Wyoming Clinical Practice Recommendations for Diabetes Mellitus



SECOND EDITION 2008

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CLINICAL RECOMMENDATIONS COMMITTEE

Welcome to the second edition of the Wyoming Clinical Practice Recommendations for Diabetes Mellitus. These recommendations are intended for use by primary care professionals and meant to be basic guidelines, not enforceable standards.

The Wyoming Diabetes Clinical Practice Recommendations Committee, in conjunction with the Wyoming Diabetes Prevention and Control Program, initially produced the recommendations as part of a statewide effort to improve the health care of people with diabetes. The Wyoming Diabetes Prevention and Control Program is coordinated by the Wyoming Department of Health and funded by a cooperative agreement from the Centers for Disease Control and Prevention.

These recommendations are offered in support of best practices consistent with current scientific knowledge. We encourage providers to modify these recommendations to meet the unique needs of each person with diabetes. These recommendations will be appropriate for treatment of most children and adults with diabetes most of the time, and the need for major modifications should not be common.

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MISSION STATEMENT PURPOSE AND GOAL

The number of patients with diabetes mellitus is growing dramatically every year. By placing importance on the excellence of care in persons with diabetes, the State of Wyoming recognizes that implementation of these standards will result in a reduction of morbidity and mortality associated with diabetes.

The purpose of these clinical recommendations is to assist in providing the highest level of care possible for the screening, management, and treatment of individuals with diabetes and related disorders.

The goal of this document is to provide a succinct, concise, and up-to-date set of recommendations for use by all health care practitioners in the State of Wyoming.

THE FOLLOWING ORGANIZATIONS SUPPORT THESE RECOMMENDATIONS:

Wyoming Association of Diabetes Educators
Wyoming Chapter, American College of Physicians
Wyoming Medical Society
Wyoming Pharmacy Association
Wyoming Podiatric Medical Association

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GLOSSARY OF ABBREVIATIONS

| A1c | Hemoglobin A1c |
|--------|--|
| AACE | American Association of Clinical Endocrinologists |
| AAP | American Academy of Pediatrics |
| ACE | Angiotensin Converting Enzyme |
| ACIP | Advisory Committee on Immunization Practices |
| ADA | American Diabetes Association |
| AHA | American Heart Association |
| ARB | Angiotensin II Receptor Blocker |
| BG | Blood Glucose |
| BMI | Body Mass Index |
| BUN | Blood Urea Nitrogen |
| CAD | Coronary Artery Disease |
| CDC | Centers for Disease Control and Prevention |
| CDE | Certified Diabetes Educator |
| CHF | Congestive Heart Failure |
| CVD | Coronary Vascular Disease |
| DBW | Desirable Body Weight |
| DKA | Diabetic Ketoacidosis |
| DM | Diabetes Mellitus |
| DSM-IV | Diagnostic and Statistical Manual of Mental Disorders, 4th |
| DSMT | Diabetes Self-Management Training |
| ECG | Electrocardiogram |
| FDA | U.S. Food and Drug Administration |
| GCT | Glucose Challenge Test |
| GDM | Gestational Diabetes Mellitus |
| GFR | Glomerular Filtration Rate |
| GI | Gastrointestinal |
| HDL | High Density Lipoprotein |
| HHS | Hyperosmolar Hyperglycemic State |
| IFG | Impaired Fasting Glucose |
| IGT | Impaired Glucose Tolerance |
| LADA | Latent Autoimmune Diabetes of Adulthood |
| LDL | Low Density Lipoprotein |
| LFT | Liver Function Test |
| MNT | Medical Nutrition Therapy |
| NCEP | National Cholesterol Education Program |
| OGTT | Oral Glucose Tolerance Test |
| PCOS | Polycystic Ovarian Syndrome |
| PDR | Proliferative Diabetic Retinopathy |
| PG | Pregnancy |
| RD | Registered Dietitian |
| RPE | Rating of Perceived Exertion |
| SMBG | Self-Monitoring Blood Glucose |
| TSH | Thyroid Stimulating Hormone |
| UA | Urinalysis |
| WHO | World Health Organization |
| | |

Edition

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I. DEFINITION AND CLASSIFICATION

A. Definition of Diabetes Mellitus

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the ß-cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action. Impairment of insulin secretion and defects in insulin action frequently coexist in the same patient, and it is often unclear which abnormality, if either alone, is the primary cause of the hyperglycemia.

B. Classification of Diabetes Mellitus

Patients with any form of diabetes may require insulin treatment at some stage of their disease. Such use of insulin does not, of itself, classify the patient.

1. Type 1 diabetes

Type 1 diabetes results from ß-cell destruction, usually leading to absolute insulin deficiency. It occurs in all ages, with the highest incidence in ten- to fourteen-year-old youth world-wide.

Immune mediated:

- 1. Type 1 diabetes is due to pancreatic islet ß-cell destruction, predominantly by an autoimmune process associated by human lymphocyte antigens and genetic factors. Insulin secretory capacity then gradually declines until it is totally lost. Approximately 90% of cases of type 1 diabetes are immune-mediated.
- 2. In adult onset type 1 diabetes, also known as latent autoimmune diabetes of adulthood (LADA), human lymphocyte antigens types may be different from those of juvenile-onset type 1 diabetes, and islet-directed antibody titers may be lower. Approximately 20% of patients diagnosed with type 2 diabetes may actually have LADA.

Idiopathic:

Other factors contribute to the development of type 1 diabetes in some patients. No evidence of pancreatic ß-cell autoimmunity is found to explain their insulinopenia or ketoacidosis.

2. Type 2 diabetes

Defects of type 2 diabetes may range from predominantly insulin resistance to a predominantly secretory defect with insulin resistance.

C. Other Specific Types & Causes

- A. Genetic defects of ß-cell function
 - 1. Chromosome 12, HNF-1 (MODY3)
 - 2. Chromosome 7, glucokinase (MODY2)
 - 3. Chromosome 20, HNF-4 (MODY1)
 - 4. Mitochondrial DNA
 - 5. Others

B. Genetic defects in insulin action

- 1. Type A insulin resistance
- 2. Leprechaunism
- 3. Rabson-Mendenhall syndrome
- 4. Lipoatrophic diabetes
- 5. Others

C. Diseases of the exocrine pancreas

- 1. Pancreatitis
- 2. Trauma/pancreatectomy
- 3. Neoplasia
- 4. Cystic fibrosis
- 5. Hemochromatosis
- 6. Fibrocalculous pancreatopathy
- 7. Others

D. Endocrinopathies

- 1. Acromegaly
- 2. Cushing's syndrome
- 3. Glucagonoma
- 4. Pheochromocytoma
- 5. Hyperthyroidism
- 6. Somatostatinoma
- 7. Aldosteronoma
- 8. Others

E. Drug- or chemical-induced

- 1. Glucocorticoids
- 2. Atypical antipsychotics
- 3. Vacor
- 4. Pentamidine
- 5. Nicotinic acid
- 6. Thyroid hormone
- 7. Diazoxide
- 8. ß-adrenergic agonists
- 9. Thiazides
- 10. Dilantin
- 11. Interferon
- 12. Others

D. Gestational Diabetes Mellitus (GDM)

Definition

GDM is any degree of glucose intolerance with onset or first recognition during pregnancy. This does not exclude the possibility that the glucose intolerance occurred prior to conception. Six weeks after the pregnancy ends the woman should be reclassified into one of the following categories: 1) diabetes, 2) pre-diabetes, or 3) normoglycemia.

REFERENCE SECTION I

American Diabetes Association. Clinical Practice Recommendations. Standards of medical care in diabetes. *Diabetes Care.* 30(Suppl. 1):S4-S41. 2007

Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care.* 26:S5-S20. 2003

Latent Autoimmune Diabetes in Adults. Diabetes Monitor. http://www.diabetesmonitor.com/lada.htm.

Tierney L, McPhee S, Papadakis, M. Current Medical Diagnosis and Treatment. 45th Edition. Lange Medical Books. McGraw-Hill. 2006

- F. Infections
 - 1. Congenital rubella
 - 2. Cytomegalovirus
 - 3. Others
- G. Uncommon forms of immune-mediated diabetes
 - 1. "Stiff-man" syndrome
 - 2. Anti-insulin receptor antibodies
 - 3. Others

H. Other genetic syndromes sometimes associated with diabetes

- 1. Down's syndrome
- 2. Klinefelter's syndrome
- 3. Turner's syndrome
- 4. Wolfram's syndrome
- 5. Friedreich's ataxia
- 6. Huntington's chorea
- 7. Laurence-Moon-Biedl syndrome
- 8. Myotonic dystrophy
- 9. Porphyria
- 10. Prader-Willi syndrome
- 11. Others

II. SCREENING AND DIAGNOSIS

A. Type 1 Diabetes

Type 1 diabetes mellitus occurs in 5-10% of the population who develop diabetes. Type 1 diabetes mellitus is usually an autoimmune disease. Although the process by which the pancreatic ß-cell is destroyed is not well understood, several risk factors and immune-related markers are known that accurately identify many first-degree relatives of patients with type 1 diabetes who will develop the disease. Because we now have the ability to predict the development of type 1 diabetes in some people, investigators have begun to explore the use of intervention therapy to halt or even prevent ß-cell destruction in such individuals.

A type of diabetes called latent autoimmune diabetes in adults (LADA) exists, which may make up 10-20% of adult non-insulin requiring diabetes at diagnosis. These individuals tend to be non-insulin dependent at diagnosis, are usually not obese, and have the same immune related markers and same genetic susceptibility as true type 1 diabetes. Later, they become truly insulin dependent.

Diabetes is one of the most common chronic diseases of childhood, with a prevalence of 0.22% or 1 in every 400-600 children aged <20 years. In the U.S., approximately 13,000 new cases are diagnosed annually. There are about 176,500 individuals <20 years of age with diabetes in the U.S.

