Insulin for Life (www.insulinforlife.org) is a non-profit organization that collects and distributes unopened and in-date insulin, test strips, and other diabetes supplies that would otherwise be wasted. Based in Australia, Insulin for Life has affiliates in the United States, Germany, Austria, and the United Kingdom. Donations come from industry, diabetes centers and clinicians, and patients themselves.

Insulin for Life helps a number of developing countries on a continuous basis, and donates to others as needed in emergency situations, such as following the Asian tsunami, the recent earthquake in Peru, and Hurricane Katrina in the US. In addition, Insulin for Life partners with the International Diabetes Federation (IDF) (www.idf.org) on its Child Sponsorship Program in Bolivia, Rwanda, Zimbabwe and Uzbekistan.

"Many of these supplies would have otherwise been wasted. Instead, they are saving many lives," said Ron Raab, President of Insulin for Life Global, who has had type 1 diabetes himself for the last 50 years.

"Until effective health care systems are put in place, organizations like Insulin for Life will need to provide help," said IDF President Martin Silink, MD, Professor of Endocrinology and Diabetes, University of Sydney, Australia.

Over the past 2 years, shipments from Insulin for Life have totaled 250,000 mL insulin (25-30 million units), 400,000 blood glucose test strips, 1,523,500 syringes, and thousands of meters and other items, with an estimated value of € 2.5 million.

During a press conference Wim Wientjens, PhD, Vice President of the IDF, further highlighted the value of these two organizations. He noted that in developing countries, diabetes care can be abysmal. It is often marked by a lack of insulin (which may be unavailable to or unaffordable for families), a lack of expert care and facilities, and a lack of affordable means of self-monitoring. "For children with diabetes in developing countries, the most common complication of diabetes is death," said Dr. Wientjens, who like Mr. Raab has type 1 diabetes.

Alicia Jenkins, MD, a Visiting Professor at the University of Oklahoma Diabetes Center, added that the aim is to "address the great inequality that exists in the world of diabetes care." To illustrate how these programs are successful, Dr. Jenkins described the work being done in support of 42 needy children in Uzbekistan, whose typical life expectancy would be only 4-7 years post-diagnosis.

Since January 2007, when the project was initiated, Uzbekistan has received over 30,000 mL of insulin and 10,000 syringes. Hospital admissions for diabetic ketoacidosis have sharply declined, and mean HbA1c has been reduced from >10% to 8%. There are now new patient advocacy associations and "healthier, happier people," she reported.

Clinicians can help these efforts by donating funds or supplies, by sponsoring a child via the IDF Life for a Child program, or by starting a distribution center in their area. For more information, visit www.idf.org or www.insulinforlife.org.

Glycemic Control Associated with Reductions in Incidence of Macrovascular Events

Results of an analysis of data from a healthcare database including nearly 70,000 patients with diabetes revealed that elevated HbA1c is a significant risk factor for acute myocardial infarction (AMI) and the need for coronary artery bypass graft surgery (CABG).

Introducing the analysis, Joseph E. Thomas, MD, Yale University School of Medicine, Connecticut, United States, said that while tight glycemic control has been associated with improved cardiovascular outcomes in both type 1 and type 2 diabetes, the relationship between glycemic control and cardiovascular outcomes in clinical practice is not well understood. Thomas and colleagues conducted a retrospective chart analysis of data from 69,418 patients with diabetes from the Integrated Health Care Information System (IHCIS).

For purposes of the analysis, patients were stratified into four index HbA1c groups: <6%, 6-7%, 7-9%, ≥9%. Mean patient age was ~57 years (~54% male), with prior AMI in 1.0-1.5% and prior CABG surgery in 0.1-0.5%. Mean follow-up was 27 months. In the HbA1c ≥9% group at baseline, total cholesterol, LDL-cholesterol, and triglycerides were higher, and HDL-cholesterol was lower than in the other groups. About a third of patients were receiving ACE inhibitors or angiotensin receptor blockers. As expected, use of oral antidiabetic agents and insulin was higher in patients with poorer glycemic control.

The unadjusted incidence rate for AMI, CABG, stroke, and their combination increased generally with increasing HbA1c with the exception of stroke (Table 1). "We were unable to explain the lower stroke incidence," Dr. Thomas said, although he commented that TIAs had been excluded.

Table 1: Unadjusted Incidence Rate per 1,000 Person-Years.

