO the patient is** will highlight intrinsic causes such as the patient’s inherent biomechanics, the duration of their diabetes, other systemic illness, the degree of neuropathy, and basic metabolic and physiologic status affecting ulcer healing such as infection, venous insufficiency, or peripheral arterial occlusive disease.

An understanding of what caused the diabetic ulcer will determine the various therapies needed to manage it. Lavery and colleagues examined patterns of contributory factors and found that a combination of neuropathy, deformity, secondary callus formation and elevated peak pressure was the most common pathway to development of a diabetic foot ulcer. The origin of high pressures is usually the result of inherent biomechanical deformities or imbalances that are often ignored as major contributory factors to foot ulcer development. Muscle atrophy and connective tissue glycation alter the degree of these deformities and reduce flexibility of the foot, increasing forefoot pressures and tissue irritations in gait and shoe wear (Figure 2).

Ideally, offloading should be a therapy designed to prevent the development of ulcerations. All too often, it is used as a therapy to address the already ulcerated limb.

Digital deformities such as hammertoes, mallet toes and contracted toes can be prevented from becoming fixed by means of podiatric interventions inside shoes. Custom shaped plantar metatarsal pads lift the plantar-flexed metatarsals, thereby extending the proximal and distal interphalangeal joints. Once digital deformities become fixed, resultant

**Table 1: Assessing the Biomechanical Risk of Patients (reprinted with permission)**

<table>
<thead>
<tr>
<th>6W Biomechanical Risk Assessment</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who</td>
<td>No neuropathy or deformity</td>
<td>Neuropathy or deformity</td>
<td>Both</td>
<td></td>
</tr>
<tr>
<td>What</td>
<td>Properly offloaded</td>
<td>Adequate offloading but not ideal</td>
<td>Inappropriate footwear or behaviour (barefoot)</td>
<td></td>
</tr>
<tr>
<td>When</td>
<td>Limited or no ambulation</td>
<td>Moderate or normal daily activity</td>
<td>Highly active</td>
<td></td>
</tr>
<tr>
<td>Where</td>
<td>Indoor limited walking on uneven surfaces</td>
<td>Moderate outdoor walking on some uneven surfaces</td>
<td>Frequent outdoor walking on multiple uneven surfaces</td>
<td></td>
</tr>
<tr>
<td>Why</td>
<td>Adherent</td>
<td>Mostly adherent</td>
<td>Average motivation</td>
<td>Non-adherent</td>
</tr>
<tr>
<td>Way</td>
<td>Short stride</td>
<td>Normal stride cadence and step length</td>
<td>Long stride</td>
<td>Fast, hard walker</td>
</tr>
</tbody>
</table>

Total scores | Low Risk | 0-3 | Moderate Risk | 4-6 | High Risk | 7-12 |
irritations from shoe or bone-to-bone contact cause increased pressure and shear to the skin (Figure 2). Loss of toe function leads to increased direct plantar pressures and skin shear, while capsular stiffness decreases the toe’s ability to absorb pressures from footwear. Loss of flexibility in the Achilles tendon and the posterior muscle group also contributes to increased forefoot pressures in gait. Inherent foot type or posture and gait changes also play important roles.

WHAT the patient wears includes an examination of the range of shoes, slippers or sandals worn and the correctness of any inserts, prescription insoles or orthotics. Footwear has been implicated as the precipitating cause in toe ulcers and a significant contributor to wounds elsewhere on the foot. However, shoes have not been shown to be an independent predictor of wound development without accompanying foot deformity, either because of a patient’s inherent foot type or because of muscle atrophy linked to glycation of motor nerves to the muscles. Properly prescribed and properly used therapeutic footwear reduces the incidence of foot ulceration.

WHEN the patient walks encompasses finding out about temporal issues of activity modification and should include education on scheduling and time management to reduce the amount of walking done in a day.

WHERE the patient walks is important to understand the stresses to which the foot is subjected in a day. Home and work environment surfaces can create very different stresses on the foot and may need modification. Some patients will ask if they can still drive if their car is an automatic. They will need counselling to find alternate means of transport (colleagues, family members or neighbours to assist).

WHY the patient walks will address the issues of motivation and adherence. The understanding of the patient of his or her condition, and how well he or she is motivated to co-operate with the clinician’s prescribed therapies, will more than any single variable, greatly affect outcomes and success of treatment.