B. Type 2 Diabetes

Of the more than 22.2 million Americans with diabetes, 90-95% of them have type 2 diabetes. Type 2 diabetes is often asymptomatic in its early stages and can remain undiagnosed for many years. Symptoms or signs of previously undiagnosed type 2 diabetes may include delayed wound healing, recurrent vaginal yeast infections, vascular disease, an unexplained neuropathy, or diabetic retinopathy. Diabetes is frequently not diagnosed until complications appear and approximately one-third of all people with diabetes may be undiagnosed. However, while there is good evidence of benefit from treating cases diagnosed through usual clinical care, there are no randomized trials demonstrating the benefits of early diagnosis through screening of asymptomatic individuals. Nevertheless, there is sufficient indirect evidence to justify opportunistic screening in a clinical setting of individuals at high risk.

The CDC estimated the prevalence of diabetes among adults over the age of 20 was 9.6% in 2005; this is expected to double by the year 2025. However, specific population subgroups have a much higher prevalence of the disease than the population as a whole. These subgroups have certain attributes or risk factors that either directly cause diabetes or are associated with it.

The incidence of type 2 diabetes in children and adolescents is increasing. Consistent with screening recommendations for adults, children and youth at substantial risk for the presence or the development of type 2 diabetes should be tested. The American Diabetes Association and the American Academy of Pediatrics recommend:

- Youths should be screened if they are overweight as defined by a BMI of >85th percentile, or weight >120% of ideal (50th percentile) for height, plus youths with any two of the following risk factors:
 - Family history of type 2 diabetes in a first or second degree relative.
 - Certain race or ethnicity such as American Indians, African American, Hispanic, Asian or Pacific Islander.
 - Signs of insulin resistance or conditions associated with insulin resistance such as acanthosis nigricans, hypertension, dyslipidemia, or polycystic ovarian syndrome.
 - Maternal history of GDM.
- Youths identified in the previous bullet should be tested every two years starting at age 10 years or at the onset of puberty if it occurs at a younger age.

Individuals with undiagnosed type 2 diabetes are at significantly higher risk for stroke, coronary heart disease, and peripheral vascular disease than individuals without diabetes. They also have a greater likelihood of having dyslipidemia, hypertension, and obesity. Early detection and prompt treatment may reduce the burden of diabetes and its complications. The chronic hyperglycemia of diabetes is associated with long-term dysfunction, damage, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

Individuals who have a fasting BG* of 100 mg/dL (6.1 mmol/l) - 125 mg/dL (7.0 mmol/l) are considered to have impaired fasting glucose (IFG), and those with 2 hr values in the OGTT of 140 mg/dL (7.8 mmol/l) - 200 mg/dL (11.1 mmol/l) are defined as having impaired glucose tolerance (IGT). Both IFG and IGT are risk factors for future diabetes. Normoglycemia is defined as BG levels <100 mg/dL (6.1 mmol/l) in the fasting BG test and a 2 hr post-load value <140 mg/dL (7.8 mmol/l) in the OGTT.

Laboratory measurement of BG concentration is performed on venous samples with enzymatic assay techniques and the above mentioned values are based on the use of such methods. The A1c test remains a valuable tool for monitoring glycemia, but it is not currently recommended for the screening or diagnosis of diabetes. Pencil and paper tests, such as the American Diabetes Association's risk test, may be useful for educational purposes but do not perform well as stand-alone tests. Capillary blood glucose testing, using home testing equipment, can be imprecise and is better used for self-monitoring rather than a screening tool.

C. Screening

The purpose of screening is to identify asymptomatic individuals who are likely to have diabetes.

1. Asymptomatic Individuals

Screen by measuring fasting plasma BG. Fasting is defined as no caloric intake for at least 8 hours.

TABLE 1 Criteria for Testing for Diabetes in Asymptomatic, Undiagnosed Individuals

- 1. Testing for diabetes should be considered in individuals at age 45 years and above, particularly in those with a BMI ≥25 kg/m2 (different BMI may be needed for some ethnic groups); if normal, repeat screening should be considered at 3-year intervals.
- 2. Testing should be considered at a younger age or be carried out more frequently in individuals with a BMI ≥25 kg/m2 (different BMI may be needed for some ethnic groups) and have additional risk factors, such as:
 - a first-degree relative with diabetes
 - are habitually physically inactive
 - are members of a high-risk ethnic population (e.g., African-American, Hispanic American, American Indians, Asian American, Pacific Islander)
 - have delivered a baby weighing ≥9 lb or have been diagnosed with GDM
 - are hypertensive (>140/90)
 - have an HDL cholesterol level ≤35 mg/dL (0.90 mmol/l) and/or a triglyceride level ≥200 mg/dL (2.82 mmol/l)
 - have PCOS
 - on previous testing, had IGT or IFG
 - have a history of vascular disease
 - * BG throughout these Recommendations means plasma or serum glucose. For a discussion on the ways of measuring glucose in the blood and their differences, see the Appendix, page 93.

2. Gestational Diabetes

All pregnant women should be considered for screening (see D2 below).

Initial screening: measure the plasma glucose concentration 1 hour after a 50 gm oral glucose load; if the glucose threshold value is >140 mg/dL (>7.8 mmol/l), then perform a diagnostic test (see below). A threshold of >140 mg/dL (>7.8 mmol/l) identifies 80% of pregnant women with GDM. A threshold of >130 mg/dL (>7.2 mmol/l) identifies 90% of pregnant women with GDM.

D. Diagnostic Criteria

1. Diabetes Mellitus

TABLE 2

Criteria for the Diagnosis of Diabetes Mellitus

1. Symptoms of diabetes plus random plasma glucose concentration ≥200 mg/dL (11.1 mmol/l). Random is defined as any time of day without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss.

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- 2. Fasting BG \geq 126 mg/dL (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 hours. Or
- 3. Two hour plasma glucose ≥200 mg/dL (11.1 mmol/l) during an OGTT. The test should be performed as described by WHO, using a glucose load containing the equivalent of 75 grams anhydrous glucose dissolved in water. (Perform OGTT if patient is high risk or high level of suspicion.)

This third measure (OGTT) is not recommended for routine screening; however, it is more sensitive than fasting plasma glucose in diagnosing early diabetes and thus should be considered in those patients who are thought to be at high risk (e.g., IFG) or in those whom the initial diagnosis is unclear.

If the patient is not acutely ill, these criteria should be confirmed by repeat testing on a different day.

2. Gestational Diabetes

Diagnosis is based on 100 gram or 75 gram Oral Glucose Tolerance Test (OGTT). The 100 gram OGTT is more commonly used and better validated. See Table 3 below. Risk assessment for GDM should be undertaken at the first prenatal visit.

- 1. High risk of GDM (marked obesity, personal history of GDM, glucosuria, or a strong family history of diabetes)-test as soon as possible in pregnancy.
- 2. Average/low risk should have testing undertaken at 24-28 weeks of gestation.

TABLE 3

Diagnosis of GDM with Oral Glucose Load

| | 100 gm mg/dL mmol/l | | 75 mg/dL | gm mmol/l |
|---------|------------------------|-------|-------------|--------------|
| Fasting | ≥95 | ≥5.3 | ≥95 | ≥5.3 |
| 1 hr | ≥180 | ≥10.0 | ≥180 | ≥10.0 |
| 2 hr | ≥155 | ≥8.6 | ≥155 | ≥8.6 |
| 3 hr | ≥140 | ≥7.8 | | |

Two or more of the venous plasma concentrations must be met or exceeded for a positive diagnosis.

REFERENCE SECTION II

American Diabetes Association. Clinical Practice Recommendations. Standards of medical care for patients with diabetes mellitus. *Diabetes Care.* 30(Suppl. 1):S4-S8. 2007

Diabesity and Our Children. Sweet Success Update. Page 1. Spring 2007

Pozzilli DM. Autoimmune Diabetes: Not Requiring Insulin at Diagnosis. *Diabetes Care*. 24:1460-1467. 2001

III. STANDARDS OF CARE FOR DIABETES IN ADULTS

TABLE 4

A. Quick Reference Guide for Adult Type 1 and 2 Diabetes

| | ASSESSMENT FREQUENCY CATEGORIES | | | | | |
|---------------------------------------|---------------------------------|--------------------------------|---------------------------------|-------------|--|--|
| | Initially | Annually | Other | Every Visit | | |
| GENERAL | | | | | | |
| Comprehensive History and Physical | X | | | | | |
| Brief History and Physical | | | | Х | | |
| Height and Weight | Х | | | Х | | |
| Blood Pressure | X | | | Х | | |
| Dilated Eye Exam | X ¹ | X* | | | | |
| Dental Exam | X | | X twice/yr | | | |
| Foot Exam | | | | | | |
| Visual | Х | | | Х | | |
| Comprehensive | X | X | | | | |
| Referral to Podiatrist | | X* | | | | |
| Referral to diabetes educator | Х | | X twice/yr* | | | |
| EKG | Х | X [*] after age 50 | | | | |
| LABORATORY EVALUATIONS | | | | | | |
| Hemoglobin A1c | X | | X quarterly | | | |
| Lipid Profile | X | X* | | | | |
| Comprehensive & Basic Metabolic Panel | Х | X* | | | | |
| UA Microalbumin/Creatine Ratio | X ² | X* | | | | |
| TSH | Х | X* | | | | |
| PREVENTION/INTERVENTION | | | | | | |
| Aspirin Therapy | X ³ | | | | | |
| Consider ACE Inhibitors/ARB | X* if B | P no <mark>t at goal or</mark> | neph <mark>ropathy pre</mark> s | sent X* | | |
| Tobacco Cessation | Х | | | Х | | |
| Immunizations | | | | | | |
| Influenza | X | Х | | | | |
| Pneumococcal | X* | | | | | |
| Pre/Post Pregnancy Counseling | X | X* | | | | |
| Multi-vitamin of Choice | X | X | | | | |
| Consider Comorbidities | Х | X | | | | |
| OTHER CONSIDERATIONS | | | | | | |
| Diabetes Self-Management Education | Х | X* | | | | |
| Barriers to Care | X | | | Х | | |
| SMBG/Blood Glucose Log | | | | X | | |
| Medical Nutrition Therapy | X | X | | | | |
| Physical Activity | X | X | | | | |
| Weight Management | X | X | | | | |
| Medication Review | X | X | | | | |
| Risks & Complications | X | X | | | | |

