AMERICAN JOURNAL OF DIABETES

All articles peer-reviewed

Vol. 2 No. 1 2005

Original articles:

Diabetes Education Methods Series

Elizabeth A Pector, MD

Care for Avoiding Complications Series

Mark H Schutta, MD, Prakash Seshadri, MD

Journal club:

Peridontal disease, bariatric surgery for obesity

Resources:

Taking care of teeth

Book reviews:

Diet, obesity, children with T1DM

Second issue for diabetes educators and physicians who care for patients with diabetes

AMERICAN JOURNAL OF DIABETES

Vol. 2, No. 1 2005

American Journal of Diabetes is a professional clinical journal focussing on the diagnosis, management and treatment of diabetes. Each issue includes articles that physicians and diabetes educators can apply in daily practice.

Articles are selected for publication on the basis of their scientific merit and relevance to the treatment of diabetes. The articles are not product endorsements or advertisements; all advertisements are clearly marked as advertisements. Authors' opinions are their own and may not be the opinions of the American Journal of Diabetes, its editorial board, its Publisher, its Editor-in-Chief or its advertisers. American Journal of Diabetes, its Publishers, Editor-in-Chief, Editorial Board and its advertisers assume no liability or responsibility for any claims, actions or damages resulting from the publications of any article.

AUTHOR INFORMATION can be downloaded from our website, americanjournalofdiabetes.com or e-mailed or faxed to you. Write, phone or e-mail your mailing address, fax number or e-mail address to Author Information, American Journal of Diabetes, PO Box 381, Haddonfield, NJ 08033; ph 856-795-2359; fax 856-427-6922; e-mail: submissions@americanjournalofdiabetes.com.

American Journal of Diabetes is published monthly by Auer-Smith Publishing, Inc. Periodical Postage at Tequesta, Florida and additional mailing offices. Postmaster: Send address changes to Auer-Smith Publishing, 177 North US Hwy 1 #255, Tequesta, Florida 33469; ph 877-335-CURE. Edited, typeset and printed in the USA.

ANNUAL SUBSCRIPTION RATES. USA: 1 year $125. Other countries: 1 year $180. Mail subscription requests to American Journal of Diabetes, 177 North US Hwy 1 #255, Tequesta, Florida 33469; ph 877-335-CURE.

CLASSIFIED ADVERTISEMENTS: Contact American Journal of Diabetes Classified Ads: fax 866-744-0068; classifieds@americanjournalofdiabetes.com; ph 877-335-CURE.

Website: americanjournalofdiabetes.com.

TABLE OF CONTENTS

American Journal of Diabetes reprints of single articles or whole issues may be ordered from Auer-Smith Publishing, 177 North US Highway 1 #255, Tequesta Florida 33469 fax 866-744-0068; ph 877-335-CURE; auersmithpub@aol.com

JOURNAL CLUB

Bariatric Surgery Outcomes in Patients with Obesity, Diabetes and Cardiovascular Risk Factors

The first article reports the results of a large randomized, prospective, controlled study from the Department of Body Composition and Metabolism, Sahlgrenska University Hospital, Goteborg, Sweden. The aim was to determine whether weight loss by bariatric surgery had long-term as well as the short-term benefits.

Swedish Obese Subjects Study Scientific Group. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 2004; 351: 2683-93.

Subject obesity was either treated with gastric surgery or by conventional therapy.

Subjects (mean age, 48 years; mean body-mass index, 41) were followed at least 2 years (n=4,047) or 10 years (n=1,703) after treatment. The follow-up rate for laboratory examinations was 86.6 % at 2 years and 74.5 % at 10 years.

At 2 years, weight was 0.1 % higher in control subjects and 23.4 % lower in surgical subjects (P<0.001). At 10 years, weight was 1.6 % higher and 16.1 % lower, respectively (P<0.001).

Energy intake was lower and physical activity higher in surgical than control subjects throughout follow-up. Rates of recovery from diabetes, hypertriglyceridemia, low levels of high-density lipoprotein cholesterol, hypertension, and hyperuricemia were better at 2 and 10 years in surgical than control subjects. Recovery from hypercholesterolemia was similar between groups. At 2 and 10 years, surgical subjects had less diabetes, hypertriglyceridemia, and hyperuricemia.

Diabetes in Minority Populations

In 2004, the Centers for Disease Control published an article describing the higher prevalence of diabetes in the ethnic Hispanic population in the Mortality and Morbidity Weekly Report. This weekly journal is freely accessible from their website, www.cdc.gov/mmwr/

Centers for Disease Control and Prevention. Prevalence of Diabetes Among Hispanics — Selected Areas, 1998–2002. MMWR 2004; 53: 941-944.

CDC scientists analyzed data from Behavioral Risk Factor Surveillance System surveys to estimate diabetes prevalence in adults classified as Hispanic and non-Hispanic white. Study subjects were surveyed in California, Florida, New York plus New Jersey, Illinois and also in Puerto Rico. The data indicated that Hispanics have a higher prevalence of diabetes than non-Hispanic whites and that disparities in diabetes between these 2 populations varied geographically.

The prevalence of diabetes in adults increased with age and was higher in all age groups for Hispanic adults. The difference was greatest in adults 55-64 who lived in California (25.6 % versus 11.7 %). In this age group, the lowest difference in Florida (12.8 % versus 11.0 %).

Overall, the age-adjusted diabetes prevalence in Hispanics was 9.8 % compared with 5.0 % in non-Hispanic whites. In Hispanics, the prevalence for men and women was similar (9.7 % versus 9.9 %), but in non-Hispanic whites, prevalence was significantly higher for men than women (5.5 % versus 4.5 %).

JOURNAL CLUB

Dental Needs and Care

American Journal of Diabetes has selected several articles on dental needs and dental care in patients with DM.

PERIODONTAL DISEASE TREATED BY TOPICAL MINOCYCLINE MICROSPHERES, SCALING AND ROOT PLANING

Skaleric U, Schara R, Medvescek M, Hanlon A, Doherty F, Lessem J. Periodontal treatment by Arestin and its effects on glycemic control in type 1 diabetes patients. J Int Acad Periodontol 2004; 6(4 Suppl): 160-5.

The first of 2 papers on periodontal disease was from the University of Ljubljana, Slovenia (e-mail: uros.skaleric@mf.uni-lj.si). The aim of this randomized pilot clinical trial was to determine if HbA1c was reduced after treatment with topical minocycline microspheres (Arestin) with scaling and root planing in adults with T1DM and periodontitis.

Subjects (n=20) had HbA1c at least 7.5 %, and periodontitis in at least 4 teeth with 5 mm periodontal pockets, including 2 with 6-9 mm pockets and bleeding on probing. All subjects received full mouth scaling and root planing at baseline. Arestin was administered to all pockets ≥ 5 mm at baseline and at 12 weeks. Probing depth, clinical attachment level, plaque index, gingival index, and HbA1c were evaluated at baseline and at weeks 6, 12, 18 and 24. Arestin significantly improved control of periodontal disease, but was ineffective at reducing Hb1Ac.

OraPharma Inc., Pennsylvania (e-mail:.kardiolog48@hotmail.com) has reported the effectiveness of Arestin therapy in a large post-marketing study in private US practices in which 895 dentists treated 2,805 subjects.

Lessem J, Hanlon A. A post-marketing study of 2805 patients treated for periodontal disease with Arestin. J Int Acad Periodontol 2004; 6(4 Suppl): 150-3.

Subjects' teeth were scaled and roots planed in all pockets ≥ 5 mm at baseline when treated with Arestin. In a second visit at 3 months Arestin was again applied. The subject was assessed in the third and final visit at 6 months.

Mean pocket depth was reduced at 3 months, 1.82 mm ($p < 0.0001$) (n=1,710) and at 6 months, 1.94 mm ($p < 0.0001$) (n=1095). Similar results were obtained in subjects who smoked, had diabetes and had a history of cardiovascular disease. After 1 treatment 62 % of sites had decreased to less than 5 mm and after 2 treatments, 6 7 %. No serious adverse events were reported.

ORAL HYGIENE

The College of Dentistry at New York University reports the effect of oral hygiene instructions on periodontal disease in 60 Saudi males examined at King Saud University, College of Dentistry, Riyadh, Saudi Arabia.

Subjects (mean age 42±13.60) were healthy males with periodontal disease (n=20) or males

The effect of oral hygiene instructions on diabetic type 2 male patients with periodontal diseases. J Contemp Dent Pract 2003; 4: 24-35.

JOURNAL CLUB

with T2DM with early or moderate periodontal disease (n=20), 3) males with T2DM with advanced periodontal disease (n=20). Oral hygiene instructions were to brush 3 times daily for 7 days for 2 minutes with a medium toothbrush. Fasting blood glucose was significantly reduced (baseline 172.67 mg/dL ±64.69), Day 7 162.20±58.78) P = 0.000). Overall, plaque scores were reduced over 47 %.

Sandberg GE, Sundberg HE, Wikblad KF A controlled study of oral self-care and self-perceived oral health in type 2 diabetic patients. Acta Odontol Scand 2001; 59: 28-33.

In a controlled study in Hogskolan Dalarna, Health and Caring Sciences, Falun, Sweden, 102 control subjects and 102 subjects with T2DM completed questionnaires on oral self-care and self-perceived oral health.

Of subjects with T2DM, 85 % had never received information about the relation between diabetes and oral health, and 48 % believed that their dentalcare professionals were unaware of their diabetes. More than 90 % in both groups brushed their teeth daily and more than half with natural teeth cleaned proximally.

Subjects with DM and control subjects were content with their teeth and mouth (83 % and 85 %). Sensation of dry mouth was common among subjects with T2DM (54 %) and subjects with hypertension exhibited dry mouth more (65 %) than those with normotension.

A report from the Armed Forces Hospital of Riyadh, Saudi Arabia. assessed 52 subjects with T1DM and T2DM (mean age 51.3±14) with adult periodontitis treated randomly either by

Al-Mubarak S, Ciancio S, Aljada A, Mohanty P, Ross C, Dandona P. Comparative evaluation of adjunctive oral irrigation in diabetics. J Clin Periodontol 2002; 29: 295-300.

ultrasonic scaling and scaling and root planing alone or additionally with subgingival water irrigation twice daily. After treatment, both groups had clinical and systemic improvement. Subgingival irrigation statistically significant reduced modified gingival index, plaque index, and bleeding on probing compared with controls ($p<0.03$) at 12 weeks and reactive oxygen species generation at 12 weeks ($p<0.012$).