WAY the patient walks. Gait is made up of cadence, stride and step length. These are measures of a patient’s assertiveness when walking and influence the amount of stress placed on the tissues of the foot. Younger patients may have very fast, aggressive gaits, which can be detrimental to their feet. Older patients may have a slower, more tentative gait. Balance training and walking aids such as canes and crutches must be used to reduce stress on the foot and modify the way the patient walks.

The concept of using different off-loading devices during the different phases of healing is all-important and too often neglected by the practitioner. A common problem among practitioners is to allow the patient to return to standard or depth footwear too early, which can result in recurrence of the ulcer.

Types of offloading devices and footwear
At first presentation, no ulcer should leave the clinical setting without some form of offloading. Even in primary care clinics with limited resources, a rolled bandage which is formed into a ‘doughnut’ can be placed over an ulcer to re-distribute pressure to the surrounding tissue, and the patient educated as to the use of a pair of crutches until such time as an offloading plan of treatment can be implemented.

Total Contact Cast (TCC)
Most practitioners treating diabetic foot ulcers are aware that the gold standard for offloading a diabetic foot wound is a TCC (Figure 3) as it has healing rates as high as 90%. However, there are strict exclusions for the use of TCCs, as listed in Table 2.
Whether because of the exclusion criteria or the time, complexity of application or cost of materials, many clinicians use alternative devices. These include:

- a removable cast walker (RCW - Figure 4),
- a non-RCW or instant total contact cast (iTC C - a moulded ankle foot orthosis, with or without a patella tendon-bearing addition),
- Charcot restraint orthopaedic walkers (CROWs),
- healing or therapeutic sandals with moulded diabetic orthotics,
- semi-compressed felt in various thicknesses,
- the ‘Football dressing’ and
- commercial offloading shoes (E.g. the wedge sandal shoe [figure 5], post-operative shoes and depth or custom-moulded footwear).

### Table 2: Exclusion criteria for the use of a Total Contact Cast (TCC)

<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Documented peripheral arterial disease</td>
</tr>
<tr>
<td>2. Ankle brachial index of less than 0.7</td>
</tr>
<tr>
<td>3. Active infection</td>
</tr>
<tr>
<td>4. Cast claustrophobia</td>
</tr>
<tr>
<td>5. Known non-compliance or non-adherence</td>
</tr>
<tr>
<td>6. Fluctuating leg oedema</td>
</tr>
<tr>
<td>7. Active skin disease</td>
</tr>
<tr>
<td>8. Sinus tract</td>
</tr>
<tr>
<td>9. Clinician has inadequate training or confidence to perform a TCC</td>
</tr>
</tbody>
</table>

**Non-removable cast walker (non-RCW) or instant total contact cast (iTCC)**

Armstrong and colleagues pioneered the use of the non-RCW or what is now termed the Instant TCC (iTCC). These modalities were prompted by studies that showed that patients with diabetes consistently remove or fail to use prescribed offloading devices. Armstrong et al found that the RCW was worn during only 28% of daily activity. The real key to healing with almost any of the offloading devices is the ability to improve patient compliance by restricting removal of the devices. The iTCC utilizes a removable diabetic walker which has been secured with overlying cast material (plaster of Paris or similar), or by applying a cable tie connector to prevent patients removing the devices.

**Semi-compressed felt (SCF) and the Football dressing**

Alternative non-removable dressings that have support in the literature for management of open wounds are Semi-Compressed Felt (SCF) and the Football dressing (Figures 6 and 7). Podiatrists regularly use SCF in thicknesses varying between 5 mm and 15 mm to create offloading pads or foot alignment corrective pads. These are affixed directly to the plantar surface of the foot. SCF is used to offload debrided areas of hyperkeratinous deposits until the patient can use custom-moulded, offloading orthoses.

Typically, a skin barrier product is applied first to prevent irritation and to ensure that the dressing does not shift position. Other skin barriers are used to prevent maceration in the case of exudate. Once the wound has been dressed, a modified surgical shoe with a moulded insole, a surgical wedge shoe or even a pre-
A fabricated walker can then be used to protect the foot. Dressings should be changed as prescribed and the protective pads are re-applied weekly until the wound is healed.