* Or as indicated per level of control

¹ In type 1, screening should start 3-5 years after the diagnosis is made

² In type 1, screening should start 5 years after the diagnosis is made

³ In type 2, start all patients on aspirin at initial visit; in type 1, start only if evidence of CAD exists

B. Initial Evaluation

Medical History

- Symptoms
- Eating patterns
- Exercise patterns
- Risk factors, including cardiac status and baseline EKG
- Presence of infections and history of frequency of infections
- Medications
 - Prescriptions and over-the-counter (including nutrient and herbal supplements)
 - Recreational including alcohol
- Family history
- Lifestyle and cultural preferences
- Tobacco history
- Reproductive and sexual history, including contraception practices
- Immunization status (e.g., Influenza, Pneumococcal, Tetanus, PPD)
- Previous diabetes education (MNT and DSMT)

Physical Examination

- Height, weight, BMI
- Vital signs
- HEENT (head, eyes, ears, nose and throat)
- Thyroid palpation
- Cardiac examination
- Abdominal examination
- Palpation of peripheral pulses
- Feet & hands examination
- Skin examination (acanthosis nigricans, necrobiosis lipoidica)
- Neurological examination (including tuning fork, Achilles tendon reflex and monofilament testing)
- Fundoscopic evaluation
- Referral to other specialties, as indicated

Laboratory Evaluation

- Hemoglobin A1c
- Lipids
- Urine for microalbumin and creatinine
- Blood glucose
- Comprehensive metabolic panel
- TSH
- Others as indicated

C. Yearly Assessments

- Dilated eye exam
- Foot exam (including pulses, tuning fork, Achilles tendon reflex and monofilament testing)
- Lab: lipids, urine microalbumin/creatine ratio, A1c, others as indicated
- Blood pressure, weight, BMI
- Updated immunization
- Updating self management skills including SMBG
- Tobacco cessation counseling
- EKG (after age 50)
- Dental exam
- Vaccinations as indicated (e.g., Influenza, Pneumococcal, Tetanus, PPD)

D. Targets

Randomized, controlled studies have demonstrated that long-term complications of diabetes can be reduced by intensive glycemic control. The Diabetes Control and Complications Trial showed at nine years the incidence of new retinopathy was 12% in the intensive therapy group versus 54% in the conventional therapy group. After 6.5 years of this study, the prevalence of new microalbuminuria was 16% in intensive therapy versus 27% in conventional therapy. In the same study, the incidence of clinical neuropathy was reduced with intensive insulin therapy by 64%.

There are a number of management goals and guidelines for diabetes recommended by various societies and organizations. These guidelines, although based on the available evidence analyzed by experts in the field, may be slightly different. Perhaps the three most commonly utilized guidelines in the United States are from the American Diabetes Association (ADA), the American Association of Clinical Endocrinologists (AACE), and the Adult Treatment Panel (ATP III) of the National Cholesterol Education Program (NCEP). One should keep in mind that these are only general guidelines and that management goals should be individualized to the patient, with consideration given to individual risk factors (e.g., the patient's age, prognosis, the presence of diabetes complications or comorbidities, and the risk for and ability to perceive hypoglycemia).

TABLE 5

Target Indicators for Glycemic Control in Diabetes

| Target Indicator | Source | | | | | |
|------------------------------|-------------------|-------------------|---------------------|--|--|--|
| Target Indicator | ADA ¹ | AACE ² | ATPIII ³ | | | |
| Preprandial/Fasting BG* | 90 - 130 | <110 | | | | |
| Postprandial/2 hr Fasting BG | <180 | <140 | | | | |
| A1c (%) | <7.0 | ≤6.5 | | | | |
| Blood Pressure | <130/80 | <130/80 | <130/85 | | | |
| Lipids | | | | | | |
| LDL | <100 ⁴ | <100 ⁴ | <100 ⁴ | | | |
| Triglycerides | <150 | <150 | <150 | | | |
| HDL | >40 men >50 women | >40 men >50 women | >40 men >50 womer | | | |

All goals must be individually tailored for patient to provide best control and preserve safety.

1 Summary of targets from Standards of Care. 2007. American Diabetes Association (ADA)

2 Summary of targets from Road Map for Treatment in Type 2 Diabetes. 2007. American Association of Clinical Endocrinologists (AACE)

3 National Cholesterol Education Program/Adult Treatment Panel III (ATP III) guidelines. 2006

4 Lower if multiple risk factors

E. Therapeutic Options

1. Use of Insulin

Insulin is available in different types and concentrations. In the United States, insulin is commercially available in U-100 and U-500 concentrations (100 or 500 units/mL; 1 unit equals ~36 mcg insulin). Outside the United States, U-40 and U-80 are commonly used, which may be useful information when managing patients who travel abroad. Syringes correspond to insulin concentrations.

* BG throughout these Recommendations means plasma or serum glucose. For a discussion on the ways of measuring glucose in the blood and their differences, see the Appendix, page 93.

TABLE 6 Insulin: Types and Action

| Type of Insulin | Brand name/ formulary status | Concen- tration | May be mixed with | Onset | Peak | Duration | Administration in relation to meals | Appear- ance | |
|--|------------------------------------|--------------------|---|-------------------|-------------------|--|---|-----------------------------|--|
| Prandial or Correction (Rapid Acting) | | | | | | | | | |
| Aspart | Novolog | 100 units/ mL | NPH | 10 to 20 min | 1 to 3 hours | 3 to 5 hours | 5 to 10 min before meal | Clear | |
| Glulisine | Apidra | 100 units/ mL | NPH | 10 to 15 min | 1 to 1.5 hours | 3 to 5 hours | 15 min before meal or within 20 min after start of meal | Clear | |
| Lispro | Humalog | 100 units/ mL | NPH | 15 to 30 min | 1 to 2 hours | 3 to 5 hours | 15 min before or immediately after meal | Clear | |
| Prandial or | Correction (S | hort Acting) | | | | | | | |
| Regular | Novolin R Nova | 100 units/ mL | NPH | 30 to 60 min | 2 to 4 hours | 4 to 8 hours | 30 min before meal | Clear | |
| Regular | Humulin R U-500 | 500 units/ mL | DO NOT MIX | 30 to 60 min | 2 to 4 hours | 4 to 8 hours | 30 min before meal | Clear | |
| Regular | Humulin R | 100 units/ mL | NPH | 30 to 60 min | 2 to 4 hours | 4 to 8 hours | 30 min before meal | Clear | |
| Basal (Intern | mediate Actin | g) | | | | | | | |
| NPH | Novolin N | 100 units/ mL | Aspart, Glulisine, Lispro, and Regular | 1 to 2 hours | 3 to 6 hours | 8 to 18 hours | If mixing, follow guideline for rapid- or short-acting insulin | Cloudy | |
| NPH | Humulin N | 100 units/ mL | Aspart, Glulisine, Lispro, and Regular | 1 to 2 hours | 3 to 6 hours | 8 to 18 hours | If mixing, follow guideline for rapid- or short-acting insulin | Cloudy | |
| Basal (Long | Acting) | | | | | | | | |
| Detemir | Levemir | 100 units/ mL | DO NOT MIX | 0.8 to 2 hours | No peak | Dose dependent 12 hr for 0.2 units/kg; 20 hr for 0.4 units/kg; up to 24 hr | Without regard to meal | Clear, but cannot mix | |
| Glargine | Lantus | 100 units/ mL | DO NOT MIX | 1 to 2 hours | No peak | 24 hours | Without regard to meal | Clear, but cannot mix | |
| Basal and Pa | randial Pre-m | nixed Combin | ations | | | | | | |
| 70% Aspart Protamine/ 30% Aspart | NovoLog Mix 70/30 | 100 units/ mL | DO NOT MIX | 10 to 20 min | NA | NA | Within 15 min of meal initiation | Cloudy | |
| 70% NPH/ 30% Regular | Novolin 70/30 | 100 units/ mL | DO NOT MIX | 30 to 60 min | NA | NA | 30 minutes before meal | Cloudy | |
| 50% NPH/ 50% Regular | Humulin 50/50 | 100 units/ mL | DO NOT MIX | 30 to 60 min | NA | NA | 30 minutes before meal | Cloudy | |
| 70% NPH/ 30% Regular | Humulin 70/30 | 100 units/ mL | DO NOT MIX | 30 to 60 min | NA | NA | 30 minutes before meal | Cloudy | |
| 75% Lispro protamine/ 25% Lispro | Humalog Mix 75/25 | 100 units/ mL | DO NOT MIX | 15 to 30 min | NA | NA | Within 15 min of meal initiation | Cloudy | |

| Type of Insulin | Brand name/ formulary status | Concen- tration | May be mixed with | Onset | Peak | Duration | Administration in relation to meals | Appear- ance |
|--|------------------------------------|-------------------------------------|-------------------------|-----------------|-----------------|----------|-------------------------------------|-----------------|
| Inhalation Insulin | | | | | | | | |
| Inhaled Recombinant Human Insulin | Exubera | 1 mg, 3 mg unit dose blisters | NA | 10 to 20 min | 30 to 90 min | 6 hours | Within 10 min of meal ingestion | NA |

Notes for Table 6:

When combining insulin products in a single syringe, use clear, then cloudy (rapid- or short-acting drawn first) NovoLog Mix 70/30 and Humalog Mix 70/25 do not contain NPH or Regular insulin

TABLE 7

Pre-Meal Dosing for Inhaled Insulin



* Approximate dosing equivalent of regular human subcutaneous insulin

Insulin Regimens

Many factors affect pharmacokinetics of insulin, including insulin type, injection technique, injection site, etc. In adults, insulin regimen should reflect the normal daily glycemic fluctuations under physiologic conditions. Insulin adjustments are based on average blood glucose readings. Frequently prescribed regimens include:

- *Twice daily injections*, consisting of a mixture of short- or rapid- and intermediate-acting insulins (before breakfast and supper).
- *Multiple daily injections*, consisting of a short- or rapid-acting insulin before meals and a long-acting insulin at bedtime.
- Insulin pump regimens of rapid-acting insulin used to mimic a basal-bolus routine.