DENTAL IMPLANTS

Morris HF, Ochi S, Winkler S. Implant survival in patients with type 2 diabetes: placement to 36 months. Ann Periodontol 2000; 5: 157-65.

The Dental Implant Clinical Research Group, VA Medical Center, Ann Arbor, Michigan implanted 2,887 prostheses (n=663) and observed the subjects for 36 months: 91 % implants were in control subjects and 8.8 % in subjects with T2DM. Implants in subjects with T2DM failed significantly more often (P=0.020). Chlorhexidine rinses after implant placement improved survival in subjects with T2DM and control subjects (9.1 % and 2.5 %) as did preoperative antibiotics (10.5 % and 4.5 %).

A second report about implants was a prospective multicenter study from Kentucky, from the University of Louisville, (e-mail j.olson@louisville.edu).

JOURNAL CLUB

Olson JW, Shernoff AF, Tarlow JL, Colwell JA, Scheetz JP, Bingham SF. Dental endosseous implant assessments in a type 2 diabetic population: a prospective study. Int J Oral Maxillofac Implants 2000; 15: 811-8.

A total of 89 male subjects with T2DM were assessed for the success of 2-stage endosseous root-form implants in the mandibular symphysis. The implants were uncovered approximately 4 months after placement, restored with an implant-supported, Hader bar clip-retained over-denture, and maintained 60 months.

No implants failed between surgical placement and uncovering, 5 failed at uncovering, 7 failed after uncovering before prosthesis placement, and 4 failed after prosthesis placement. Only duration of diabetes ($P<0.025$) and implant length ($P<0.001$) were statistically significant predictors of implant failure. Failure rates between the 3 different implant systems were similar.

RESOURCES

A page on Oral Health & Oral Hygiene is included on the the American Diabetes Association's site at *www.diabetes.org/type-1-diabetes/mouth-care.jsp.*

The site is aimed at patients, telling them to take care of their teeth because diabetes brings higher risk for gum disease, and gum disease makes diabetes harder to control.

The ADA recommends

1) learning how gum problems start

2) brushing teeth twice a day, flossing teeth every day, looking for early signs of gum disease and visiting a dentist at least twice a year to remove plaque and built-up tartar.

This site explains the consequences of ignoring these recommendations, tells a patient how to interact with a dentist during a dental visit and warns of the increased risk of other oral diseases including oral infections, fungal infections, and dry mouth.

A second site on oral health is posted by the Centers for Disease Control (CDC) at *www.cdc.gov/diabetes/pubs/tcyd/dental.htm.*

The messages at this site are similar to those on the ADA site, stressing that bad oral health can make blood glucose harder to control. This site recommends

1) brushing teeth twice or more a day

2) the patient giving the dentist the name and telephone number of the diabetes health care provider

3) planning dental visits in order to keep constant the times of day that insulin and meals are taken.

ORIGINAL ARTICLE

Effectiveness and innovations of group diabetes education and support. Part 1: Traditional and Internet groups

Elizabeth A Pector, MD

Spectrum Family Medicine, SC, 1220 Hobson Road, Suite 216, Naperville, IL 60540
E-mail synspectrum@yahoo.com

Abstract

The objective was to assess the effectiveness of group diabetes self-management education (DSME) and psychosocial support for patients with diabetes. Literature searches of Medline, Cochrane review abstracts, and Psycinfo were analyzed and summarized. Education and psychosocial support were found to be effective in improving disease knowledge, self-care behavior, metabolic outcomes, and quality of life. Group DSME is cost effective and is equal or superior in effectiveness to individualized instruction. Psychosocial interventions are effective for depressed patients with diabetes, and stress management instruction can improve metabolic control for all patients. Positive results from small trials of cognitive behavioral therapy for diabetic patients with eating disorders or self-destructive behavior need to be replicated. Internet support groups foster meaningful improvements in diet and psychosocial factors, but produce only modest benefits in behavior and biological measures. *EA Pector. Effectiveness and innovations of group diabetes education and support. Part 1: Traditional and Internet groups. Amer J Diabetes. 2005; 2(1):7.*

Introduction

As the incidence of diabetes mellitus increases in the US, group interventions for diabetes education and psychosocial support become an attractive way to allocate fixed resources to meet growing needs. Individualized instruction is not always possible: by 1998, only 40 % of patients had ever received any formal diabetes self-management education (DSME).(1) In addition, with the increasing prevalence of diabetes in minorities, obese adolescents, and senior citizens, educators are challenged to devise innovative yet effective modes of instruction, such as Internet-based initiatives.

To address the comprehensive needs of patients and their families, a biopsychosocial approach to treatment has been recommended.(2,3)

Accordingly, DSME is increasingly based on psychological theories of counseling and behavior change.(2) Regrettably, few studies have reported on quality of life, and psychosocial outcomes are only more recently being assessed.(4,5) Previous reviews of diabetes research have generally analyzed educational interventions separately from psychosocial support, and thus the present review separates the informational aspects of support from emotional and psychological support, while recognizing that all components work together to optimize the health of a person with diabetes.(1,2,6,7)

This paper, Part 1 of a series, examines the effectiveness of traditional individual and group diabetes education and support. Because diabetes Internet support groups are a popular resource, their functions and efficacy are also explored.

Methods

Medline literature was searched for "diabetes group education," "diabetes self-help," "diabetes psychological support," "diabetes emotional support," "diabetes Internet group" and "diabetes self-help groups support." Cochrane review abstracts were searched for the terms "diabetes education," "diabetes group," and "diabetes support." Selected references from review articles were also obtained. Information pertinent to diabetes was obtained from review articles that discuss face-to-face and online support groups for a variety of medical conditions. Review articles, meta-analyses, and newer randomized controlled trials (RCTs) are summarized below.

Results

Challenges in assessing effectiveness of interventions

Unfortunately, few DSME studies adhere to desired quality criteria, in the opinions of many authors.(1,3,4,6,8) Two novel approaches to grading studies are noted in Table 1. Eakin et al. used a "RE-AIM" framework to review diabetes studies from both an individual and a community setting perspective.(3) Muhlhauser and Berger defined stages along a continuum of increasing evidence.(8) In reviewing German literature on diabetes education, they discovered that 20 years may elapse between theoretical studies and post-implementation assessments.(8)

Even when studies are well conducted, the diversity of study populations, educational approaches, and evaluation criteria makes meta-analyses hard to conduct and interpret.(1,8) Although some authors try to isolate the specific components of complex interventions that contribute to efficacy.(6) Muhlhauser and Berger argue that some elements of a multimodal approach, ie coping skills, lifestyle behaviors, and diet adherence, are not easily separated for analysis, especially since dietary recommendations have changed.(8)

In the expanding arena of Internet support groups, reports of clinical trials and observational studies of diabetes support forums have been published. Except for a single larger controlled trial, studies have been small and uncontrolled, and additional work is needed to replicate benefits and quantify risks.(9,10)

Effectiveness of DSME

Bearing in mind the limitations of research conducted to date, large-scale studies, systematic reviews and meta-analyses reveal that group education effectively improves health status and self-care behavior. For instance, a comprehensive outreach to improve personal health practices, the Chronic Disease Self-Management Program, (CDSMP) is used by health organizations in 31 states and 9 countries.(11) CDSMP uses a community-based, 6-week, 2.5-hour session format that addresses dietary change, exercise, medications, community resources, prob-

RE-AIM (Individual and Setting levels) (3)	Continuum of Evidence (8)
Reach (individual): What proportion of potentially eligible participants take part? How representative are they of the underlying population?	Preclinical/theoretical: Defining treatment goals and methods
Effectiveness (individual): Positive and negative outcomes, including process, intermediate outcomes, and quality of life, measured in all participants who began program	Modeling: Pilot studies of intervention components
Adoption (setting): What proportion of eligible settings (eg work sites, schools, medical offices) offer the intervention, and how representative are they?	Exploratory trials: Prospective assessments before and after assessments
Implementation (setting): How well do settings adhere to study protocol in delivering intervention components?	Randomized controlled trials
Maintenance: Individual: outcomes 6 to 12 m after intervention Setting: continuation of intervention components in the setting after trial completion	Long-term Implementation: Individual and population outcomes, replication and transfer of programs to different settings, effectiveness in different settings

Table 1. Approaches to grading studies by Eakin et al (3) and Muhlhauser and Berger (8).

lem solving, and decision-making. Two-year longitudinal followup of CDSMP participants revealed improvements over baseline in health and energy, fewer emergency and outpatient visits and improved self-efficacy.(11)

In regard to patients with T2DM, the US Task Force on Community Preventive Services concluded that diabetes self-management education (DSME) can be recommended in community centers or faith institutions for adults with T2DM.(3) In support of this recommendation are the results of a meta-analysis of 72 studies of individual and group DSME in T2DM.(6) Knowledge about diabetes increased significantly, and was boosted by regular reinforcement. Despite the lack of long-term weight loss, patients increased self-monitoring, reported dietary improvement, and exhibited short-term benefits in glycemic control. Group interventions were more effective than individual approaches in achieving weight loss and glucose control, while both individual and group settings positively affected diet and self-care behaviors.(6) Moreover, Norris et al. conducted a meta-analysis of RCTs to calculate the effect of self-management education on HbA1c in T2DM.(1) Interventions in the 31 selected studies decreased HbA1c by an average of 0.76 % at immediate followup, but the effect declined to just 0.26 % after 4 or more months of followup.(1) A drop of 1 % in HbA1c was seen for every 23.6 hours of contact between patient and educator. Previous meta-analyses and meta-regression by Brown also documented the efficacy of diabetic self-

management education.(1) In order of greatest to least magnitude, the positive effects in Brown's studies were on knowledge, dietary compliance, skill performance, metabolic control, psychological outcomes, and weight loss.(1)

Other investigators found significant benefits of DSME in T1DM, but variable results in T2DM. For instance, Loveman et al evaluated 18 RCTs and 6 controlled clinical trials (CCTs) for efficacy of patient education in T1DM and T2DM.(4) Their systematic review was restricted to studies with 12 months of follow-up data. For patients with T1DM, 4 studies documented significant and enduring improvements in metabolic control, with reduced complications.(4) In contrast, diverse educational approaches for T2DM led to inconsistent effects on control. In 4 studies that included patients with T1DM and T2DM, results were again inconsistent, with lower-quality studies producing statistically significant findings.(4) The US Task Force on Community Preventive Services endorsed home DSME for children and adolescents with T1DM.(3) Additionally, Muhlhauser and Berger's review of older German studies found diabetes education was effective in T1DM, with improved long-term glycemic control and fewer hypoglycemic episodes.(8) Finally, a controlled trial of group education for over 1,300 intensively-treated insulin users resulted in a 6-month decline of 0.82 % in HbA1c for T1DM patients, and a 0.48 % drop for patients with T2DM, compared with a roughly 0.2 % HbA1c decrease in controls.(12) Similar to Muhlhauser and Berger's findings, hypoglycemia was less frequent.