Index HbA1c (%)	AMI	CABG	Stroke	AMI/ CABG/ Stroke
<6	16.5	4.4	63.3	76.5
6-7	18.2	6.0	65.0	80.5
7-9	21.6	6.9	63.8	81.7
≥9	20.6	6.9	48.1	65.2
Overall	19.4	6.1	60.0	76.0

After adjusting for baseline characteristics (gender, age, baseline hypertension, AMI, congestive heart failure, peripheral vascular disease, and cardiovascular disease), hazard ratios for survival and AMI increased with worsening glycemic control (HR=1.57 for HbA1c ≥9%, p<0.001) when compared with the baseline <6% HbA1c group. The same pattern persisted for survival and CABG (HR=1.19 for index HbA1c 6-7, HR=1.56 for index HbA1c 7-9, HR=1.38 for index HbA1c ≥9). With adjusted survival and stroke, however, differences were not significant.

Dr. Thomas concluded, "Elevated index HbA1c is a significant risk factor for AMI, CABG and poorer survival. Glycemic control is associated with real-world, long-term macrovascular outcomes." The data suggest, he added, that "early intervention with intensive diabetes treatment may reduce macrovascular risks." Finally, he noted that ongoing trials (ORIGIN, ACCORD, VADT) are addressing the potential benefits of insulin therapy in patients with cardiovascular disease.

Limitations of this study include the fact that it was an observational study with short follow-up and that because the data were taken from the IHCIS managed care employee database, the population was likely to have been healthier and younger than the usual diabetes database.

Diabetic Peripheral Neuropathy: More Effective Treatments Needed

In a pooled analysis of 1,510 patients enrolled in seven randomized controlled trials, pregabalin (150-600 mg/day) provided significant improvements in pain, sleep interference due to pain, and global health, said Roy Freeman, MD, Harvard Medical School, Boston, Massachusetts, United States. Improvements in pain were dose-related; a clinically meaningful (≥30%) improvement in pain was noted by 43- 62%, though 37% of placebo patients also reported this level of improvement.

"There was a dose-related rapid onset of durable pain relief," Dr. Freeman reported. While pregabalin was well tolerated overall, there was also a dose-related increase in weight gain of approximately 2 kg. For 4% of the 600 mg group, the weight gain was a clinically meaningful increase of at least 7% of body weight. Peripheral edema occurred in 10% (300 mg) to 16% (600 mg). "Clearly the 600 mg dose was more effective, though there were more side-effects," Dr. Freeman said.

Results of another international study, the NATHAN 1 Study, showed that antioxidant treatment with α-lipoic acid improved some neuropathic deficits and symptoms in mild to moderate diabetic neuropathy, but did not affect nerve conduction, based on a composite neurological assessment. The randomized study included 454 subjects given α-lipoic acid 600 mg/day. After 4 years of treatment, the difference between the treatments based on the changes of the composite score including clinical signs (neuropathic deficits) and nerve conduction was only 0.7 points, but the neuropathic deficits did improve in the α-lipoic acid-treated group compared to placebo administration. Dan Ziegler, MD, German Diabetes Center, Dusseldorf, Germany, noted that the "marginal progression" of neuropathy in the placebo arm made it difficult to show a treatment effect. "The designs of future trials must assume a long-term stable neuropathic condition," he said.

Perspective

MD Conference Express asked Nicolaas C. Schaper, MD, PhD, Professor of Endocrinology and Diabetes at University Hospital, Maastricht, the Netherlands, and session moderator, to comment on the studies reported at the Novel Therapies for Peripheral Neuropathy session.

He first noted that there are problems with clinical trials of agents. "You see a huge placebo effect in many studies, as in this study with pregabalin, and many are too short to be clinically relevant," he pointed out. Another problem is the inconsistency between epidemiologic data and clinical trial data, he said. Epidemiologic data suggest there is a steady deterioration in nerve function over time however, a study reported at this EASD showed very little deterioration among trial subjects. "Clinical trials, therefore, may not reflect our clinical practice with this complication," he said.

In studies reported at the EASD α-lipoic acid and aldose reductase inhibitors were found to be either problematic or with relative small effects. "While there may be short-term efficacy in reducing pain with pregablin, there were some relevant side-effects, including edema and weight gain. If these appear by 13 weeks, as shown in this study, then what happens after treatment for 10 years? We need to think carefully about this issue," he continued. "Although we currently have treatments such as tricyclic antidepressants (eg, amitriptyline) and anticonvulsants