Dosage Guidelines

Insulin dosages vary greatly and can change over time. The following should be included in the routine review and reassessment of patients:

Weight change

- Duration of diabetes
- Skin/tissue condition at injection sites
- Exercise patterns
- Daily routine
- Results of SMBG and A1c
- Intercurrent illness

Distribution of Dose

A basal/bolus insulin regimen would generally include 3 components:

- 1. Basal insulin: this component covers the glucose that enters the circulation from the liver during fasting hours (glycogenolysis). This requirement is usually provided by a long-acting insulin given at bedtime, or two doses of intermediate-acting insulin, approximately 12 hours apart.
- 2. Prandial insulin: this component covers the glucose that enters the circulation after a meal. This is usually provided by a rapid- or short-acting insulin as several boluses in a day, given prior to meals. An insulin/carbohydrate ratio is utilized in modifying meal boluses. Insulin to carbohydrate ratio must be individualized based on insulin sensitivity.
- 3. Supplemental insulin (also known as sliding scale or correctional insulin): this component is intended to lower the blood glucose when it is higher than the target and is given in boluses of rapid- or short-acting insulin, when needed.

In otherwise healthy patients with type 1 diabetes, the typical total daily dose requirement is about 0.5-1 U/kg. In type 2 diabetes, this requirement is about 1-1.5 U/kg. The proportion of basal and bolus insulins are usually close to 50-50 percent, with the 50% bolus divided by the number of meals.

If initiating insulin pump therapy, the total daily dose of insulin is usually reduced by 25-30%. This reflects the higher efficiency of insulin when delivered in a continuous fashion by pump. The basal dose is distributed in 24 hours, based on different requirements at various times of the day. Bolus doses are divided based on the number and carbohydrate content of meals.

2. Oral Pharmacotherapy

Many advances have been made in the pharmacologic treatment of type 2 diabetes within the past five years. All agents have tissue-specific sites of action to improve glycemia. As stated in AACE Guidelines for Management of Diabetes, "these agents can be used in combination to utilize their respective mechanisms of action for reversing multi-factorial pathophysiology of beta cell dysfunction, insulin resistance, increased hepatic glucose production, and decreased peripheral glucose utilization."

TABLE 9

Classifications of Non-Insulin Anti-Diabetic Agents

| Drug Class | Generic Name | Brand Name | Dosing Range* | Dura- tion (hrs) | Average Cost (month) |
|--------------------|----------------|-------------------|---------------|------------------------|----------------------------|
| Sulfonylureas | Tolazamide | Tolinase | 100 mg-1 gm/d | 6-12 | \$15-\$80 |
| | Tolbutamide | Orinase | 500-2000 mg/d | 6-12 | \$15-\$60 |
| | Chlorpropamide | Diabinese | 100-500 mg/d | up to 60 | \$9-\$21 |
| | Glimepride | Amaryl | 1-8 mg/d | 12-24 | \$10-\$30 |
| | Glipizide | Glucotrol | 2.5-20 mg/d | 10-24 | \$7-\$40 |
| | Glyburide | Micronase/Diabeta | 1.25-20 mg/d | 10-24 | \$8-\$32 |
| Biguanides | Metformin | Glucophage | 500-2500 mg/d | 10-12 | \$25-\$210 |
| Thiazolidinediones | Pioglitazone | Actose | 15-45 mg/d | 24 | \$103-\$165 |
| | Rosiglitazone | Avandia | 2-8 mg/d | | \$67-\$175 |

| Drug Class | Generic Name | Brand Name | Dosing Range* | Dura- tion (hrs) | Average Cost (month) |
|---------------------------|--------------|------------|---------------|------------------------|----------------------------|
| Incretin-Based Agents | | | | | |
| - Incretin Mimetic Agents | Exenatide | Byetta | 10-20 mcg/d | 2.4 | \$200-\$230 |
| - DPP-IV Inhibitors | Sitagliptin | Januvia | 100 mg/d | | \$164 |
| Amylin Analog | Pramlintide | Symlin | 45-360 mcg/d | <1 | \$52-\$414 |
| a-Glucosidase Inhibitors | Acarbose | Precose | 75-300 mg/d | 3-4 | \$74-\$90 |
| | Miglitol | Glyset | 75-300 mg/d | | \$60-\$77 |
| Meglitinides | Nateglinide | Starlix | 360 mg/d | | |
| | Repaglinide | Prandin | 0.5-16 mg/d | 4.5 | \$120-\$130 |

* Although the maximum dose can often be safely exceeded, reaching the maximum dose usually indicates that it is time to move on to another type of therapy because dosing above the maximum dose usually does not produce any significant results, but does increase the cost of therapy.

Sulfonylureas

Mode of Action: The primary effect is to stimulate insulin secretion by blocking the potassium channel of the beta cell. A secondary effect is to decrease hepatic glucose production, and possibly improve insulin sensitivity at the receptor and post-receptor levels.

Profile: Sulfonylurea agents differ in potency, cost, and pharmacokinetics; use as adjunct to diet and exercise; may be used as monotherapy or combination therapy; most useful in thin patients; not effective in type 1 diabetes; not to be used in pregnancy (only Glyburide may be considered during the later part of pregnancy); not recommended for use in association with major surgical procedures or general anesthesia, severe infection, stress, trauma, or predisposition to severe hypoglycemia.

Dosing:

- Tolazamide Initial: 100-250 mg/day (blood glucose <200 = 100 mg, >200 = 250 mg) with breakfast. Increase by 100-250 mg increments per week. Doses above 500 mg/day should be given in 2 divided doses. Maximum daily dose is 1 gm/day.
- **Tolbutamide** Initial: 1-2 gm/day as a single dose in the morning or in divided doses throughout day. Maintenance dose is 0.25-3 gm/day; doses greater than 2 gm/day are seldom needed.
- Chlorpropamide 250 mg/day in mild to moderate, middle-aged and stable patients. Older patients start at 100-125 mg/day. Adjust dose by 50-125 mg every 3-5 days. Maintenance dose generally 100-250 mg/day. Avoid doses greater than 750 mg/day.
- Glimepride Initial: 1-2 mg once daily with breakfast. Usual maintenance dose is 1-4 mg/day. After 2 mg/day dose add 2 mg increments at 1-2 week intervals. Maximum dose is 8 mg/day.
- Glipizide Initial: 5 mg/day, increase at 2.5-5 mg increments after several days. Immediate release maximum once daily dose is 15 mg; maximum total daily dose is 40 mg. Doses greater than 15 mg should be divided. Sustained action tablet maximum daily dose is 20 mg.
- Glyburide Regular tabs: 2.5-5 mg/day initially, increase at no more than 2.5 mg increments at weekly intervals. Maintenance is 1-20 mg as once daily or divided doses. Maximum dose is 20 mg/ day. Micronized tablets: 1.5-3 mg initially, increase in increments of 1.5 mg/day in weekly intervals. Maintenance dose is 0.75-12 mg/day in single or divided doses. Maximum dose is 12 mg/day.

Warnings: Hypoglycemia due to overdosage, decreased caloric intake, severe or prolonged exercise, ethanol ingestion, or combination with other glucose lowering drugs. Renal or hepatic impairment necessitates dosage adjustment. Chemical similarities exist between sulfonylureas and sulfonamide, thiazides, loop diuretics and carbonic anhydrase inhibitors. Caution should be exercised in patients with sulfonamide allergy. Weight gain is a common side effect of this classification of medications. It may be necessary to discontinue therapy and administer insulin if the patient is exposed to significant stress such as infection, surgery, trauma or fever.

Contraindications: Sulfonylureas are contraindicated in advanced liver or kidney disease, known hypersensitivity to the drug, and diabetic ketoacidosis.

Biguanides

Mode of Action: Metformin has insulin-sensitizing properties and decreases hepatic glucose production by improving insulin action on the liver. A secondary effect is to enhance muscle glucose uptake and utilization.

Profile: Used as monotherapy or in combination with other classes or insulin. Biguanides are usually the first line of medications used in diabetes. This class of drugs is usually weight neutral in most people.

Dosing: Immediate release tablets, begin at 500 mg twice daily or 850 mg once daily. Allow at least one week between increments of 500 mg per week or 850 mg every other week. Meaningful decrease in BG levels are seldom seen with doses less than 1500 mg per day, but GI adverse effects are better tolerated with lower doses and slower titration upwards. Doses of up to 2000 mg/day may be given in divided twice daily dosing, however if greater doses are needed, it may be better tolerated in three daily doses. Maximum daily dose is 2550 mg per day. Extended release tablets begin with 500 mg per day at the evening meal, titrate up at 500 mg increments. If greater than 2000 mg/day is required, convert to immediate release tablets and split doses. The greatest side effects are usually seen in doses above 2500 mg/day.

Warnings: Lactic acidosis is a rare but potentially severe consequence of therapy with metformin. Caution should be exercised in any situations pre-disposing to lactic acidosis. Metformin is substantially excreted by the kidney and care must be exercised in renal (creatine clearance < 60-70 mL/min) or hepatic insufficiency.

Contraindications: Patients prone to metabolic acidosis or hypoxic states, including renal dysfunction with serum creatinine >1.5 mg/dL for males or >1.4 mg/dL for females, or liver dysfunction; dye procedures (temporarily discontinue drug for 24 hr pre- and 48 post-IV iodinated contrast and follow-up with a BUN-to-creatine ratio test). Use cautiously in patients >80 years old.