Many trials have determined that group DSME compares favorably to individual education. In patients with a HbA1c over 8.5 %, a RCT showed that a multidisciplinary, 3.5-day intensive group educational program delivered to 50 patients was as effective as mailings sent every 3 months to 56 control group patients, with about a 2 % drop in HbA1c in both experimental and control patients.(13) A similar trial for T1DM and T2DM patients, the DOIT (Diabetes Outpatient Intensive Treatment) program, evaluated a multi-day group program with education, skills training, and daily medical management.(14) This was followed by 6 months of case management. Controls only received standard diabetes care and quarterly educational mailings. Of the 167 randomized patients, 117 were reassessed at 6 months, and the active group had significantly greater HbA1c drop than controls, and better dietary and self-monitoring behaviors.(14) In a third trial, 170 T2DM patients were randomly assigned to group or individual education.(15) In the entire study population, HbA1c decreased from 8.5-6.5 % at 6 months. The group intervention resulted in a 2.5 % reduction in HbA1c in contrast to the individual condition's 1.7 % drop, a marginally significant difference (P=0.05).(15) A 4th study in Spain demonstrated no significant difference between individual and group education in a cohort of 68 recently diagnosed patients with T2DM.(16) Disease knowledge, HbA1c, HDL-C, BMI, systolic blood pressure, and self-monitoring improved significantly in both conditions.(16) Finally, a Swedish study evaluated pharmacist-led "study circles" conducted over 1 year for T2DM patients, using a standardized group format that used patient experiences as a basis for discussions.(17) At the start of the study 51 % of patients had HbA1c below 6.5 % , and by the end, 63 %. Patients with high BMI, higher initial HbA1c, and loneliness were less likely to attain pre-defined goals.(17)

Another successful approach involves integrating group education into group medical visits. Italian investigators evenly divided 102 patients

Basic information about online support groups. Website: www.mentalhelp.net/selfhelp/
Rick Mendosa's comprehensive list of resources. Website: www.mendosa.com/faq.htm
Message boards of Joslin Diabetes Center. Website: www.joslin.harvard.edu/managing/help.shtml
List of organizations related to diabetes, from the National Organization of Rare Disorders database list of organizations concerned with diabetes. Website: rarediseases.org/search/
Catalog of Internet resources. Website: dmoz.org/Health/Support_Groups/
Short list of diabetes groups. Website: psychcentral.com/
Diabetes resources. Website: www.supportpath.com/sl_d/diabetes.htm

Table 2. Internet support resources. These links were all current on 01 Mar 2004.

with T2DM into a group care condition, with routine care provided in interactive group visits, and a control group, with individualized consultation and education.(18) Both groups were followed for 51 months. Diastolic blood pressure and relative cardiovascular risk decreased similarly in both the group-care and control patients. In controls, HbA1c increased, but in group-care patients, BMI decreased and HDL-C, quality of life, disease knowledge and health behaviors all improved.(18) A similar study in 120 uninsured or underinsured US residents found that patients receiving group diabetes care, as opposed to those getting individual care, reported an increased sense of trust in the physician, better coordination of care, better community orientation, and more culturally competent care.(19)

Cost-effectiveness of group education

Although few cost-benefit analyses of group DSME have been done, the most recent opinions suggest that results justify the cost. Before 2001, studies that assessed economic outcomes and health care utilization found no improvements, except for a decrease in emergency room visits in 1 study.(6) A cognitive theory-based lifestyle intervention that decreased cholesterol and improved dietary habits was estimated to cost $137 per patient.(6) Another team found a 1 % change in HbA1c cost $56 per patient in direct costs at 6 months.(6) Most analyses have not accounted for indirect costs or health care utilization in their calculations.(6) Nevertheless, Loveman et al., assuming modest positive effects of diabetes education, deemed it cost-effective at 500-600 GBP per patient, equalling at least $1,060 based on the 2003 exchange rate.(4,20) An intervention in Starr County, Texas was estimated at $384 per person, excluding self-monitoring supply expenses, hence cost was not felt to be a barrier to larger-scale implementation of a culturally sensitive intervention.(21) Group care in an Italian diabetes clinic required nearly 200 minutes and $756 per patient, compared with 150 minutes and $666 per control patient.(18) Thus, according to Loveman's criteria, group DSME interventions in several countries are cost-effective; a formal analysis based on US data would be welcome.

Outcomes of psychosocial interventions

Psychological and behavioral factors are impor-

tant in self-management and quality of life in patients with diabetes.(2,5) Indeed, patients often actively seek psychosocial support. After adjusting for disease prevalence, diabetes ranked eighth out of 20 health conditions in prevalence of support groups in a 4-city survey.(22)

A review by Snoek and Skinner concludes that psychosocial interventions are moderately effective in improving metabolic and psychological well being for patients with diabetes, with no reported adverse effects.(2) However, in a RCT of intensively treated patients who received several days of education, those randomized to a supplementary 8-session social support group had no additional improvement after 7 months in their metabolic control, diabetes knowledge, self-management behaviors, or emotional adjustment.(23) Psychosocial interventions for adolescents will be considered in Part 2 of this series.

A review of interventions for diabetic patients with depression, eating disorders, anxiety or stress, self-destructive behavior, and interpersonal/family conflicts revealed few empirical studies of good quality, with small, uncontrolled studies dominating the literature.(2) Cognitive behavioral therapy (CBT) effectively treats depression and improves HbA1c in patients with T2DM. Moreover, pilot studies indicate positive effects of CBT on stress management, eating disorders and self-destructive behavior, but these findings need to be confirmed.

Surwit et al. found that group stress management instruction improved diabetes control.(24) All 108 participants attended 5 group diabetes education classes, and they were randomly assigned to a control group or a group that received stress management instruction. The stress management training was effective, but this was only evident after 1 year of followup. HbA1c readings declined significantly, by 0.5 % from the baseline of 8.14 %.(24) Efficacy of the training did not depend on the initial level of the patient's anxiety, indicating that even less anxious individuals benefit from stress management interventions.(24)

Internet group education and support

Internet health support groups are increasingly popular, and are widely used by people with diabetes. A recent American Pew Internet Project survey revealed that 54 % of American adults who seek health information online visit support web sites for health or social situations.(25) In a tabulation of the number of online support groups available for 20 health conditions, diabetes ranked 8th when adjusted for disease prevalence.(22) Table 2 lists online resources, including Rick Mendosa's comprehensive listing of Web- and non-Web-based support forums for a striking variety of demographic categories.(26) However, interest in online support is not global. A survey of patients with T1DM in Spain revealed that only half of the 59 % with Internet access had ever accessed a health-related web site. Those who had visited a health-related site were better educated, and also experienced severe hypoglycemia more often. Metabolic control was the same among patients who visit health-related sites and those who did not.(27)

In general, benefits of online group support include 24-hour-a-day access, and availability of support for people who are isolated by geography, disability, or caregiving responsibilities.(28,29) Additionally, online anonymity conceals social or demographic factors, atypical behavior, or disturbing appearance that might preclude acceptance in a face-to-face group. Anonymity also facilitates discussion of sensitive topics such as sexuality.(10,29) Empathy, information, advice, and opportunities for leadership and advocacy are found in online

forums.(10,29)

There are some disadvantages to online group activity.(10,29) Misinformation is possible, but has not often been seen in diabetes-related studies. Only 2 % of the messages in 1 study contained potentially dangerous errors and no instances of misinformation were noted in the 10 months of the D-Net trial.(9,30) Another drawback is the loss of nonverbal cues such as facial expression, vocal inflections, and gestures, which may lead to misunderstandings and anger.(10,26) Other negative aspects include large email burden, social withdrawal in introverts or teens who use the Internet heavily, and Internet addiction.(10,29) Risks that have been reported in other online groups, but not in diabetes groups, are loss of privacy, deception, identity theft, and cyber stalking.(10) Adolescents may be particularly vulnerable online.(10,31)

Despite the popularity of online diabetes groups in the US, outcome measures are sparse. An uncontrolled study in Italy of a professional moderated chat with 43 adolescents with T1DM revealed a drop in HbA1c over 3 months, from 8.9-7.8 %.(32) Only 1 randomized controlled trial has been conducted.(9,33) In the D-Net study, 160 primary care patients were recruited and divided into 4 groups. Most were novices to the Internet, and average age in the sample was 59 years. The control group received online access to information about diabetes, but no direct support. Experimental groups included 1) a personal coach; 2) support with online forums and chats; or 3) combined coach and support.(33) At 3 months, perceived social support was significantly increased.(33) Website use was greatest in the first 3 months in the study, dropping thereafter until the trial's end at 10 months.(9) Participants assigned to peer support or an online coach tended to use the system more than controls. The most significant improvement in all groups occurred in diet, followed by psychosocial outcomes of perceived barriers and support, and depression.(9) There were modest but significant changes in behavior (improved medical care) and biological measures (reductions of 12 mg/dL in total cholesterol, 8 mg/dL in LDL-C, and 16 mg/dL in triglycerides).(9) There were no significant differences in HbA1c in any group, and peer support or coach outcomes were not significantly different from controls, except for psychological outcomes. Overall, the study was moderately successful in using the Internet to deliver a diabetes educational intervention.(9) RCTs have also shown Internet group support an effective part of programs for weight loss or maintenance.(34,35)

Observational studies have found patients are generally well informed, polite, and supportive in Internet diabetes support groups.(30,33,36) Major discussion topics include diet, exercise, medications, doctor-related issues, and online resources.(30,37) In some studies, emotional support garners relatively little interest, with only 18 % of messages in Zrebiec's study posted on this topic, and few messages about social companionship in Loader's analysis.(30,37) In contrast, a small study of 30 rural Montana middle-aged women randomized to computer and non-computer groups revealed that 77 % felt the computer intervention provided a great deal of support.(28)

Conclusions

A wide variety of group DSME and psychosocial support interventions have been proven effective for patients with both T1DM and T2DM. Patients have achieved significant improvements in disease knowledge, diet, exercise, self-management skills, quality of life, and metabolic control. Group DSME is cost effective, and it can

be as effective as individual instruction.