The Football dressing (Figure 7), developed by Rader and Barry, is a viable option on top of a 15mm SCF wound offloading pad in instances of forefoot ulceration for which a TCC is contraindicated and a cast walker cannot be sourced because of finance limitations or other circumstances. The football dressing uses several layers of woven cast padding, followed by crepe bandage, overlaid with more padding. Additional woven gauze roll bandage or crepe bandage and lastly a layer of self-adherent wrap (cohesive bandage) keep it in place. The football dressing can be fabricated to fit into an existing cast walker or a wedged sandal. Further layers of various modalities of specialized open cell foam can be placed inside the cast walker or wedged sandal for additional pressure relief.

A football dressing eliminates the claustrophobic feeling some patients experience when they are restrained in a non-removable device. If a patient takes the RCW off, the Football dressing (which is perceived as a large bandage) will protect the foot if a few limited steps are taken outside the device (E.g. trips to the bathroom at night).

A return to standard or depth footwear too early can result in the recurrence of the ulcer, so it is best to involve a patient’s caregivers, family and friends to achieve a better overall outcome. We need to foster a relationship of trust to gain adherence to treatment plans. McGuire and others believe that a further three to four weeks should pass to allow maturation of the epidermis before the prescription of therapeutic footwear. Patients should not return to the original footwear implicated as a cause of the ulcer.

The importance of custom moulded total contact orthoses (as manufactured by podiatrists and orthotists) cannot be over-emphasized. Thin, dynamically moulded materials are just not enough, either to offload the diabetic foot or to reduce shear-producing sliding. Custom moulded orthoses must be thick enough to take up room in the shoe necessary to give the patient a snug yet not too tight fit, and fill the midfoot arches for proper pressure redistribution. They should reflect the professionalism and care of the dispensing podiatrist and not be a prefabricated over-the-counter or heat-moulded device.

**REFERENCES AVAILABLE ON REQUEST**
Hypoglycaemia is one of the most well-known and feared possible acute complications of treated diabetes. Health care providers and patients alike should easily recognize the acute symptoms of palpitations, tremor and sweating. If left untreated, confusion, seizure and coma will follow.

This discussion will review the literature on the risks associated with hypoglycaemia.

Hypoglycaemia and the fear thereof is one of the main reasons why many patients with both type 1 and type 2 diabetes do not achieve their blood glucose targets. This is despite overwhelming evidence that good glycaemic control prevents microvascular complications of diabetes.

In both the Diabetes Control and Complications Trial (DCCT) and the follow-up Epidemiology of Diabetes Interventions and Complications (EDIC) study, it was clear that lower mean HbA1c levels resulted in fewer microvascular complications.

In type 2 diabetes, the United Kingdom Prospective Diabetes Study (UKPDS) showed that intensive glycaemic control resulted in less microvascular events - each one percent drop in HbA1c led to a 35% reduction in microvascular complications.

In the UKPDS, the following rates of hypoglycaemia were seen:
- 0.7% of patients had severe hypoglycaemia (divided between glibenclamide and insulin treatment)
- Oral treatment alone showed a 16% risk
- Insulin therapy showed a 30% risk

Rates of hypoglycaemia are however, underestimated. This is because patients take corrective measures when measuring below-target blood glucose values and because mild hypoglycaemia is more common and less reported.

Brain tissue is dependent on a continuous glucose supply. The brain registers hypoglycaemia at a blood glucose level of 3.6 to 3.8 mmol/l. At this level, the counter regulatory hormones adrenaline and glucagon are secreted. Glucagon prevents the further fall of glucose and reverses the suppressive action of insulin on the liver. This action will increase the glucose output by the liver through glycogenolysis and gluconeogenesis. Adrenaline stimulates the liver directly to produce glucose and additionally suppresses peripheral usage of glucose.

Important is that these counter-regulatory hormone responses occur in the absence of any warning symptoms. Warning symptoms only occur at a blood glucose level of 3.2 mmol/l if there is no blunting of hypoglycaemic awareness present.