Thiazolidinediones (TZDs)

Mode of Action: This class of medications enhances tissue sensitivity to insulin in muscle through activation of intracellular receptors. A secondary effect is suppression of hepatic glucose production. There is no stimulatory effect on insulin secretion.

Profile: Used as monotherapy or in combination with sulfonylureas and metformin; both TZDs are FDA approved for use in combination with insulin therapy. Useful in patients with insulin resistance or azotemia. May take several weeks for onset of action and several months for peak action. Assess serum transaminase levels at start of therapy and every 2-3 months for 1 year, then periodically.

Dosing:

- Pioglitazone Initial dosing is 15-30 mg once daily. If response is inadequate, increase in 15 mg increments up to maximum daily dose of 45 mg.
- Rosiglitazone Initial dose is 4 mg in a single or divided daily dose. If there is insufficient response after 8-12 weeks of therapy, increase to 8 mg per day in a single or divided dosage. Clinically, the greatest decreases in glucose and A1c were seen with the 4 mg twice daily dosing.

Warnings: Weight gain, increase in total cholesterol, edema, and heart failure. Currently there is much controversy as to whether or not Avandia can increase overall cardiovascular morbidity and mortality. No adjustment of dose is needed with mild to moderate renal impairment. However, clearance is significantly lower in hepatic impairment. Treatment should not be started if the patient exhibits active liver disease or increased transaminases.

Contraindications: Known hypersensitivity or allergy to the drug or its components, severe renal impairment, clinical evidence of active liver disease, abnormal transamines >2.5 times upper limit of normal for pioglitazone or >2.5 times upper limits of normal for rosiglitazone, and CHF (NY Heart Assoc. Class III and IV).

Incretin-Based Agents

Incretin hormones cause increased insulin synthesis and release from pancreatic beta cells and inhibit the release of glucagon from pancreatic alpha cells. Decreased glucagon secretion results in decreased hepatic glucose synthesis. Incretin hormones along with glucose-dependent insulinotropic polypeptide regulate normal glucose homeostasis, and are released throughout the day, but are increased with response to meals.

- Incretin Mimetics: Exenatide

Mode of Action: This analog of the hormone GLP1 is among a group of hormones that have direct and indirect influences on the increased secretion of insulin, promotion of beta cell growth and replication, and the slowing of gastric emptying. The medication may lead to decreased food intake.

Profile: Exenatide is approved for use in type 2 patients that are already on metformin, sulfonylureas, or both and are not experiencing optimal glycemic control with mono or combination oral therapy. It is also approved for use with thiazolidinediones. Addition to metformin therapy seldom requires decreased dose of metformin. However, presence of hypoglycemia upon addition to sulfonylureas dictates that the sulfonylurea dose be decreased. The medication promotes weight loss in most people.

Dosing: Initial dosing is 5 mcg subcutaneously (thigh, abdomen, upper arm) twice daily within 60 minutes prior to meals. After 1 month the dose may be increased to 10 mcg twice daily, based on response and tolerance. Gradual dose escalation decreases side effects.

Warnings: Nausea is the most common side effect with exenatide. Nausea decreases with decreased food intake. Initiation of therapy in patients with severe GI disease has not been studied. Other common side effects include diarrhea, vomiting, headache and dizziness. Renal adjustment of dosing is not necessary with creatinine clearance levels above 30 mL/minute, however, below 30 mL/minute Exenatide is not recommended. Exenatide can cause hypoglycemia, generally characterized as mild to moderate in severity. Hypoglycemia is much more pronounced when Exenatide is added to a sulfonylurea (sulfonylurea dose should be decreased at the initiation of Exenatide).

Contraindications: Exenatide requires the presence of insulin, so use in type 1 diabetes or ketoacidosis is not recommended. Exenatide use is not recommended in severe renal failure and gastroparesis. Dose dependent gastrointestinal side effects are common and may respond to gradual titration and continued use.

- Dipeptidyl Peptidase-IV Inhibitors (DPP-IV): Sitagliptin

Mode of Action: Sitagliptin inhibits dipeptidyl peptidase-IV which breaks down endogenous incretin hormones. Incretin hormones are rapidly destroyed by DPP-IV enzyme.

Profile: This agent is used at a dose of 100 mg per day as monotherapy or in combination with metformin or thiazolidinediones.

Dosing: 100 mg once daily.

Warnings: The most common adverse effects of sitagliptin are upper respiratory tract infections, nasopharyngitis, and headache. Hypoglycemia was not elevated in combination use with metformin or pioglitazone. There are no current studies combining sitagliptin with agents known to cause hypoglycemia such as sulfonamides or insulin. Renal insufficiency does change dosing; decrease the daily dose to 50 mg for creatinine clearances of 30-50 mL/minute or serum creatinine between 1.7-3 mg/dL in men or 1.5-2.5 mg/dL in women. In severe renal impairment (creatinine clearance less than 30 mL/min or serum creatinine greater than 3 mg/dL) drop the daily dose to 25 mg. Sitagliptin requires the presence of insulin, so use in type 1 diabetes or ketoacidosis is not recommended.

Contraindications: Dosage reduction should be considered in patients with moderate or severe renal impairment and use of this medication has not been studied in severe hepatic failure. Administration is contraindicated with allergy to Sitagliptin or any component of the formulation.

Amylin Analogs - Pramlintide

Mode of Action: This synthetic analog of Amylin, which is co-secreted with insulin, decreases postprandial glucose elevations via the following mechanisms: 1) prolongation of gastric emptying time; 2) decreased glucagon secretion; and 3) centrally mediated appetite suppression resulting in reduced caloric intake.

Profile: Adjunctive treatment with insulin in type 1 patients, or type 2 patients with insulin and with/ without concurrent sulfonylurea and/or metformin that have not obtained optimal glycemic control.

Dosing:

- Type 1 diabetes: 15 mcg subcutaneously immediately prior to meals. Titrate in 15 mcg increments every 3 days if not experiencing significant nausea. Target dose is 30-60 mcg before meals. Consider discontinuation if intolerant of 30 mcg dose. When initiating pramlintide therapy, decrease current insulin dose (rapid and mixed analogs) by 50% to avoid hypoglycemia.
- Type 2 diabetes: 60 mcg subcutaneously immediately prior to meals; after 3-7 days increase to 120 mcg prior to meals if no significant nausea occurs. If nausea occurs at 120 mcg, reduce dose to 60 mcg.

Warnings: Pramlintide has been associated with an increased incidence of insulin induced severe hypoglycemia, generally seen within 3 hours of doses. Frequent pre- and post-dose glucose readings are necessary. Renal dosing adjustment is not required; dialysis patients have not been evaluated. Caution: potential for patient errors due to confusion with measurement of doses (see table below).

The table below is a combination of the tables included in professional and patient education inserts. The first three columns under 'professional' are what is contained in the professional insert. The last two columns illustrate how information is presented in patient leaflets. Issues of concern expressed by the Institute for Safe Medication Practices are that the measurements in professional inserts relate to volume in units, and cc or mL, while patient information describes measurements only in units. Go to http://www.ismp.org/ for more information and counseling tips on how to decrease risk of accidental overdose with pramlintide.

TABLE 10

Professional vs. Patient Information for Pramlintide

| Pramlintide Professional Table | | | Pramlintide Patient Handout Table | | | |
|--------------------------------|---|----------------------|-----------------------------------|-----------------------------------|--|--|
| | | | Pramlintide D | ose Conversion | | |
| Dosage Prescribed (µg) | Increment using U-100 Syringe (Units) | Volume (cc or mL) | If your dose amount is: | Draw up this amount in syringe | | |
| 15 | 2.5 | 0.025 | 15 micrograms | 2 ¹ /2 units | | |
| 30 | 5.0 | 0.050 | 30 micrograms | 5 units | | |
| 45 | 7.5 | 0.075 | 45 micrograms | 7½ units | | |
| 60 | 10.0 | 0.100 | 60 micrograms | 10 units | | |
| 120 | 20.0 | 0.200 | 120 micrograms | 20 units | | |

Contraindications: Known hypersensitivity to pramlintide or any component of the formulation (including Metacresol); diagnosis of gastroparesis (caution with drugs that cause hypomotility); or hypoglycemia unawareness.

Alpha-Glucosidase Inhibitors

Mode of Action: These medications act locally in the small intestine by inhibiting the *a*-glucosidase enzyme to slow digestion of ingested carbohydrates, delay glucose absorption, and reduce the increase in postprandial blood glucose.

Profile: Used as monotherapy or in combination with other medications. Effectiveness has been demonstrated with all agents and insulin and this class of agents modestly reduces glycosylated hemoglobin. Alpha-Glucosidase inhibitors have a high discontinuation rate due to GI side effects.

Dosing:

- Acarbose Initial dose is 25 mg three times daily with first bite of each meal. Increase dose based on effect and tolerance. Maintenance dose is 50-100 mg three times daily. Maximum dose in patients less than 60 kg is 50 mg three times daily; in patients greater than 60 kg it is 100 mg three times daily.
- **Miglitol** Initial dose is 25 mg three times daily with the first bite of meals. Dose is increased to 50 mg three times daily after 4-8 weeks. Maximum dose is 100 mg three times daily.

Warnings: Alpha-glucosidase inhibitors can increase hypoglycemia caused by sulfonylureas. Treatment emergent elevations in transaminases can occur in up to 15% of patients, and are generally asymptomatic and reversible. Gastrointestinal side effects (pain, diarrhea, flatulence) are very common, but tend to abate with time. The mechanism of action makes treatment of hypoglycemia more problematic; complex sugars will not be effective; glucose tablets or IV glucose may be needed.

Contraindications: Major GI disorder (i.e., inflammatory bowel disease, chronic ulceration, malabsorption, or partial intestinal obstruction).