More research is needed on long-term effectiveness of DSME, and on quality of life and psychosocial outcomes. The influence of psychosocial attributes such as depression, social support, and problem-solving abilities on diabetic control needs to be further assessed.(1,2) In addition, future investigations could focus on effectively maintaining long-term behavioral change to reduce HbA1c.(1,3) Studies must include clearly designed RCTs, based on explicit hypotheses, and should report on many long-term outcomes.(1,4) Details must be provided for participant demographics, program settings, intervention protocols, and contact time for intervention and control groups.(1,3) Attrition of participants should be minimized, and target populations need to be sampled scientifically, with estimates of how closely the study participants represent the target group, so research outcomes can be reliably generalized to the real world.(1,3) Likewise, knowledge of the percentage and representativeness of eligible settings that actually engage in a study can aid in wide-scale program design and deployment.(3,8) Lastly, controlled trials of Internet group support could better assess the balance of benefit and risks for a popular, but not entirely benign, support format.

Given the demonstrated benefit of DSME, it is imperative to reach many more patients with multidisciplinary group instruction. With roughly 1 in 12 Americans diagnosed with diabetes, and even greater prevalence expected in the future, it would be tragic for patients to be deprived of education and support that can help them forestall long-term complications.

References

1.Norris SL, Lau J, Smith SJ, Schmid CH, Engelgau MM. Self-management education for adults with Type 2 diabetes. A meta-analysis of the effect on glycemic control. Diabetes Care 2002; 25: 1159-71.

2.Snoek FJ, Skinner TC. Psychological counseling in problematic diabetes:does it help? Diabet Med 2002; 19: 265-73.

3.Eakin EG, Bull SS, Glasgow RE, Mason M. Reaching those most in need: a review of diabetes self-management interventions in disadvantaged populations. Diabetes Metab Res Rev 2002; 18: 26-35.

4.Loveman E, Cave C, Green C, Royle P, Dunn N, Waugh N. The clinical and cost-effectiveness of patient education models for diabetes: a systematic review and economic evaluation. Health Technol Assess 2003; 7: 1-190.

5.Mensing C, Boucher J, Cypress M, Weinger K, Mulcahy K, Barta P, Hosey G, Kopher W, Lasichak A, Lamb B, Mangan M, Norman J, Tanja J, Yauk L, Wisdom K, Adams C. National standards for diabetes self-management education. Diabetes Care 2004; 27 (Suppl 1): S143-50.

6.Norris SL, Engelgau MM, Narayan KM. Effectiveness of self-management traning in Type 2 diabetes: a systematic review of randomized controlled trials. Diabetes Care 2001; 24: 561-87.

7.Renders CM, Valk GD, Griffin S, Wagner EH, Eijk JThM van, Assendelft WJJ. Interventions to improve the management of diabetes mellitus in primary care, outpatient and community settings (Cochrane Methodology Review). In: The Cochrane Library, Issue 4, 2003. Chichester, UK: John Wiley & Sons, Ltd.

8.Muhlhauser I, Berger M. Patient education-evaluation of a complex intervention. Diabetologia 2002; 45: 1723-33.

9.Glasgow RE, Boles SM, McKay HG, Feil EG, Barrera M Jr. The D-Net diabetes self-management program: long-term implementation, outcomes, and generalization results. Prev Med 2003; 36: 410-9.

10.Pector EA. Internet health support groups: their uses, formats, benefits, risks, facilitation, and research approaches. Technol Health Care 2003; 11: 346-7.

11.Lorig KR, Ritter P, Stewart AL, Sobel DS, Brown BW Jr, Bandura A, Gonzalez VM, Laurent DD, Homan HR. Chronic disease self-management program: 2-year health status and health care utilization outcomes. Med Care 2001; 39: 1217-23.

12.Koev DJ, Tankova TI, Kozlovski PG. Effect of structured group education on glycemic control and hypoglycemia in insulin-treated patients. Diabetes Care 2003; 26:251.

13.Raji A, Gomes H, Beard JO, MacDonald P, Conlin PR. A randomized trial comparing intensive and passive education in patients with diabetes mellitus. Arch Intern Med 2002; 162: 1301-4.

14.Polonsky WH, Earles J, Smith S, Pease DJ, Macmillan M, Christensen R, Taylor T, Dickert J, Jackson RA. Integrating medical management with diabetes self-management training: a randomized control trial of the Diabetes Outpatient Intensive Treatment program. Diabetes Care 2003; 26: 3048-53.

15.Rickheim PL, Weaver TW, Flader JL, Kendall DM. Assessment of group versus individual diabetes education: a randomized study. Diabetes Care 2002; 25: 269-74.

16.Dalmau Llorca MR, Garcia Bernal G, Aguilar Martin C, Palau Galindo A. Group versus individual education for type-2 diabetes patients. Aten Primaria 2003; 32: 36-41.

17.Sarkadi A, Rosenqvist U. Field test of a group education program for Type 2 diabetes: measures and predictors of success on individual and group levels. Patient Educ Couns 2001; 44: 129-39.

18.Trento M, Passera P, Bajardi M, Tomalino M, Grassi G, Borgo E, Donnola C, Cavallo F, Bondonio P, Porta M. Lifestyle intervention by group care prevents deterioration of Type II diabetes: a 4-year randomized controlled clinical trial. Diabetologia 2002; 45: 1231-9.

19.Clancy DE, Cope DW, Magruder KM, Huang P, Salter KH, Fields AQ. Evaluating group visits in an uninsured or inadequately insured patient population with uncontrolled Type 2 diabetes. Diabetes Educ 2003; 29: 292-302.

20.Department of the Treasury. Treasury rates of exchange on 31 December 2003. http://www.fms.treas.gov/intn.html [accessed 24 Jan 2004]

21.Brown SA, Garcia AA, Kouzekanani K, Hanis CL. Culturally competent diabetes self-management education for Mexican Americans: The Starr County Border Health Initiative. Diabetes Care 2002; 25: 259-68.

22.Davison KP, Pennebaker JW, Dickerson SS. Who talks? The social psychology of illness support groups. Am Psychol 2000; 55: 205-17.

23.Maxwell AE, Hunt IF, Bush MA. Effects of a social support group, as an adjunct to diabetes training, on metabolic control and psychosocial outcomes. Diabetes Educ 1992; 18: 303-9.

24.Surwit RS, van Tilburg MA, Zucker N, McCaskill CC, Parekh P, Feinglos MN, Edwards CL, Williams P, Lane JD. Stress management improves long-term glycemic control in type 2 diabetes. Diabetes Care 2002; 25: 30-4.

25.Fox S, Fallows D. Internet health resources. 2003 Jul 16. http://www.pewintenet. org/ [accessed 09 Jan 2004]

26.Mendosa R. On-Line diabetes resources. 2003 Nov. http://www.mendosa.com/faq.htm [accessed 20 Jan 2004]

27.Gimenez-Perez G, Gallach M, Acera E, Prieto A, Carro O, Ortega E, Gonzalez-Clemente JM, Mauricio D. Evaluation of accessibility and use of new communication technologies in patients with Type 1 diabetes mellitus. JMIR 2002; 4: e16.

28.Smith L, Weinert C. Telecommunication support for rural women with diabetes. Diabetes Educ 2000; 26: 645-55.

29.White M, Dorman SM. Receiving social support online: implications for health education. Health Educ Res 2001; 16: 693-707.

30.Loader BD, Muncer S, Burrows R, Pleace N, Nettleton S. Medicine on the line? Computer-mediated social support and advice for people with diabetes. Int J Soc Welfare 2002; 11: 53-65.

31.Mitchell KJ, Finkelhor D, Wolak J. Risk factors for and impact of online sexual solicitation of youth. JAMA 2001; 285: 3011-4.

32.Iafusco D, Ingenito N, Prisco F. The chatline as a communication and educational tool in adolescents with insulin-dependent diabetes: preliminary observations. Diabet Care 2000; 23: 1853.

33.Barrera M Jr., Glasgow RE, McKay HG, Boles SM, Feil EG. Do Internet-based support interventions change perceptions of social support?: An experimental trial of approaches for supporting diabetes self-management. Am J Community Psychol 2002; 30: 637-54.

34.Tate, DF, Wing RR, Winett RA. Using Internet Technology to Deliver a Behavioral Weight Loss Program. JAMA 2001; 285 :1172-7.

35.Harvey-Berino J, Pintauro SJ, Gold EC. The feasibility of using Internet support for the maintenance of weight loss. Behav Modif 2002; 26: 103-16.

36.Muncer S, Loader B, Burrows R, Pleace N, Nettleton S. Form and structure of newsgroups giving social support: a network approach. Cyberpsychol Behav 2000; 3: 1017-29.

37.Zrebiec JF, Jacobson AM. What attracts patients with diabetes to an internet support group? A 21-month longitudinal website study. Diabet Med 2001; 18: 154-8.

BOOK REVIEWS

Obesity and Diabetes

American Journal of Diabetes has received several books addressing the issue of obesity in children and adults leading to diabetes.

Diabesity: The Obesity-Diabetes Epidemic That Threatens America — And What We Must Do to Stop It. Francine R.Kaufman. Bantam, 2005, 336 pp, ISBN 0553803840, $27.

The first is a chatty description of a diabetes physician's approach to life as she treats patients with obesity and diabetes.