Cognitive impairment appears at a blood glucose level of 3.0 mmol/l.
What makes mild hypoglycaemia dangerous?
If mild hypoglycaemia (blood glucose ~3.3 mmol/l) occurs at least once a day, counter regulatory hormone adaptation will occur. Hypoglycaemic symptoms are masked because the threshold for their appearance will be shifted to a much lower level. The absence of early hypoglycaemic detection (blood glucose 3.3-3.6 mmol/l) will increase the risk of prolonged and severe hypoglycaemic events as well as events that are more frequent.

Blunting of counter regulatory hormone responses
Sudden strict diabetes control (HbA1c fall from 10.4 % to 6.7 % over 6 months) with diabetes duration of 6 years or longer will cause blunting of the autonomic nervous system responses to hypoglycaemia. A study done by Stephan Davis showed that adrenalin levels in these patients decreased by 50 %, thus blunting their heart rate and blood pressure responses.

Severe hypoglycaemia
Severe hypoglycaemia is defined as a blood glucose level equal to or lower than 2.8 mmol/l.

Data from the Action in Diabetes and Vascular Disease: Preterax and Diamicon Modified Release Controlled Evaluation (ADVANCE) trial showed that severe hypoglycaemia is a marker for increased vulnerability to adverse outcomes.

Severe hypoglycaemia has acute effects on:

1. **Sympathoadrenal activity:** The increased secretion of catecholamine has an acute adverse effect on the myocardium and vascular system. The higher level of adrenalin leads to platelet activation and increased coagulation. It has the potential to trigger a cardiovascular event.

2. **Inflammation:** Hypoglycaemia increases the following mediators acutely:
   - Interleukin 6 (Il-6)
   - C-reactive protein (CRP)
   - Vascular endothelial growth factor (VEGF)
   - Tumour necrosis factor alpha (TNF-alpha)
   Intravascular inflammation is activated and will eventually contribute to atherosclerosis.

3. **Endothelial dysfunction:** Hypoglycaemia increases production of the potent vasoconstrictor, endothelin 1, by vascular endothelial cells.

4. **Cardiac ischaemia:** Severe hypoglycaemia is associated with approximately twice the risk of cardiovascular disease. A meta-analysis done by Atsushi on 903 510 people with type 2 diabetes showed more cardiovascular disease among those with hypoglycaemia. This association is biologically plausible due to the increase in catecholamine.

5. **Fatal arrhythmias:** A prolonged QT interval due to increased adrenalin and lower potassium levels can lead to torsade de pointes and fatal dysrhythmias in both type 1 and type 2 diabetes. Hypoglycaemia can also cause other ECG changes including a decreased PR interval and ST segment depression.

6. **Brain structure, cognitive impairment and brain dysfunction:** Severe hypoglycaemia has shown to alter brain structure and cause significant cognitive damage. The risk of dementia increases with 2.4 % per year with hypoglycaemic events. Severe hypoglycaemia can also lead to an increased risk of seizures, coma and death.

7. **Weight gain:** One of the most common signs of recurrent hypoglycaemia is weight gain. This is the result of defensive eating. Weight gain causes more insulin resistance and usually leads to an increase in blood glucose levels and up titration of medicine.

8. **Financial:** The financial burden due to hypoglycaemia includes the costs of increased hospitalisation as well as loss of income due to absence from work. The risk of car accidents and resultant increased medical costs is higher with hypoglycaemia.

9. **Emotional:** People with diabetes feel a loss of quality of life due to the fear of recurrent hypoglycaemia. Depression may be a consequence due to the frustration of not being able to be in complete control. In addition, the unpredictability of the events contribute to the risk of depression.

It is thus vital to recognise the patient at high-risk for severe hypoglycaemia and to tailor treatment to try to minimize these events. High-risk patients include those with:

- A long duration of diabetes
- Recurrent mild hypoglycaemia
- Hypoglycaemia unawareness
- Kidney failure
- Sudden, strict onset of glycaemic control
- A history of alcohol abuse
- Low energy intake
- Lower HbA1c values and
- The very old and the very young

Type 2 diabetes mellitus is a multi-factorial disease with various potential complications. We must be aware of the risks of hypoglycaemia in this population as it can contribute to the progression of atherosclerosis. Due to its possible adverse health consequences, even ‘mild’ hypoglycaemia should be avoided by choosing more reliable and predictable diabetes therapies.

REFERENCES AVAILABLE ON REQUEST
Health benefits of weight reduction in patients with diabetes

Overweight and obesity account for about 80-90% of all cases of type 2 diabetes and are important obstacles to the successful long-term management of diabetes.