Meglitinides

Mode of Action: Meglitinides are insulin secretagogues, lowering blood glucose by stimulating release of insulin in response to a glucose load. They close adenosine triphosphate-dependent potassium channels in beta cell membranes, resulting in increased calcium influx that induces insulin secretion. They lower both fasting and postprandial blood glucose, with greatest effect postprandially.

Profile: Usually taken 15-30 minutes before meals; can be used as monotherapy or in combination with metformin.

Dosing:

- Nateglinide Initial and maintenance dose is 120 mg three times daily within 15-30 minutes before meals. Patients close to A1c goal may be started at 60 mg three times daily.
- Repaglinide Patients not previously treated or whose A1c <8% start at 0.5 mg within 15-30 minutes of each meal. If already treated or A1c greater than 8%, start at 1-2 mg before each meal. Dosing adjustments are made on fasting blood glucose readings and preprandial doses can be doubled up to 4 mg per dose. Allow at least 1 week before dose adjustments. Maximum daily dose is 16 mg per day.

Warnings: Use caution in patients with moderate to severe hepatic or renal impairment. Hypoglycemia may occur due to over dosage, decreased caloric intake, after severe or prolonged exercise, ethanol ingestion, or combination with other glucose lowering agents. It may be necessary to discontinue therapy and administer insulin if the patient is exposed to significant stress such as infection, surgery, trauma or fever.

Contraindications: Diabetic ketoacidosis, with or without coma; known hypersensitivity to the drug or its inactive ingredients.

TABLE 11Available Anti-Diabetic Combination Products

| Generic Names | Brand Names | Strengths Available |
|--------------------------|--------------|--|
| Glyburide/Metformin | Glucovance | 1.25 mg/250 mg, 2.5 mg/500 mg, 5 mg/500 mg |
| Glipizide/Metformin | Metaglip | 2.5 mg/250 mg, 2.5 mg/500 mg, 5 mg/500 mg |
| Rosiglitazone/Metformin | Avandamet | 1 mg/500 mg, 2 mg/500 mg, 2 mg/1,000 mg, 4 mg/500 mg, 4 mg/1,000 mg |
| Pioglitazone/Metformin | ActoPlus Met | 15 mg/500 mg, 15 mg/850 mg |
| Pioglitazone/Glimepride | Duetact | 30 mg/2 mg, 30 mg/4 mg |
| Rosiglitazone/Glimepride | Avandaryl | 4 mg/1 mg, 4 mg/2 mg, 4 mg/4 mg |
| Sitagliptin/Metformin | Janumet | 50 mg/500 mg, 50 mg/1,000 mg |

REFERENCE SECTION III

AACE Medical Guidelines for Clinical Practice for the Management of Diabetes Mellitus. *Endocrine Practice.* 13(Suppl 1):3-66. May/June 2007

American Diabetes Association. Clinical Practice Recommendations. Standards of medical care in diabetes. *Diabetes Care*. 30(Suppl. 1):S4-S41. 2007

Cada J, Levien T, Baker D. Exenatide Injection. Hospital Pharmacy. 40(11):994-1003. 2005

Cada J, Levien T, Baker D. Pramlintide Acetate. Hospital Pharmacy. 40(7):599-613. 2005

Cada J, Levien T, Baker D. Sitagliptin Phosphate. Hospital Pharmacy. 42(2):133-140. 2007

Drug Facts and Comparisons. Wolters Kluwer Health. 287-312. 2007

Gavin J, Beaser R, Gerich J. Diabetes, Glycemia, and New Hormonal Paradigms: Understanding the Links. Medscape CME Lecture. June 2006

Nogid A, Pham D. Adjunctive Therapy with Pramlintide in Patients with Type I or Type II Diabetes Mellitus. *Pharmacotherapy*. 26(11):1626-1640. 2006

IV. STANDARDS OF CARE FOR DIABETES IN CHILDREN AND ADOLESCENTS

TABLE 12

A. Quick Reference Guide for Pediatric Type 1 and 2 Diabetes

| | ASSESSMENT FREQUENCY CATEGORIES | | | | | | |
|--|---------------------------------|--------|----------------|-------|-------------|-------|-------------|
| | Initially | | Annually | | Other | | Every Visit |
| CENERAL | í. | | | | | | |
| Comprehensive History and Physical | X | | | | | | |
| Brief History and Physical | | | | | | | x |
| Height and Weight | X | | X | | | | X |
| Blood Pressure | X | | X | | | | x |
| Dilated Eve Exam | X (type 2) | | X ¹ | | | | |
| Dental Exam | X | | | | X twice/yr | | |
| Foot Exam | | | | | | | |
| Visual | x | | X (type 1) | | | | X (type 2) |
| Comprehensive | X | | X | | | | |
| Referral to Podiatrist | X^* (type 2) | | X* | | | | |
| Referral to diabetes educator | X | | | | X* | | |
| EKG | X ² | | X2* | | | | |
| Referral to Pediatric Endocrinologist | X* | | | | X quarterly | | |
| LABORATORY EVALUATIONS | | | | | | | |
| Hemoglobin A1c | X | | Х | | X quarterly | | |
| Lipid Profile | Х | | X if no. | rmal, | every 2 yrs | | |
| Comprehensive & Basic Metabolic Panel | X | | Х | | | | |
| UA Microalbumin/Creatine Ratio | X (type 2) | | X ³ | | | | |
| TSH | X* | | Х* | | | | |
| Celiac Disease Screening | X (type 1) | | | | | | |
| Liver Panel | X (type 2) | | X (type 2) | | | | |
| PREVENTION/INTERVENTION | | | | | | | |
| Consider ACE Inhibitors/ARB | X* (type 2) | | Х* | | | | |
| Tobacco Cessation | X* | | | | | | X* |
| Immunizations | X assess cu | rent s | tatus | | X follow AA | P gui | delines |
| Pre/Post Pregnancy Counseling | X* | | X* | | | | |
| Multi-vitamin of Choice | Х | | Х | | | | |
| Consider Comorbidities | Х | | Х | | | | |
| SELF-MANAGEMENT EDUCATION | | | | | | | |
| Psycho-social adjustment | X | | Х | | | | |
| Knowledge of disease (Risks/Complications) | Х | | Х* | | | | |
| Barriers to Care | Х | | | | | | X |
| SMBG/Log | | | | | | | Х |
| Nutrition (MNT) | Х | | Х | | | | |
| Physical Activity | Х | | Х | | | | |
| Weight Management | Х | | Х | | | | |
| Medication Review | X | | Х | | | | |

* Or as indicated per level of control or symptoms

¹ In type 1, 3-5 yrs after diagnosis if >9 years of age

² NA in type 1, as indicated in type 2

³ In type 1, within 5 years of diagnosis or puberty

About 176,500 people aged 20 years or younger have diabetes. This represents about 0.2% of all people in this age group. Approximately one in every 400-600 children and adolescents has type 1 diabetes (www.cdc.gov/diabetes/pubs/estimates05.htm).

Although type 2 diabetes can occur in youth, the nationally representative data that would be needed to monitor diabetes trends in youth by type are not available. Clinically-based reports and regional studies suggest that type 2 diabetes, although still rare, is being diagnosed more frequently in children and adolescents; particularly in American Indians, African Americans, and Hispanic Americans (www. cdc.gov/diabetes/pubs/estimates05.htm).

A team equipped to manage both the physical and emotional growth needs of the child, while working in partnership with parents/guardians, should provide the care for these patients. Early consultation and referral to a pediatric endocrinologist should be strongly considered.

The primary goals of diabetes management in childhood are:

- Ensure an adequate level of knowledge of diabetes to all caregivers and increase self-care so the child can take over the responsibility of the disease as he/she matures.
- Maintain optimal glycemic control to prevent acute and chronic complications.
- Ensure normal growth and development of the child.
- Assist in providing a good quality of life for the child and family.

B. Initial Evaluation

A complete medical evaluation should be performed to diagnose the patient, detect the presence or absence of diabetes complications, formulate a management plan and provide a base for continuing care.

History and Physical Examination

Components of the initial visit for a new diagnosis should include:

Medical History

- Symptoms:
 - Type 1 usually presents with polyuria, polydipsia, polyphagia, weight loss and fatigue; vomiting, abdominal pain and dehydration may be the immediate symptoms that bring the child to medical care
 - Type 2 usually presents as glycosuria, ketones may or may not be present, absent or mild polyuria and polydipsia, ketosis may be present in 25% of the cases, hypertension and lipid disorders may also occur
- Eating patterns, nutritional status, growth and development patterns
- Exercise history
- Presence or history of any infections (urinary tract infections, boils, exacerbation of acne, genital or perineal candidiasis)
- Medications, both prescriptions and over-the-counter (including nutrient and herbal supplements)
- Risk factors for atherosclerosis
- History and treatment of other conditions, including endocrine and eating disorders
- Family history of diabetes and other endocrine disorders (consider PCOS in females with type 2 DM)
- Lifestyle, cultural, psychosocial, educational, and economic factors that might influence the management of diabetes
- Behavior changes/poor performances in school
- Tobacco, alcohol, and/or controlled substance use
- Contraception and reproductive and sexual history
- Immunizations

Physical Exam

- Height and weight (use growth charts for ht/wt, and BMI)
 - Type 1 usually presents as normal or underweight, with recent weight loss (with the increase in childhood obesity this may not always be present), growth failure may also be present
 - Type 2 usually presents as overweight (weight for height is greater than the 85 percentile) with little or no weight loss
- Sexual maturation staging
- Blood pressure and pulse
- Fundoscopic evaluation
- HEENT (head, eyes, ears, nose and throat)
- Thyroid palpation
- Cardiac examination
- Abdominal examination (e.g., for hepatomegaly)
- Evaluation of pulses
- Hand/finger and foot examination
- Skin examination (for acanthosis nigricans in type 2)
- Neurological examination
- Signs of disease that can cause diabetes