This book is aimed at general audiences but takes many pages getting information across. Consequently, it satisfied neither a professional or general audience. Those who enjoy reading about the life and work of a diabetes physician may find it interesting.

This book is being heavily marketed. If it stops a single child from developing obesity and diabetes it will be worth the price. *American Journal of Diabetes* applauds that aim but does not see how this book could achieve it.

Help For Your Child With Type 1 Diabetes

A Child in Your Care Has Diabetes: A Collection of Information. Elisa Hendel. Hen House Press, Inc. 2003, 2002, 66 pp, ISBN 0971861218, $24.95.

This book is spiral-bound and glossy, and looks like a manual, which is the idea.

The author, Elisa Hendel is the mother of a young girl who was diagnosed with diabetes at the age of 6 during a family vacation in Puerto Rico. On their return to New Jersey Ms Hendel's reaction to her daughter's illness was to learn everything she could to care for her daughter and make sure everyone with responsibility for her daughter was in a position to care for her.

Ms Hendel desire to teach her daughter's caregivers and teachers started with giving them all detailed notes in which were explained the symptoms of hypoglycemia and hyperglycemia, emergency responses, foods. This book is a polished compilation of these notes, with a forward by Jo Nuzzo, CDE, MSN.

The copy reviewed by *American Journal of Diabetes* was the second edition, which was upgraded from the first edition by additional charts, lists and letters from patients who use the pump.

The 2004-2005 US School Nurse of the Year selected by the 11,400-member National Association of School Nurses is Mrs Loretta Macconi, RN, MSN, CRNP of Elizabeth Haddon School, Haddonfield, New Jersey. Mrs Macconi has been involved in a diabetes initiative in her school district. She told *American Journal of Diabetes* that she has had several students with T1DM who need isulin during the school day and she has been called in hypoglycemic emergencies. She said the book looked like a resource that would be useful for her and other school nurses.

The New Low-Carb Way of Life. Rob Thompson, Diane Stafford. M Evans and Company, Inc., 2005, 288 pp, ISBN 1590770315, $21.95.

This chatty book is written in big type. *American Journal of Diabetes* were scared by "low-carb" in the title and the covering letter's second sentence: "Dr Atkins has proven to the world that low carb diets work to lose weight..." The next statement starts "but..". This "but" is, in our opinion, in the right direction but does not alleviate our dread of having theories presented as facts.

Rob Thompson is an internist and cardiologist and Diane Stafford is a writer. They have collaborated on a readable book which explains why eliminating dietary carbohydrates is bad and why reducing fat intake is good. A weakness is the lack of references, consequently *American Journal of Diabetes* could not distinguish information backed by scientific evidence from author opinion.

American Journal of Diabetes sees an audience for this book in patients who want step-by-step instructions and explanations on how to lose and maintain weight.

American Journal of Diabetes will review more books related to lifestyle and diabetes in an expanded section next month.

ORIGINAL ARTICLE

Diabetes Complications: Overview and Review of Diabetic Retinopathy and Diabetic Nephropathy

Mark H Schutta, MD and Prakash Seshadri, MD

Rodebaugh Diabetes Center, University of Pennsylvania School of Medicine, 3400 Spruce St, Philadelphia, PA 19104. Website: www.uphs.upenn.edu/endocrin

Abstract

Complications of diabetes account for a significant percentage of hospitalizations in the United States; diabetic neuropathy is the primary complication and the most likely cause of morbidity and mortality related to diabetes. Large studies show that glycemic control is essential to prevent diabetic neuropathies. *Schutta MH, Seshadri P. Diabetic Complications: Overview and Review of Diabetic Retinopathy and Diabetic Nephropathy. Amer J Diabetes. 2005; 2(1):17-26.*

Introduction

Before insulin was isolated, physicians reported strong associations between glycemic control and complications of diabetes, and pathologic findings unique to patients with diabetes.(1,2) Decades later, the Kumamoto Trial, the Diabetes Control and Complications Trial (DCCT), and the United Kingdom Prospective Diabetes Study (UKPDS) firmly associated improved glycemic control with reduction in microvascular complications.(3,4,5) Both DCCT and UKPDS associated better glycemic control with a trend towards lower incidence of cardiovascular events.(4,5)

General Prevention

The DCCT evaluated 1,401 patients with T1DM who were initially evaluated for microvascular complications. They were randomized into 2 cohorts, either given conventional therapy (primary prevention group) or intensive insulin therapy (secondary intervention group).(5) Primary prevention patients had diabetes < 5 years and had neither retinopathy nor nephropathy. Secondary intervention patients had diabetes < 15 years, at least 1 microaneurysm, little or moderate nonproliferative retinopathy, and excreted albumin up to 200 mg/24 h. Primary prevention patients received 1-2 insulin injections daily, and intensive patients received 3-4 injections daily. Goals for secondary intervention patients included maintenaining fasting and preprandial glucose < 120 mg/dL, postprandial glucose < 180 mg/dL,

and HbA1c < 7.0 %. Subjects were observed over a mean of 6.5 years with follow-up of 3-9 years. In primary prevention patients, onsets were reduced: diabetic retinopathy by 76 %, nephropathy by 35 %, and clinical neuropathy by 70 %. In secondary intervention patients, progression of retinopathy was reduced by 54 %, nephropathy by 56 %, and neuropathy by 58 %. The 41 % reduction in risk for cardiovascular events was not statistically significant. Glycemic control impacted other cardiovascular risk factors, including a 34 % reduction in LDL-C.

The risk reductions demonstrated in the DCCT extend beyond the 6.5 years of the study as demonstrated by the Epidemiology of Diabetes Interventions and Complications (EDIC) study. The benefits of intensive control persisted at least 7 years.(6)

Reduced microvascular complications were observed when patients with T2DM had improved glycemic control in the Kumamoto trial and the UKPDS.(3,4) Intensive insulin therapy over 6 years reduced HbA1c from 9.3 % to 7.1 % in a population of thin Japanese adults with diabetes, and microvascular complications were consequently reduced.(3) The UKPDS followed over 4,000 obese and nonobese patients with newly diagnosed T2DM and found that intensive step therapy with sulfonylurea, metformin or insulin significantly reduced microvascular endpoints by 25 %.(4) Since that study was published, research has consistently found that intensive therapy is beneficial and that fasting euglycemia may be insufficient to reduce microvascular and macrovascular complications.(7) Postprandial hyperglycemia increases the risks of microvascular and macrovascular complications. Reductions in postprandial hyperglycemia were associated with reductions in retinopathy and nephropathy in the Kumamoto study. Additionally, results from several robust prospective epidemiological studies strongly associate postchallenge and postprandial hyperglycemia and cardiovascular risk.(8,9,10) These include the Honolulu Heart Program and the Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE). The investigators from the Honolulu Heart Program observed that men who did not have diabetes had a progressive increase in cardiovascular mortality directly related to their 1-hour post-challenge glucose excursions.(11)

The largest study to examine postchallenge glucose and mortality is Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE).(2) Subjects with impaired glucose tolerance had a higher mortality than those with impaired fasting glucose. The study concluded that fasting blood glucose cannot predict mortality related to hyperglycemia and, therefore, does not meet the criteria for an evidence-based screening test for the most serious consequence of hyperglycemia. Postprandial hyperglycemia is a more important determinant of glycemic control and correlates better to HbA1c.(12)

In January 2002, the American College of Endocrinology Consensus Statement on Guidelines for Diabetes Control gave stringent glycemic targets: HbA1c should be < 6.5 % and 2-hour postprandial glucose levels should be < 140 mg/dL.(13) With 24-hour peakless insulin glargine; rapid-acting forms, such as insulin lispro and insulin aspart; and the meglitinides, short-acting insulin secretagogues, patients may be able to reach these targets by starting insulin therapy earlier and using a basal/bolus approach to glycemic control. The glycemic targets of the American Diabetes Association are: HbA1c, 7 % and postprandial glucose, <180 mg/dL; however the guidelines recommend lower target values can be considered in individual patients.(14,15)

Retinopathy

Diabetic retinopathy is the leading cause of visual loss and blindness in US patients between the ages of 20 and 74. While patients with T1DM have a higher risk for developing severe retinal complications and visual loss than patients with T2DM, they represent 10 % of patients with diabetes. Therefore, the great majority of diabetic retinopathy is seen in patients with T2DM. The National Eye Institute estimates that 90 % of blindness from diabetes is preventable in 90 % of all cases.(16)

The first signs of diabetic retinopathy are microaneurysms and dot intraretinal hemorrhages referred to as mild, proliferative background retinopathy. These complications are seen in patients living 20 years with diabetes, in most with T1DM and approximately 80 % with T2DM.(17,18)

The DCCT demonstrated the importance of glycemic control in retinopathy prevention, but the differences between the control group and intensive group did not appear until 2.5 years after intensive therapy was initiated.(5) In addition, about 10 % of patients with preexisting retinopathy suffered decline in their retinopathy after initiation of the intensive regimen.(19)

Progression of diabetic retinopathy advances from a mild, nonproliferative stage to a pre-proliferative stage manifested as larger hemorrhages, soft and hard exudates, venous beading and dilatation, and intraretinal microvascular changes and macular edema. These abnormalities do not affect vision. However, if untreated, the more severe form of proliferative retinopathy, characterized by fibrous accumulation, neovascularization, and preretinal and vitreous hemorrhage, can lead to blindness.(23) When allowed to progress, the new vessels grow over the retinal surface and the posterior surface of the vitreous. These vessels are fragile and rupture easily inducing preretinal and vitreous hemorrhage. Retinal detachment, visual loss and neovascular glaucoma are the most severe consequences. In patients diagnosed 10 years, proliferative retinopathy occurs in nearly 50 % of patients with T1DM and 10 % of patients with T2DM respectively. In patients with T2DM, the incidence of proliferative retinopathy is higher in insulin-requiring patients.(18,19)

Prevention. Several risk factors for progression of diabetic retinopathy have been identified. The DCCT and UKPDS demonstrated the importance of intensive glycemic control in slowing the development and progression of this condition, with each percentage point reduction in HbA1c associated with a 35 % decrease in risk.(4,5) Tight control of blood pressure was also examined in the UKPDS and resulted in a 25 % reduction in microvascular diseases.(4) The UKPDS randomly assigned hypertensive patients to either a beta-blocker or an angiotensin-converting enzyme (ACE) inhibitor and found no statistically significant difference in benefit between the 2 groups.(4,20)

Elevated serum lipids are also associated with disease progression and specifically with hard exudates in the retina. Both the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) and the Early Treatment Diabetic Retinopathy Study (ETDRS) demonstrated this relationship.(17,24) The ETDRS, an observational study, found that the severity of hard exudates was the strongest risk factor for the development of subretinal fibrosis in patients with diabetic macular edema. Increased triglycerides were also associated with an increased risk of proliferative diabetic retinopathy.(20a)

In addition to hyperglycemia, other factors implicated in development or progression of diabetic

retinopathy include hypertension and hypercholesterolemia. Excessive polyol production during periods of hyperglycemia appears to deposit on the lens and optic nerve.(16) Nonenzymatic glycation end products causing protein cross links have been shown to impede retinal blood flow.