The underlying metabolic abnormalities of diabetes are the result of obesity and predispose patients to hypertension and cardiovascular disease. Weight reduction is an important goal in treating type 2 diabetes and some consider it the cornerstone of diabetes therapy. Not only does it result in physiological benefits, it also increases longevity.

Modest weight loss (5-10%) provides the most striking benefits:

- Increases life expectancy of overweight patients with type 2 diabetes by 3-4 years
- Reduces diabetes-related deaths by more than 30%
- Fall of up to 50% in fasting glucose in those newly diagnosed with diabetes
- 40-60% fall in incidence of diabetes for people at risk, such as those with impaired glucose tolerance

Weight loss may improve glucose homeostasis through various mechanisms:

a) Reduction in hepatic glucose output and fasting glucose levels
b) Improvement in postprandial glucose excursions and peripheral insulin resistance
c) Enhancement of β-cell sensitivity to insulinoergic stimuli

duromine™

Effective interventions for weight management should commence as soon as diabetes is diagnosed (or at the diagnosis of impaired glucose tolerance or abdominal obesity). It has been demonstrated clinically that people with type 2 diabetes experienced more difficulties losing weight than overweight people without diabetes. Failure to achieve and maintain weight loss may not be due to non-adherence, but rather due to the altered metabolism of diabetes. Added to this is the fact that too many ‘diets’ focus on improvement of blood glucose and lipids, rather than a focus on weight management.

In a survey done of specialist physicians who treat obesity, phentermine ranked as the most prescribed anti-obesity medication.

Duromine (phentermine) is a sustained action anorectic agent used in obese patients as a short-term adjunct in a medically monitored comprehensive regimen of weight reduction based, for example, on exercise, dietary interventions and behaviour modification.

Duromine in conjunction with dietary interventions and exercise helped patients with obesity and type 2 diabetes achieve early and significant weight loss.

Gershberg et al demonstrated that patients lost significantly more weight with Duromine than on diet alone and also achieved significant reductions in blood pressure and serum cholesterol.

With Duromine, patients can conservatively expect to achieve an average weight loss of 1.19 kg per week in the first 4 weeks and 0.56 kg per week in weeks 5-12.

Faster initial weight loss is associated with a greater likelihood of achieving 10% weight loss and preventing weight regain in the long run.

Dosage and directions for use:

15 mg or 30 mg capsule once daily at approximately 7 a.m.

**Duromine is not indicated in children under 12 years old.

References:

The CDE is again offering a series of advanced 1-Day Master Classes for Healthcare Professionals who have a special interest in diabetes. These Courses are designed to provide an in-depth understanding of therapeutic options aligned with the latest principles of diabetes management. Insulin therapy in the management of type 1 and type 2 diabetes and insights into evidence-based treatment guidelines for oral agents are the subject of these cutting-edge sessions.

Healthcare Professionals can look forward to a series of interactive lectures presented by an Academic Faculty of Senior Endocrine and Diabetes Specialists, followed by discussion of relevant case studies.

We will present the following sessions in 2014:

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<tr>
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<th>Insulin Therapy</th>
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<tr>
<td><strong>Course Date</strong></td>
<td><strong>Venue</strong></td>
</tr>
<tr>
<td>31 May 2014</td>
<td>Cape Town</td>
</tr>
<tr>
<td>7 June 2014</td>
<td>Durban</td>
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<tr>
<td>21 June 2014</td>
<td>Johannesburg</td>
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<td>27 September 2014</td>
<td>Port Elizabeth</td>
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Each Master Class has been accredited for 5 CPD points for registered Medical and other Healthcare Practitioners. Please visit the following page on the CDE Website www.cdecentre.co.za/for-healthcare-professionals/diabetes-courses for further information.
In December 2013, the World Diabetes Congress was held in Melbourne, Australia. I attended lectures in my areas of interest including those on narrative medicine, mental health, the prevention of type 2 diabetes, youth with diabetes, the elderly patient, nutrition and exercise. All of these lectures had some pearls of wisdom to share; some that we know and some that we don’t, but I have selected just a few to share. It is difficult to do them justice in a short summary so I have tried to pick out the key points of interest in each talk.