Initial Laboratory Evaluation

- If DKA suspected: serum glucose, electrolytes, arterial or venous pH, serum or urine ketones
- If diagnosis of type of diabetes is uncertain, consider testing islet cell antibodies, insulin or c-peptide levels; consultation with a pediatric endocrinologist is recommended prior to testing
- A1c
- Microalbuminuria, if type 2
- TSH yearly in all type 1 patients, in type 2 diabetes if clinically indicated
- Screen for celiac disease in type 1 if family history or clinical suspicion
- Lipid profile once blood glucose control has been achieved

Referrals

- Pediatric endocrinologist, preferably at time of diagnosis
- Diabetes Self-Management Training, including medical nutrition therapy and self-blood glucose monitoring; education goals should be age-specific
- Eye exam in newly diagnosed children with type 2 diabetes (refer children with type 1 within 5 yrs. of diagnosis or at puberty)
- Behavioral specialist, as indicated
- Other specialties and services as appropriate
- Family planning for adolescent females who are sexually active
- Screening for depression in children ≥10 years of age

C. Follow-up Evaluation

Quarterly Assessments:

The health care team should see the child with diabetes at least quarterly. Follow-up visits with the diabetes care team should include assessment of:

- Height, weight, BMI (placed on growth charts)
- Other health or developmental problems, including associated disorders (thyroid or celiac disease; skin, foot, bacterial or fungal problems; eating disorders; depression)
- Glycemic control, including incidence of hypo- and hyperglycemia, A1c
- Injection sites and techniques
- Self-management skills including nutrition, physical activity, and self-blood glucose monitoring

- Changes in performance or behavior (particularly school absences/problems), leisure and sport activities, and psychosocial progress
- Information on driving, employment, tobacco use, sexual activity, drugs and alcohol
- Address any concerns that occur within the family due to having a child with diabetes
- Make referrals to other specialists as needed
- Frequency of hypoglycemia and presence of hypoglycemia unawareness

Yearly Assessments Should Include:

- Screenings for complications including blood and urine tests, blood pressure, eye tests, TSH, lipids, and dental exams
- Puberty and sexual maturation
- Growth
- Immunization status
- Contraceptive use and family planning for sexually active adolescents
- Updating self-management goals with more responsibility for self-care given to the child or adolescent and less with the parent or guardian based upon stage of development and maturity
- For older adolescents, discuss transitioning to adult care
- Screening for family and patient dynamics that may impact diabetes management

D. Target Indicators of Glycemic Control

The American Diabetes Association has published a statement for the care of children and adolescents with type 1 diabetes. The established goals are age specific and set as a reference point. Glycemic control goals must be individualized based upon the age of the child, history of hypoglycemia, and presence of other risk factors.

TABLE 13

| Age-specific values | Preprandial BG* | Bedtime/overnight BG | A1c |
|---------------------|-----------------|----------------------|--|
| < 6 years old | 100-180 mg/dL | 110-200 mg/dL | < 8.5% (but >7.5%) |
| 6-12 years old | 90-180 mg/dL | 100-180 mg/dL | <8% |
| 13-19 years old | 90-130 mg/dL | 90-150 mg/dL | <7.5% or lower if it can be achieved without excessive hypoglycemia |

Age-Specific Target Indicators for Children/Adolescents with Type 1 Diabetes

E. Prevention and Management of Diabetes Complications

Acute

Hypoglycemia

Hypoglycemia is the most frequent acute complication in type 1 diabetes. Mild forms may cause a variety of reversible signs and symptoms characteristic of neurological dysfunction. Severe prolonged hypoglycemia with convulsions has the potential to cause permanent central nervous system impairment, especially in young children.

The blood glucose threshold for an autonomic response will vary based upon the level of metabolic control. With poor control, the response will occur at a higher blood glucose level. In a child with good control, the response will occur at a lower blood glucose level.

^{*} BG throughout these Recommendations means plasma or serum glucose. For a discussion on the ways of measuring glucose in the blood and their differences, see the Appendix, page 93.

Nocturnal Hypoglycemia

The autonomic threshold is lowered during sleep. Nocturnal hypoglycemia is frequent, often prolonged and usually asymptomatic. Counter-regulatory responses may be impaired during sleep. Nocturnal hypoglycemia should be suspected if the pre-breakfast blood glucose is low, or if any of the following occur: nightmares, seizures, periods of confusion with lethargy on awakening, morning headaches, or altered moods. Severe glucosuria with or without mild ketonuria upon arising is considered to be evidence of rebound hyperglycemia following insulin-induced hypoglycemia (Somogyi effect). Testing blood glucose at regular intervals during the night or use of continuous glucose monitoring may confirm nocturnal hypoglycemia. Bedtime blood glucose levels are not predictable of nocturnal hypoglycemia; however, predictability improves with midnight readings.

Prevention

Educating children, adolescents, their families, and other caregivers about hypoglycemia is important. Particular attention should be given to:

- Early warning signs and symptoms
- Usefulness of frequent BG monitoring
- Effects of increased exercise
- Preventive effects of food items high in carbohydrates (especially fiber or those containing resistance starch)
- Emergency source of glucose or sucrose always available
- Providing glucagon and educating on its use
- Understanding of insulin action time and management
- Appropriate BG targets for the day and bedtime
- Wearing proper ID stating the child or adolescent has diabetes

Treatment

It is important to test BG levels to confirm hypoglycemia. When confirmation is made and the child is conscious, administer 5–15 gm of glucose or simple carbohydrates (sports drink, juice, low fat milk, regular soft drink, etc.), wait 15 minutes, retest BG level. If BG has improved, then follow treatment with the next meal or a snack. If BG level has not improved, repeat treatment.

If the child has lost consciousness and/or is having convulsions, treatment is urgent. Administer glucagon 0.5 mg for ages less than 12 years, 1.0 mg for ages 12 years or older, (or 0.1-0.2 mg/10 kg body weight). It is best administered intramuscular. If glucagon is not available, advise family or caregivers to call for emergency personnel.

Diabetes Ketoacidosis (DKA)

DKA can occur under a variety of circumstances. Children may present at diagnosis or after having the disease. DKA presents a greater risk of cerebral edema in children, especially <15 years old. Physicians with experience in dealing with children and DKA (pediatric endocrinologists or intensivists) should direct the care as much as possible. DKA that occurs after diagnosis is commonly due to insulin omission. This may be due to other illnesses, trauma, surgery, emotional stress, eating disorders, or undiagnosed pregnancy. Proper evaluation of children or adolescents with recurrent DKA should occur. Referrals for self-management and/or psychological counseling for the child and family may be recommended.

Chronic

Hypertension

Children and adolescents with diabetes should have their blood pressures obtained and evaluated at each visit. Upward trends even within a normal range may indicate need for further investigation. Parental hypertension can pre-dispose the child to hypertension. Reassessment of the parents' blood pressure should occur as the parents get older.

Definition

Hypertension is defined as an average systolic or diastolic blood pressure \geq 95th percentile for age, gender and height percentile measured on at least 3 separate days. "High-normal" blood pressure occurs when the average systolic or diastolic blood pressure is \geq 90th and <95th percentile for age, gender, and height percentile over 3 different days. Two references are available at:

- www.nhlbi.nih.gov/health/prof/heart/hbp/hbp_ped.pdf
- www.cdc.gov/nchs/about/major/nhanes/ggrowthcharts/charts.htm

Treatment

Lifestyle intervention should be started. Referral for MNT related to hypertension and the DASH guidelines (Dietary Approaches to Stop Hypertension) and exercise should be initiated. Tobacco cessation should occur if indicated. If lifestyle interventions are not enough, then ACE inhibitors can be considered with titration to achieve a blood pressure below the 90th percentile. Additional antihypertensive medication can be considered if ACE inhibitors alone do not control the blood pressure. Educate adolescent females that ACE inhibitors are not indicated in pregnancy.

Dyslipidemia and Cardiovascular Disease

According to the National Education Cholesterol Program for Pediatrics (NCEP-Peds), factors contributing to atherosclerosis in children and youth are the same as adults. Screening should be performed on children with type 1 diabetes >2 years of age after diagnosis once blood glucose control has been established, if there is a family history for CVD or the family history is unknown. Children with type 2 diabetes should be screened once blood glucose control has been resolved. If normal lipid values are obtained, screening should be repeated every 5 years. Optimal lipid levels are based upon the Third Adult Treatment Panel (ATPIII) and the American Heart Association (AHA):

- LDL <100 mg/dL
- HDL >35 mg/dL
- Triglycerides <150 mg/dL.

Treatment

When lipid values are above the recommended targets, the following interventions are recommended:

- Maximize BG control
- Provide nutrition counseling implementing the AHA step 2 diet (dietary cholesterol <200 mg/day and saturated fat <7% of total calories)
- Increase physical activity and decrease sedentary behavior
- Retest lipids at 3 and 6 months to determine if the interventions were effective; if lipid goals are reached retest yearly
- When lipid goals are not met, further intervention is needed based upon LDL levels
 - LDL 100-129 mg/dL maximize nonpharmacologic treatment
 - LDL 130-159 mg/dL consider medication, basing the treatment decision on the child's complete CVD risk profile
 - LDL greater than or equal to 160 mg/dL begin medication
 - Resins are considered first-choice treatment for this age group
 - Statins can be used if compliance with resins is poor and age is >10 years; start at lowest dose and increase based upon LDL levels and side effects; monitor LFTs and discontinue medication if LFTs are greater than three times the upper limit of normal or if child complains of muscle pain or soreness; carefully consider use of statins in sexually active females; discuss the risks associate with this drug in relationship to pregnancy
 - Ezetimibe is recommended if statins alone do not improve the LDL level; carefully consider use of lipid-lowering agents in sexually active females; drug-therapy should be stopped if pregnancy is known or suspected
- When triglycerides are above target, maximize BG control and lifestyle interventions; if levels are greater than 1000 mg/dL, consider treatment with a fibric acid or fish oils
- Minimize other CVD risk factors; achieve and maintain a healthy weight and blood pressure; discourage tobacco use

Retinopathy

The first eye exam should be obtained when the child is ≥ 10 years old and has had diabetes 3-5 years. Annual follow-up is recommended unless otherwise directed by the eye care specialist. A young woman planning pregnancy should receive an eye exam prior to conception and the first trimester. Follow-up exams are at the discretion of the physician.