A recent study of elderly patients with diabetes found that only 50-60 % had annual dilated eye exams.(21) Many patients develop blindness because of the lack of appropriate treatment.(8) This vision loss was avoidable in many of these patients. Proper therapy, including photocoagulation and vitrectomy, reduces the 5-year risk of blindness for patients with proliferative retinopathy by 90 %, with a 50 % reduction in the risk of visual loss associated with macular edema.(9) The failure to evaluate high risk patients is possibly of more consequence in the elderly.

The incidence and progression of diabetic retinopathy risk factors were evaluated in the WESDR.(18) A population-based examination of patients with either T1DM or T2DM over 4-year intervals spanned 1980 through 1994. Patients were divided into 2 cohorts: diabetes onset before 30 years of age and diabetes onset after 30 years of age. The older cohort was further divided into 2 groups; whether or not they were treated with insulin.(18) Retinopathy was seen in 13 % of patients diagnosed with diabetes < 5 years and in 90 % of patients diagnosed with diabetes 10-15 years. Approximately 25 % of patients with T1DM diagnosed up to 15 years had proliferative diabetic retinopathy. In the group of patients whose diabetes was diagnosed < 5 years after age 30, 40 % of patients taking insulin had retinopathy and 24 % of patients not treated with insulin had retinopathy. The incidence increased to 84 % and 53 %, respectively, in patients who have had diabetes for 15-19 years.(18) On follow-up at 4 and 10 years after the study began, HbA1c was significantly related to incidence of retinopathy, progression of retinopathy, and progression to proliferative retinopathy in all study groups.(12)

Detection. Because retinopathy is often asymptomatic, guidelines for screening and follow-up have been developed by the ADA, American Academy of Ophthalmology, and the American College of Physicians, (Table 1). Current guidelines recommend that a patient with diabetes undergo initial examination by an ophthalmologist as early as possible after T2DM has been diagnosed and within 3 to 5 years after T1DM has been diagnosed, except for children under 10. Subsequent ophthalmologic examinations should be scheduled annually, although patients with progressing retinopathy should be examined more frequently.(22)

A controlled prospective study and several case series suggest that pregnancy in patients with T1DM may aggravate retinopathy. When planning pregnancy, women with diabetes should have a comprehensive eye examination during the first trimester of pregnancy and subsequently throughout the pregnancy.

Treatment. The NIH-sponsored large randomized, controlled trials: the Diabetic Retinopathy Study (DRS), the ETDRS, and the Diabetic Retinopathy Vitrectomy Study (DRVS) provide the strongest evidence for preserving vision with laser photocoagulation and early vitrectomy.(23,27) The DRS enrolled 1,742 patients with severe nonproliferative or proliferative diabetic retinopathy and randomly assigned 1 eye to either xenon arc or argon laser while the other eye was untreated.(23) A reduction in visual loss of 50 % or more resulted in the eyes treated with panretinal photocoagulation. The DRS defined

high-risk criteria for panretinal laser photocoagulation including neovascularization accompanied by vitreous hemorrhage or obvious neovascularization on or near the optic disc unaccompanied by vitreous hemorrhage.

The ETDRS assessed the value of treatment in earlier stages of retinopathy, the benefit of aspirin, and the treatment of macular edema. Patients studied (n=3,711) had mild to severe nonproliferative retinopathy or early proliferative diabetic retinopathy with or without macular edema.(24) In each patient, eyes were randomly assigned to either immediate panretinal photocoagulation or examination every 4 months with treatment only if high-risk proliferative retinopathy was detected. The 5-year rates of severe visual loss were low in both groups. Because early treatment caused reduced visual acuity and visual fields, the authors concluded that panretinal photocoagulation should not be used for mild or moderate nonproliferative disease. The risk-benefit ratio improved as the severity of retinopathy advanced. In cases of macular edema, focal photocoagulation to the areas of edema was also initiated, resulting in a reduction in visual loss of 50 % or more.(24) Edema that threatens areas close to the fovea benefit most, and treatment should be deferred for edema located away from the center of the macula.(24) Aspirin did not affect the progression of retinopathy and did not increase the risk of vitreous hemorrhage in patients with proliferative retinopathy, so is therefore not contraindicated.(16,17) Follow-up demonstrated minimal benefit in early treatment of proliferative disease.

Techniques for performing vitrectomy have improved dramatically and, when done in conjunction with photocoagulation, can reduce the incidence of blindness in patients with diabetes. The DRVS wrote guidelines for vitrectomy indications and timing.(25-28) Patients with advanced, active proliferative diabetic retinopathy and visual acuity of 10/200 or better were randomly assigned to receive either early vitrectomy or conventional therapy. Of the early vitrectomy group, 44 % attained visual acuity of 10/20 or better versus 28 % in the conventional group at 4 years. In cases of vitreous hemorrhage, attaining visual acuity of better than 20/40 was increased in patients who had early intervention compared to those who were deferred for 1 year. This advantage was only noted in patients with T1DM, not T2DM. As reflected in the improved retinopathy outcomes in the DCCT, Kumamoto, and UKPDS studies, intense glycemic control is important to delay or prevent retinopathy. The UKPDS also demonstrated a reduced risk for retinal photocoagulation in patients with hypertension who were treated with beta-blockers or ACE inhibitors.(4) In the WESDR and the ETDRS, patients who had elevated serum cholesterol had a higher incidence of retinal hard exudate deposition.(17,24) In the ETDRS, elevated triglycerides were associated with increased risk of proliferative retinopathy.(24) The findings from these observational studies suggest that lowering lipids in patients with diabetes maintains retinal health.

Other ocular problems occur more frequently with diabetes include cataracts, glaucoma and ischemic optic neuropathy. Early screening is crucial to detecting and treating all of these causes of visual loss. All newly diagnosed patients should have a dilated indirect ophthalmoscopy with biomicroscopy or seven standard field stereoscopic 30 0 fundus photography. Frequency of further dilated exams depends on disease severity. The necessity for annual dilated exams in patients without retinopathy is not

clearly defined as evidence suggests that progression to either proliferative diabetes or macular edema is slow and therefore annual exams may not be cost effective.(29,30) Meeting accepted guidelines for blood pressure, glycemic control and blood lipids is also critical to prevention of diabetic retinopathy.

Nephropathy

Diabetic nephropathy accounts for approximately 40 % of all new cases of end-stage renal disease (ESRD).(31) Nearly 20 % of patients with T1DM and 30 % of those with T2DM develop evidence of nephropathy, but a smaller percentage of patients with T2DM progress to ESRD.(17) However, 60 % of patients with ESRD have T2DM. The incidence of diabetic nephropathy in patients who have had diabetes > 25 years is decreasing, perhaps because of improved glycemic control. In addition, recent evidence demonstrates that onset can be prevented and progression can be attenuated.

The clinical definition of nephropathy is the persistent presence of total urinary protein excretion of more than 300 mg/24 hour. Diabetic nephropathy is a slow, progressive disease. The risk of ESRD in the US depends on ethnicity, with African American, Native American, and Hispanic patients with diabetes at greater risk than other ethnic groups.(32)

The first sign of renal involvement is the appearance of low but abnormal concentrations of albumin in the urine (30 or more mg/day or 20-200µg/min).(33) Detection of microalbuminuria marks the earliest stage of nephropathy. Progression to overt nephropathy or clinical macroalbuminuria (300 mg/24 h or more than 200µg/min) occurs in 20-40 % of patients over a period of 15-20 years after onset of diabetes.(34) After macroalbuminuria develops, creatine clearance declines at a variable rate. In untreated patients, the average reduction is 10-12 mL/min/yr.(22) After onset of overt nephropathy, only 20 % of patients will have progressed to ESRD. Hypertension and proteinuria may accelerate progression to ESRD. The detection of microalbuminuria is a marker for cardiovascular disease, so the finding of microalbuminuria should prompt further screening for possible vascular disease and aggressive treatment of other cardiovascular risk factors.

Early renal abnormalities may be observed soon after diabetes is first diagnosed. Hyperglycemia induces intraglomerular hypertension and renal hyperperfusion.(23,24) Increased glomerular hyperfiltration rate (GFR) is partially a result of poor metabolic control. Intensive glycemic control reduces GFR to normal.(25) At levels greater than 135 mL/min/1.73 m^3, GFR has been observed in 20-40 % of patients newly diagnosed with insulin-dependent diabetes. Hyperglycemia results in increased blood volume and increased glomerular plasma flow rate leading to hyperperfusion, increased filtration, and resultant elevation in glomerular transcapillary hydraulic pressure. If this situation is sustained, cellular injury ensues increasing mesangial matrix, proteinuria, and glomerulosclerosis. Other potential mediators of hyperfiltration include ketone bodies and the counter-regulatory hormones (glucagon, growth hormone and insulin-like growth factor). Nonenzymatic glycosylation and lipoprotein abnormalities also appear to contribute and preliminary data support a genetic basis for susceptibility.(35,36)

Prevention. Diabetic nephropathy prevention focuses on aggressive glycemic control and hypertension treatment with emphasis on early use of ACE inhibitors and angotensin receptor

blockers.