South Africa contributed to the Congress in special ways. Keegan Hall, one of our Youth with Diabetes (YWD) leaders became the President of the IDF group “Young Leaders in Diabetes”. Kerry Kalweit, Chairperson of Youth with Diabetes in South Africa, presented a research paper entitled “A cross-sectional study on the management and perceptions of SA school children regarding their type 1 diabetes diagnosis.” She found that 47.5 % of her sample of 80 children who had had diabetes for an average duration of 4.6 years, had poor metabolic control. She noted that 84 % of these children used no correction doses. She found that family background played a part in metabolic control - children from two-parent homes did a lot better than did children from single-parent homes. Almost 29 % of the children who stated they had poor quality of life had parent issues, worries about diabetes and negative health perceptions.

Dr Stephen Green, chairman of the International Society for Pediatric and Adolescent Diabetes (ISPAD) revisited the goals of good care of diabetes in children, which included making sure they are correctly diagnosed, the setting goals and targets, determining outcomes by keeping good records of patient progress, offering good multi-disciplinary service and encouraging research of best practice and into a cure.

A schoolteacher from the UK and mother of a teenager with diabetes shared some ideas of how children with type 1 diabetes should be treated at school to make them proud of their scholarly achievements and the self-management of their diabetes. They need praise for what they do right, and as much motivation to stretch their boundaries as other children have. The teacher needs to understand the course of the diabetes, the feelings the child may have towards their diabetes, and acceptance that sometimes the child knows more about their diabetes than does the teacher. Parents should provide a comprehensive and detailed individual health care plan for the teacher. With each transition to another teacher, this should be redone, no matter the age of the child.
Dr G. Vijayakumar from South-West India spoke of a large primary prevention programme, the kNOw Diabetes Project, undertaken in Kerala Province, which has the largest prevalence’s of types 1 and 2 diabetes in India. Changes in traditional lifestyle, changes in dietary habits, an increase in mental stress, and an increase in life expectancy were some of the reasons given why the prevalence of diabetes, particularly type 2, increased from 2.3% in 1972 to 14.6% in 2007. This study used students and teachers as a medium for change in the community because they believed they were the best agents who could influence the community. They targeted 845 schools with 300,000 children from the 5th – 12th grade. Their objectives were to enhance awareness about diabetes among parents and teachers and to educate them regarding lifestyle diseases, risk factors and prevention strategies. By the end of February 2013, they had established 7 Centres for Healthy Living and 100 ‘Walk to Health’ annual events. Diabetes exhibitions were in place in 7 schools and distribution of seeds and plants for healthy eating was undertaken in 100 schools. Furthermore, they had developed a model for primary prevention of diabetes in a population at high risk, and showed that schoolchildren are an ideal group through which to reach the community.

Another talk from India by Dr Mohan et al from the Madras Diabetes Research Foundation and Harvard School of Public Health, reported on a trial to assess the effects on blood glucose and insulin levels in Asian Indians, of substituting white with brown rice. They noted that the refined grains of white rice provide half the calories among South Indian adults. This contributed to a higher glycaemic load and thus increased the risk of type 2 diabetes. They postulated that if they replaced white rice with whole grain brown rice, rich in nutrients and phytonutrients, it would decrease the risk of type 2 diabetes. 150 overweight adults aged between 25 and 65 years, who were at-risk for diabetes (judged by these investigators using fasting glucose and insulin levels) and who were not on any medications for diabetes, participated. Substituting brown rice for white, helped to reduce glucose levels significantly throughout the day. It also helped to reduce serum insulin levels. They concluded that brown rice might help to prevent and control diabetes in rice-eating populations.

Changes in traditional lifestyle, changes in dietary habits, an increase in mental stress, and an increase in life expectancy were some of the reasons given why the prevalence of diabetes, particularly type 2, increased from 2.3% in 1972 to 14.6% in 2007.

Dr. C. Yuan from the USA discussed the long-term effects of intensive lifestyle interventions in type 2 diabetes. He commented that previous research has shown that exercise and eating patterns play a key part in managing this condition. Patients, however, often do not follow any exercise routine or dietary recommendations. He suggested that part of the reason for this apathy for exercise was a lack of time and that the recommendations of the amount of time required for exercise were too long. He asked the question “How little time can you exercise to gain health benefits?” He showed that a single bout of high intensity exercise reduces postprandial blood glucose and hyperglycaemia in patients with type 2 diabetes. He found that if patients do 18 one-minute bursts of high intensity walking a day (for example running/walking at brisk pace up a staircase) before breakfast, lunch and supper, they reduced their post-prandial glucose by 0.6%. This was more than if they had had a longer period of continuous exercise once in the day. He labelled this “exercise snacking”. The effects of exercise snacking together with nutritional intervention (especially high-protein diets) had the best effect to lower HbA1c levels and increase insulin sensitivity. If the patient could sustain this practice, he or she could extend the exercise where possible.

Dr Rob Andrews, from the University of Bristol, gave an excellent and detailed talk on managing blood glucose in type 1 diabetes, before, during and after exercise. He discussed the type and timing of exercise in relation to taking insulin, and in relation to the time of day, and showed the impact of changes in each on blood glucose.

He provided the following conclusions:

- With aerobic exercises, blood glucose tends to fall, while with anaerobic exercise blood glucose tends to rise.
- Glucose falls quicker during exercise when insulin is around.
- Insulin sensitivity increases during exercise, and then for an hour after exercise and at 6-8 hours post exercise.
- Glucose levels need monitoring at these two time points.
- Hyperglycaemia and hypoglycaemia will limit glucose availability during exercise. Good glucose control aids the athlete.
- Patients doing more than an hour of moderate exercise per day should have their carbohydrate intake assessed by a dietician – most patients will not be taking enough carbohydrate.
Dr Bing-Ru Gau and his team from Taiwan looked at preventing adverse foot outcomes among patients with diabetes. He noted that 70% of leg amputations occur in those with diabetes and the incidence of diabetic foot ulcers (DFU) is as high as 25%. In Taiwan, the amputation rate was up to 29% in those with diabetes. He stated that our quest should be to identify amputation risk factors and provide treatment to preserve limbs.

The aim of their study was to answer the question “Does nutrition affect the outcome for patients with diabetes?” They evaluated 480 patients admitted for limb-threatening treatment from 2011 to 2012. They looked at a number of factors that had a bearing on limb health including, medical history, wound severity (Wagner classification), infection level (blood tests), and peripheral circulation (ankle-brachial index and Duplex waveform). The age, smoking habits, and duration of the diabetes were also taken into account. The patients were given multi-disciplinary care in the hospital. Dieticians evaluated their nutritional status within 48 hours of admission using the Mini Nutritional Assessment (MNA) and the Geriatric Nutritional Risk Index.

They found that the nutrition scores correlated with the treatment outcomes of DFU’s. Low nutrition scores were associated with higher amputation rates. They concluded that patients with DFU’s had a relatively poor nutrition status. Both MNA and GNRI are useful tools for predicting outcomes in the treatment of DFU’s.

Professor Tom Sanders from Kings College in London pointed out that 65% of fad diets have insufficient evidence of effectiveness, 4% are possibly effective, 16% probably so and 12% are convincing. He highlighted some ‘diet’ myths like magical combinations of food that promote weight loss, that weight can be lost quickly or weight loss can be easily sustained. People had exaggerated expectations of physical activity and he suggested that there were no good or bad carbohydrates. He showed that less than 5 g of salt or very high intakes of salt per day increased mortality and culture. They will have moments of trust, self-discipline, imagination, humour, self-centredness, and creativity. In our search for knowledge, we should tap into our own creativity to improve the patient’s journey. Patients will do what they want anyway – a creative approach can help to change this. From the patient’s point of view, ‘creativity is a unique place where I can be what I am using imaginary scenarios’.

Dr Tiziana Assal from Geneva, Switzerland facilitates painting workshops and a 3-day theatre workshop for her patients with diabetes, which she calls “The theatre of lived experience”. She believes that artistic expression improves the patient’s ability to cope with anxiety and allows the patient to discover inner resources. A medical doctor supervises the development of a workshop with his patients as participants. His/her presence is mandatory. The patient writes a script on a significant personal experience, which is then acted out by the group of patients at the workshop. Each participant becomes the stage director of his own script. A patient comment on this was, ‘I can use an actor as a spokesman to say what I don’t have the strength to say myself and what you don’t have the strength to hear’. For patients with diabetes, being creative in this way stimulates a new self-awareness and promotes resilience and empowerment while reducing the sense of isolation and solitude.