Intensive insulin therapy diminishes metabolic and pathologic changes associated with diabetic nephropathy. In patients with T1DM treated with continuous subcutaneous insulin, albuminuria was stabilized, skeletal muscle capillary membrane thickness was reduced, and as mentioned earlier, GFR was also reduced.(26,27) Systolic and diastolic hypertension accelerates the progression of diabetic nephropathy, but intensive antihypertensive therapy decreases the rate of fall in GFR. The present American Diabetes Association position statement for patients with diabetes who are not pregnant and are older than18 years of age is to maintain systolic pressure of less than 130 mm Hg and diastolic pressure of less than 80 mm Hg. In cases of isolated systolic hypertension of 180 mm Hg or higher, treatment is gradual and blood pressure can be lowered further provided initial goals are met and well tolerated.(14)

Detection. The presence of microalbuminuria predicts renal insufficiency in 80 % of patients with T1DM and in 20-40 % of patients with T2DM. Thus, early recognition and intervention are crucial in delaying progression of renal disease.(37) Because microalbuminuria rarely occurs in short-duration T1DM, screening should begin 5 years after diagnosis but not before onset of puberty. Because of the difficulty in predicting onset of T2DM, a routine dipstick urinalysis should be performed on all newly diagnosed T2DM patients. If this test is positive for protein, a 24-hour urine collection should be obtained with evaluation of creatinine clearance to quantitate urinary protein excretion. Negative findings on dipstick urinalysis require a more sensitive method to detect microalbuminuria, which should be repeated annually if negative. Currently, the 3 methods available to screen for microalbuminuria are measurement of albumin-to-creatinine ratio in a random spot urine collection; 24-hour collection with evaluation of creatinine clearance; and timed collection (eg, overnight or 3-4 h). Positive results should be confirmed with a 2nd measurement because of the high rate of transient elevations in urine microalbumin levels caused by hyperglycemia, exercise, urinary tract infections, hypertension, acute febrile illness, and congestive heart failure. The role of annual screening after microalbuminuria is detected and addressed is less clear, but many experts recommend continuous surveillance to evaluate response to therapy and progression of disease. Retinopathy is strongly associated with nephropathy; if it is present, albuminuria can be attributed with confidence to nephropathy. If the patient has no evidence of retinopathy, other causes of albuminuria should be sought.(38)

Treatment. Four modalities impact progression to nephropathy after albuminuria is detected. In addition to glycemic control and treatment of hypertension, reduction of glomerular capillary pressure using ACE inhibitors and angiotensin II-receptor blockers (ARBs) take stress off the kidney by dilating the efferent arteriole. The 4th intervention involves dietary protein restriction, which decreases renal perfusion rate.

Control of Hypertension. In patients with T2DM, 30 % have hypertension at the time of diagnosis. Of those with nephropathy, 70 % have hypertension.(39) Antihypertensive therapy slows development and progression of nephropathy in patients who initially have a normal albumin level as well as those patients who have overt nephropathy.(40,41) Drugs affecting the renin-angiotensin system seem to be effective in treat-

ing hypertension in patients with diabetes. Multiple studies have shown that ACE inhibitors reduce albuminuria and reduce the rate of nephropathy progression more than any other class of antihypertensive drug that reduces blood pressure by the same degree. Side effects of ACE inhibitors include nonproductive cough, which occurs in approximately 10 % of subjects, and hyperkalemia, which develops in patients with bilateral renal artery stenosis or hyporeninemic hypoaldosteronism. The Heart Outcomes Prevention Evaluation (HOPE) study demonstrated that initiating an ACE inhibitor without blood pressure reduction resulted in a 24 % relative reduction in rate of progression from normal or microalbuminuria to overt nephropathy than placebo.(42)

Reduction of Glomerular Capillary Pressure. Angiotensin receptor blockers are also renal protective, and several large studies support their efficacy. In a study of patients with T2DM and microalbuminuria administered irbesartan, urinary albumin excretion was reduced 38 % and progression to macroalbuminuria was reduced 70 % compared with patients administered placebo .(43) The Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) study showed that adding losartan to conventional therapy (no ACE inhibitors) decreased the rate of urinary protein excretion by 35 % and reduced the risk of ESRD by 28 %.(44)

Calcium channel blockers vary in their effects on diabetic nephropathy. Drugs such as verapamil and diltiazem and other nondihydropyridines may decrease proteinuria in T2DM.(45) However, the dihydropyridines may accelerate diabetic renal deterioration. This effect may be ameliorated by the addition of ARBs as demonstrated in the RENAAL study where the effect of losartan persisted when administered with dihydropyridines. Beta-blockers were as effective as ACE inhibitors in reducing the incidence of microalbuminuria and macroalbuminuria in both the UKPDS and the DCCT. To achieve targets for blood pressure, combination therapy is recommended. In a recent study, combining an ACE inhibitor and an ARB was more effective than either drug used alone.(46)

Dietary Restriction. In a study of dietary protein restriction in patients with T1DM and overt nephropathy, limiting intake of protein (0.6 g/kg/day) and phosphorus (500-1000 mg/day) decreased hypertension and reduced the decline in GFR in some subjects.(47) In another study of patients with T1DM on a diet that included the recommended daily allowance of protein, the rate of progression to ESRD was reduced.(48)

REFERENCES

1.Krowlewski AS, Warram JH, Christlieb, AR Onset, course, complications, and prognosis of diabetes mellitus. In: Marble A, Krall LP, Bradley RF , et al., eds. Joslin's diabetes mellitus. 12th ed. Philadelphia; Lea & Febiger, 1985, pp251-77.

2.Kimmelstiel P, Wilson C. Intercapillary lesions in the glomeruli of the kidney. Am J Pathol. 1936; 12: 83-97.

3.Ohkubo Y, Kishikawa H, Araki E, Miyata T, Isami S, Motoyoshi S, Kojima Y, Furuyoshi N, Shichiri M. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. Diabetes Res Clin Pract. 1995; 28: 1037.

4.United Kingdom Prospective Diabetes Study Group. Effect of intensive blood glucose control with metformin on complications in overweight patients with type 2 diabetes. Lancet. 1998; 352: 854-865.

5.The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993; 329: 977-986.

6.UK Prospective Diabetes Study Group. Intensive blood glucose control with sulfonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. Lancet. 1998; 352: 837-53.

7.Resnick HE, Harris MI, Brock DB, Harris TB. American Diabetes Association diabetes diagnostic criteria, advancing age, and cardiovascular disease risk profiles: results from the Third National Health and Nutrition Examination Survey.Diabetes Care. 2000; 23: 176-80.

Moss SE, Klein R, Klein BE. Factors associated with having eye examinations in persons with diabetes. Arch Fam Med. 1995; 4: 529-34.

9.Will JC, German RR, Schuman E, Michael S, Kurth DM, Deeb L. Patient adherence to guidelines for diabetes eye care: results from the diabetic eye disease follow-up study. Am J Public Health. 1994; 84: 1669-71.

10.Hanefeld M, Fischer S, Julius U, et al. Risk factors for myocardial infarction and death in newly detected NIDDM; the Diabetes Intervention Study, 11 year follow-up. Diabetologia. 1996; 39: 1577-83.

11.Honolulu Heart Program.Donahue Postchallenge glucose concentration and coronary heart disease in men of Japanese ancestry. Diabetes 1987; 36: 689-92.

12. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. Glycosylated hemoglobin predicts the incidence and progression of diabetic retinopathy. JAMA. 1988 18; 260: 2864-2871.

13.ACE Consensus Statement on Guidelines for Glycemic Control. Endocrine Practice 2002; 8 (Suppl 1): 6-11.

14.ADA Consensus Guidelines. Diabetes Care, 2004; 27 (Supp 1).

15.ACE Consensus Statement on Guidelines for Glycemic Control. Endocrine Practice 2002; 8 (Suppl 1): 6-11.

16. Early Treatment Diabetic Retinopathy Study Research Group.Effects of aspirin treatment on diabetic retinopathy. ETDRS report number 8.Ophthalmology. 1991; 98(Suppl 5): 757-765.

17.Chew EY, Klein ML, Murphy RP, Remaley NA, Ferris FL 3rd. Effects of aspirin on vitreous/preretinal hemorrhage in patients with diabetes mellitus. Early Treatment Diabetic Retinopathy Study report no. 20. Arch Ophthalmol. 1995 ; 113: 52-5.

18.Klein R, Klein BEK, Moss SE, Davis MD, DeMets DL. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. Arch Ophthalmol 1984; 102: 527-32.

19.Early worsening of diabetic retinopathy in the Diabetes Control and Complications Trial. Arch Ophthalmol. 1998; 116: 874-86. Erratum in: Arch Ophthalmol 1998; 116: 1469.

20.UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ. 1998; 317: 703-13.

20a.Chew EY, Klein ML, Ferris FL 3rd, Remaley NA, Murphy RP, Chantry K, Hoogwerf BJ, Miller D. Association of elevated serum lipid levels with retinal hard exudate in diabetic retinopathy. Early Treatment Diabetic Retinopathy Study (ETDRS) Report 22.Arch Ophthalmol. 1996; 114: 1079-84.

21.Lee PP, Feldman ZW, Ostermann J Brown DS, Sloan FA. Ophthalmology 2003; 110: 1952-9.

22.ADA: Clinical practice recommendations 2002. Diabetes Care 2002; 25 (suppl 1): S1-S147.

23.Ritz E, Orth SR. Nephropathy in patients with type 2 diabetes mellitus. N Engl J Med. 1999; 341: 1127-33.

24.Christiansen JS, Gammelgaard J, Frandsen M, Parving HH. Increased kidney size, glomerular filtration rate and renal plasma flow in short-term insulin-dependent diabetics. Diabetologia. 1981; 20: 451-6.

25.Dahl-Jorgensen K, Hanssen KF, Kierulf P, Bjoro T, Sandvik L, Aagenaes O. Reduction of urinary albumin excretion after 4 years of continuous subcutaneous insulin infusion in insulin-dependent diabetes mellitus. The Oslo Study. Acta Endocrinol (Copenh). 1988; 117: 19-25.

26.Diabetic Retinopathy Vitrectomy Study Research Group. Early vitrectomy for severe vitreious hemorrhage in diabetic retinopathy: two-year results of a randomized trial. DRVS (2). Arch Opthal 1985; 103: 1644.