Henri Matisse said, “To create is to express what one has in oneself”. In this way, the painting workshops allow patients to do this, revealing not only to the doctor but also to the patient himself, the feelings he has about his diabetes.
Presents a Five-Day Advanced Course in Diabetes Care for Health Professionals 2014

DIABETES ~ THE BURDEN, THE RELIEF

Conservative estimates place the prevalence of Diabetes Mellitus in South African adults aged 20-79 years at 6.5% and the prevalence is increasing. 50-85% of persons with the condition are undiagnosed and at risk from disabling and life-threatening complications. Diabetes, together with its associated cardiovascular risk factors is one of the leading causes of death, either directly or indirectly, in our population.

Over the past two decades, it has become evident that good control of diabetes, as well as the common co-morbidities of hypertension and the dyslipidaemias, is vital to prevent or delay the devastating long-term complications of diabetes. To achieve this, people with diabetes need to understand their largely silent condition and the correct principles of self-care.

Health professionals often do not have access to updated approaches to a chronic, mostly self-managed condition such as diabetes – vital opportunities for therapeutic interaction and patient education are lost. Additionally, insight is needed into the ever-widening range of available medications and treatment strategies as well as the relationships between cardiovascular and other risk factors and diabetes.

As health services evolve, there is a move towards Team Management of Chronic Conditions. This has resulted in the rest of the Health Care Team (Nurses, Pharmacists, Dieticians, Podiatrists, Biokineticists and others) playing an ever-increasing role in diabetes care.

WHO SHOULD ATTEND THE COURSE?

This is an Advanced Course, and is aimed at Health Care Professionals who have a basic knowledge and understanding of diabetes mellitus. It is designed to give an extensive overview of the core principles of modern team diabetes management, so enabling the participants to understand the condition in sufficient depth, to make a real difference in the lives of people with diabetes. Pre and Post Course multiple-choice knowledge evaluation tests are administered, to allow for evaluation of the learning experience.

Attendance is also part of the contractual requirements for Practitioners wanting to open CDE affiliated “Centre for Diabetes Excellence” Branches.

CPD ACCREDITED

The Course offers 34 contact hours. The Course is accredited to provide 30 CPD points for Medical Practitioners and other Healthcare Practitioners registered with the Health Professions Council of South Africa.

Pre-Course readings will be supplied by e-mail to all delegates and an electronic manual of all speaker notes will be provided on the first day of each Course. Official completion certificates will be provided to delegates who achieve a mark of at least 60% in the final Post-Course Knowledge Evaluation.

COMMENTS FROM DELEGATES TO PREVIOUS 5-DAY COURSES:

I realise that I had been blundering around in the dark in treating my patients with diabetes and now someone has turned on the light! This a life changing Course. You have reformed my medical practice forever - General Practitioner
PROGRAMME SUMMARY

The Course is aligned with the latest evidence-based treatment guidelines. Case studies and problem solving approaches are a vital part of the learning process.

TOPICS INCLUDE:
- Holistic Team Care Philosophy & Educational Approaches
- Diagnosis, Classification, Pathophysiology & Prevention of Type 1 & Type 2 Diabetes Mellitus
- Other types of diabetes including Gestational Diabetes
- Treatment of Type 1 & Type 2 Diabetes
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- Meal Planning & Nutrition in Diabetes
- The Importance of Exercise in Diabetes
- The Medical Management of Diabetic Ketoacidosis
- The Foot of the Person with Diabetes
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ANSWERS TO FREQUENTLY ASKED QUESTIONS

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Specialist Physician

It was a superb Course & should result in a marked improvement in the care of people with diabetes -
Registered Nurse

I enjoyed the Course thoroughly. I will manage patients with diabetes with more self-confidence. The talks were excellent, well organized and well presented - Registered Dietician

The message that you convey is that you care. The variety of topics was great. The balance between active participation and listening was great. The great teaching skills in all lectures promote learning - Registered Nurse

All speakers were excellent and displayed an impressive knowledge of their subjects. Your commitment as professionals is highly commendable. I learned a lot from this superb Course. Consequently, I will be able to treat my patients better - Medical Specialist
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