27.Diabetic Retinopathy Vitrectomy Study Research Group. Early vitrectomy for severe hemorrhage in eyes with useful vision: results of a randomized trial. DRVS report no 3. Ophthal 1988; 95: 1307.

28.The Diabetic Retinopathy Vitrectomy Study Research Group. Early vitrectomy for severe proliferative diabetic retinopathy in eyes with useful vision. Clinical application of results of a randomized trial—Diabetic Retinopathy Vitrectomy Study Report 4. Ophthal. 1988; 95: 1321-1334.

29.Batchelder T, Barricks M. The Wisconsin

Epidemiologic Study of Diabetic Retinopathy. Arch Ophthalmol. 1995; 113: 702-3.

30.Vijan S, Hofer TP, Hayward RA. Cost-utility analysis of screening intervals for diabetic retinopathy in patients with type 2 diabetes mellitus. JAMA. 2000, 283: 889-96.

31.Excerpts from US Renal Data System 1991 annual data report. Am J Kidney Dis. 1991; 18(5 Suppl 2): 1-127.

32.Tull ES, Roseman JM. Diabetes in African Americans. In: National Diabetes Data Group. Diabetes in America. 2nd ed. National Institute of Diabetes and Digestive and Kidney Diseases 1995; pp613-30.

33.Ruggenenti P, Remuzzi G. The diagnosis of renal involvement in non-insulin-dependent diabetes mellitus. Curr Opin Nephrol Hypertens. 1997; 6: 141-5.

34.UKPDS IX: Relationships of urinary albumin and N-acetylglucosaminidase to glycaemia and hypertension at diagnosis of type 2 (non-insulin-dependent) diabetes mellitus and after 3 months diet therapy. Diabetologia. 1993; 36: 835-42.

35.Vlassara H, Place MR. Diabetes and advanced glycation endproducts. J Intern Med. 2002; 251: 87-101

36.Rippin JD, Patel A, Bain SC. Genetics of diabetic nephropathy. Best Pract Res Clin Endocrinolo Metab. 2001; 15: 345-58.

37.Viberti GC, Jarrett RJ, Keen H. Microalbuminuria as prediction of nephropathy in diabetics.Lancet 1982; 2: 611.

38.Remuzzi G, Schieppati A, Ruggenenti P. Clinical practice. Nephropathy in patients with type 2 diabetes. N Engl J Med. 2002; 346: 1145-51.

39.Mogensen CE. Microalbuminuria, blood pressure, and diabetic disease: Origin and development of ideas. In: Mogensen CE, ed. The Kidney and Hypertension in Diabetes Mellitus, 5th ed. Boston, MA: Kleuwer; 2002: pp655-706.

40.Ordonez JD, Hiatt RA. Comparison of type II and type I diabetics treated for end-stage renal disease in a large prepaid health plan population. Nephron 1989; 51: 524-9.

41.National Kidney Foundation Hypertension and Diabetes Executive Committees Working Group. Preserving renal function in adults with hypertension and diabetes: a consensus approach. Am J Kidney Dis. 2000; 36: 646-661.

42.Heart Outcomes Prevention Evaluation Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Lancet. 2000; 355: 253-9. Erratum: Lancet 2000; 356: 860.

43.Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria Study Group. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. N Engl J Med. 2001; 345: 870-8.

44.RENAAL Study Investigators. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med. 2001; 345:861-9.

45.Smith AC, Toto R, Bakris GL. Differential effects of calcium channel blockers on size selectivity of proteinuria in diabetic glomerulopathy. Kidney Int. 1998; 54: 889-896.

46.Mogensen CE, Neldam S, Tikkanen I, Oren S, Viskoper R, Watts RW, Cooper ME. Randomised controlled trial of dual blockade of renin-angiotensin system in patients with hypertension, microalbuminuria, and non-insulin dependent diabetes: the candesartan and lisinopril microalbuminuria (CALM) study. BMJ. 2000; 321: 1440-4.

47.Zeller K, Whittaker E, Sullivan L, Raskin P, Jacobson HR. Effect of restricting dietary protein on the progression of renal failure in patients with insulin-dependent diabetes mellitus. N Engl J Med. 1991; 324: 78-84.

48.Hansen HP, Tauber-Lassen E, Jensen BR, Parving HH. Effect of dietary protein restriction on prognosis in patients with diabetic nephropathy. Kidney Int. 2002; 62: 220-8.

MEETINGS CALENDAR

January 9-12, 2005. California Childhood Obesity Conference, San Diego, California. Website: nature.berkeley.edu/

February 4-6, 2005. American Diabetes Association 52nd Annual Advanced Postgraduate Course, New York, New York. Website: diabetes.org/

February 10-11, 2005. University of Washington Cardiovascular Care Conference. Shireline Conference Center, Seattle, Washington. Website: www.son.washington.edu/cne/

February 10-14, 2005. Children with Diabetes Cruise. Royal Caribbean International Cruise Line Cruise into Spring. Website: www.childrenwithdiabetes.com

February 11-13, 2005. 4th World Congress on Prevention of Diabetes and its Complications, Royupuram, Chennai, India. Website: www.mvdiabetes.com/wcpd.htm/

February 13-15, 2005. The First Gulf Group for the Study of Diabetes International Diabetes Conference. Dubai International Convention Center, Dubai, United Arab Emirates. Website: www.arabhealthonline.com/

February 14-18, 2005. Fourteenth Annual Cardiovascular Conference at Park Hyatt Beaver Creek, Colorado. Website: www.beaumonthospitals.com/

March 3-6, 2005. The University of the West Indies Outreach Project 11th International Diabetes Conference on Diabetes and Ageing. Starfish Resort, Jamaica. Website: uwimona.edu.jm

March 6-9, 2005. The American College of Cardiology's 54th Annual Scientific Session, Orlando. Website: www.acc.org/

March 20-24, 2005. 21st Annual Cardiovascular Conference, Fairmont Chateau Lake Louise Hotel, Lake Louise, Alberta, Canada. Website: www.acclakelouise.com/

April 4-7, 2005. 24th Joint Meeting of the British Endocrine Societies, Harrogate, United Kingdom. Website: www.endocrinology.org/

April 20-22, 2005. Diabetes UK Annual Professional Conference. Scottish Exhibition and Conference Centre, Glasgow. Website: www.diabetes.org.uk/apc/

June 10-14, 2005. American Diabetes Association 65th Scientific Sessions, Convention Center, San Diego, California. Website: web.diabetes.org/

May 2-5, 2005. CDC Diabetes Translation Conference. The Radisson Hotel 1601 Biscayne Boulevard, Miami, Florida. Website: cdc.confex.com/

May 13-15, 2005. Children with Diabetes: Focus on the Future. Sheraton Hotel, Colorado Springs, CO. Website: www.childrenwithdiabetes.com

July 6-9, 2005. Friends for Life Conference and Expo. Disney's Coronado Springs Resort, Lake Buena Vista, Florida. Website: www.diabetes123.com/

September 3-7, 2005. European Society of Cardiology Congress. Stockholm, Sweden. Website: escardio.org/

September 9-11, 2005. Children with Diabetes: Focus on Pumping. San Diego Marriott Mission Valley, San Diego, California. Website: www.childrenwithdiabetes.com/

October 15-19, 2005. NAASO Annual Scientific Meeting Co-Sponsored by ADA. Convention Center, Vancouver, British Columbia, Canada. Website: web.diabetes.org/

American Journal of Diabetes will list your meeting up to 12 months ahead if you contact us and tell us the meeting dates, venue and the website where healthcare professionals can find more information.

INFORMATION FOR AUTHORS

We provide up-to-date information about diabetes research, FDA-approved devices and therapies to healthcare professionals so that they have the information they need to enable persons with diabetes to lead long and productive lives. Articles are targeted at the physician in clinical practice and the diabetes educator, and our goal is to build bridges between our target audience and academic scientists so that laboratory and clinical findings can be rapidly disseminated in a form that can be applied in the daily practice of medicine. Our Editorial Board includes scientists, physicians, and diabetes educators and other healthcare professionals, some of whom are themselves living with diabetes.

For consideration by the editorial board, all manuscripts must be written according to the uniform requirements for manuscripts submitted to biomedical journals, which are posted on www.icmje.org. We accept letters, review articles and articles giving original research. Original articles need to be in the form Abstract (200 words maximum), Introduction, Methods, Results, Discussion. Articles should generally have under 3,000 words.

Each article is reviewed by at least 2 members of the editorial board and the Editor-in-Chief, and outside reviewers as the need arises. We adhere to the requirement of the National Library of Medicine for inclusion of journals in their database is that "neither the advertising content nor commercial sponsorship should raise questions about the objectivity of the published material."

Publication of the journal is supported by advertising FDA-approved diabetes medications and devices, events, meetings of interest to healthcare professionals working with patients with diabetes. The articles are selected for review by the Editor-in-Chief, working independently of the Publishers, who select the advertisers.

All articles published are required to meet the standards of the National Library of Medicine. Our major criteria for selecting each article are scientific merit, relevance to our target audience and quality of writing. We invite submission of articles reporting clinicaland preclinical studies, reviews of current clinical and pre-clinical studies, discussion of devices and medications, case reports on treating adults and children with type 1 and type 2 diabetes, case reports on preventing diabetes in patients at risk. Submissions of review articles and case reports must be preceded by communication with the Editor-in-Chief. We also invite submission of letters to the Editor, which should address observations in clinical practice, early results of studies, discussion of applications of basic research to clinical practice or discussion of clinical guidelines.

The preferred form for submission is by attaching articles prepared electronically to e-mails. First send an e-mail with a cover letter, then send a second e-mail with the article attached. For us to lay out the article, it needs to be in MS Word or an equivalent program.

When we accept the article for review, we will e-mail or fax you a form which you need to sign, stating that you are the senior author of the article under review and that all tables and figures are either original or you have proof that you are permitted to reproduce them and that you assign copyright of your article to the American Journal of Diabetes when it is accepted for publication.

Send articles to:

Dr SJ Dodgson, Editor-in-Chief
submissions@americanjournalofdiabetes.com
Ph: 856-795-2359 or 215-596-8512
Fax: 856-427-6922 or 215-596-7536