Nephropathy

Annual microalbuminuria screening should be started once the child is 10 years old and/or has had diabetes for 5 years. An abnormal value should be repeated since a number of factors can impact albumin excretion. Once diagnosis is confirmed, an ACE inhibitor can be titrated to normalize the microalbumin excretion, but exercise caution in females who may become pregnant. Cessation of tobacco use, obtaining normal blood pressure, and treatment of elevated LDL should also occur, when indicated. If this treatment is not successful, referral to a nephrologist is recommended.

Neuropathy

Children do not typically develop neuropathy if they have satisfactory blood glucose control. Education on foot care should be done initially and annually thereafter. Annual foot exams should begin at puberty. In the presence of poor control, patients should be questioned and examined for:

- Symptoms of numbness, pain, cramps, and paresthesia
- Skin sensation, vibration sense and light touch
- Ankle reflexes

F. Therapeutic Options

1. Type 1 Diabetes

Children with type 1 diabetes are dependent on insulin for survival. The most widely used insulin concentration is 100 units/mL (U 100).

Please refer to Table 6 on page 10-11 for a listing of insulins.

Pre-mixed insulin preparations are also available. The use of pre-mixed insulins removes the flexibility offered by separate adjustments of the two types of insulin and is not recommended in the treatment of children.

Insulin Regimens

The choice of the insulin regimen will depend on glycemic goals, age of child, duration of diabetes, lifestyle, and patient/family preferences. Consultation with a pediatric endocrinologist is advised. Frequently used regimens include the following:

- *Two injections daily* of a mixture of short or rapid and intermediate-acting insulins (before breakfast and the main evening meal).
- *Three injections daily* of short or rapid-acting insulin before each meal; intermediate-acting insulin with the evening meal; or variations on this dosing.
- Basal-bolus regimen of short-acting or rapid-acting insulin before main meals; intermediate or long acting insulin at bedtime, and/or before breakfast and/or at lunchtime.
- Insulin pump regimens of rapid-acting insulin used to mimic a basal-bolus routine.

Dosage Guidelines

Insulin dosage varies greatly and changes over time. It requires regular review and reassessment including:

- Age
- Weight
- Stage of puberty
- Duration and phase of diabetes
- State of injection sites

- Nutritional intake and distribution
- Physical activity patterns
- Daily routine
- Results of BG monitoring and A1c
- Intercurrent illness

During the "honeymoon" period, daily insulin dose is often less than 0.5 units/kg/day. Pre-pubertal children usually require 0.7-1.0 units/kg/day. During puberty, requirements may range up to 2 units/kg/ day. The correct dose of insulin is that which achieves the best attainable glycemic control for the child or adolescent.

Distribution of Dose

Children on twice daily regimens may require more (approximately two-thirds) of their total daily insulin in the morning, and less (one-third) in the evening. Approximately one-third of the insulin dose may be short-acting insulin and two-thirds may be intermediate acting insulin, although these ratios change with advanced age and maturity of the child.

On basal-bolus regimes, night time intermediate or long-acting insulin may represent 30-50% of the total daily insulin; 50-70% as rapid or short-acting insulins divided up between three and four pre-meal boluses.

When switching to an insulin pump, the total daily dose of all insulin used may be decreased by approximately 25%. This amount is then divided in half to establish an initial basal rate. The remaining amount is used for the bolus. The basal-bolus amount will vary based upon the child and previous factors listed. Switching to an insulin pump should be done only under the supervision of a pump educator working with the diabetes specialist.

Development of skills in the independent adjustment of insulin doses varies greatly among children and families. Self-management training can assist in helping children and their families become proficient in insulin adjustment techniques.

2. Type 2 Diabetes

Fewer than 10% of youth with type 2 diabetes can be treated with diet and exercise alone; pharmacological intervention is generally required.

Currently, metformin is the only oral medication approved for use in children 10 years and older. Dosage starts at 500 mg once or twice a day. If needed, it can be increased by 500 mg each week to a maximum dose of 2000 mg per day. Consultation with a pediatric endocrinologist is recommended if pharmacological intervention is considered. Renal function should be checked before and then annually, thereafter. Metformin is contraindicated if serum creatinine levels are greater than or equal to 1.4 mg/dL (females) and 1.5 mg/dL (males).

Insulin can also be used to reach euglycemia either alone or with metformin. Insulin regimens may be similar to the type 1 population or basal insulin alone may be needed.

Further Information

The American Diabetes Association (ADA) has further information regarding the management of children with diabetes in schools and camps. This can be found in the ADA Clinical Practice Recommendations or at www.diabetes.org. Other sources for information include:

- Juvenile Diabetes Association: www.jdfcure.org
- Children with Diabetes: www.childrenwithdiabetes.com

REFERENCE SECTION IV

American Diabetes Association. Clinical Practice Recommendations. Standards of medical care in diabetes. *Diabetes Care*. 30(Suppl. 1):S4-S41. 2007

American Diabetes Association. Clinical Practice Recommendations. Management of dyslipidemia in children and adolescents with diabetes. *Diabetes Care*. 26:S194-S197. 2003

American Diabetes Association Statement. Care of Children and Adolescents with Type 1 Diabetes. *Diabetes Care*. 28:186-205. 2005

American Diabetes Association. Type 2 diabetes in children and adolescents. *Diabetes Care*. 23:381-389. 2000

International Society for Pediatric and Adolescent Diabetes (ISPAD). Consensus Guidelines 2000

Kaufman FR. Type 2 diabetes mellitus in children and youth: a new epidemic. *J Pediatric Endocrinology Metabolism*. 15(Suppl. 2):737-744. 2002

Steinberger J, Daniels S. Obesity, insulin resistance, diabetes, and cardiovascular risk in children. AHA Scientific Statement. *Circulation*. 107:1448-1453. 2003

A. Hypertension

Screening and Diagnosis

- Blood pressure should be measured at every routine diabetes visit. Patients found to have systolic blood pressure above 130 mmHg or diastolic blood pressure above 80 mmHg should have blood pressure confirmed on a separate day.
- Orthostatic measurement of blood pressure should be performed to assess for the presence of autonomic neuropathy when clinically indicated.

Treatment

- Patients with diabetes should be treated to a systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg. However, many are now suggesting that lower blood pressure goals may be appropriate.</p>
- Patients with a systolic blood pressure of 130-139 mmHg or a diastolic blood pressure of 80-89 mmHg should be given lifestyle/behavioral therapy alone for a maximum of 3 months. If targets are not achieved, pharmacological intervention should be initiated.
- Patients with systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg should receive drug therapy in addition to lifestyle/behavioral therapy.
- Some drug classes (ACE inhibitors, ARBs, ß-blockers, calcium channel blockers and diuretics) have been repeatedly shown to be particularly beneficial in reducing CVD events during the treatment of uncomplicated hypertension and are therefore preferred agents for initial therapy. All patients should receive at least an ACE inhibitor or an ARB.
- If ACE inhibitors are not tolerated, ARBs may be used. Additional drugs may be chosen from these classes or another drug class to achieve blood pressure goals.
- If ACE inhibitors, ARBs, diuretics, or Tekturna (a direct renin inhibitor) are used, monitor renal function and serum potassium levels.
- Hypertensive patients with micro or macroalbuminuria:
 - In patients with type 1 diabetes, with any degree of albuminuria, ACE inhibitors have been shown to delay the progression of nephropathy.
 - In patients with type 2 diabetes, hypertension and microalbuminuria, ACE inhibitors and ARBs have been shown to delay the progression to macroalbuminuria.
 - In those with type 2 diabetes, hypertension and macroalbuminuria (>300 mg/day), nephropathy, or renal insufficiency, an ARB should be strongly considered and has been shown to delay the progression of nephropathy.
 - In patients with microalbuminuria or overt nephropathy, in whom ACE inhibitors or ARBs are not well tolerated, a non-dihydropyridine calcium channel blocker or ß-blocker should be considered.
 - Whether or not Tekturna slows or prevents the progression of diabetic nephropathy is not yet known.
- In pregnant patients with diabetes and hypertension, blood pressure target goals of 110-129/65-79 mmHg are suggested in the interest of long-term maternal health and minimizing impaired fetal growth. ACE inhibitors and ARBs are contraindicated during pregnancy.
- In patients with a recent myocardial infarction, ß-blockers should also be considered to reduce mortality.
- In elderly hypertensive patients, blood pressure should be lowered gradually to avoid complications.
- Patients not achieving target blood pressure on three drugs, including a diuretic, and patients with a significant renal disease should be referred to a nephrologist.
- See nutrition recommendations for medical nutrition therapy guidelines (pages 49-55).
B. Dyslipidemia

Screening

- Because of frequent changes in glycemic control in patients with diabetes and its effects on levels of lipoprotein, levels of LDL, HDL, total cholesterol, and triglyceride should be measured every year in adult patients.
- Patients with high risk levels who are under treatment for dyslipidemia, or who have high risk comorbid medical conditions, may require measurement of lipids more frequently.
- In children with diabetes, consideration should be given to measuring lipoproteins after age 2 years, as suggested by the National Cholesterol Education Program (NCEP) Report of the Expert Panel on Blood Cholesterol in Children and Adolescents. The recommended frequency for remeasuring lipoproteins in children with diabetes is unknown.

Treatment of Dyslipidemia

- Because all individuals who have diabetes should be considered a CVD risk equivalent:
 - The primary goal is an LDL <100 mg/dL (2.6 mmol/l).
 - Drug therapy is optional for an LDL of 101-129 mg/dL.
 - Drug therapy should be seriously considered for an LDL of >130 mg/dL.
 - A lower LDL cholesterol goal of <70 mg/dL (1.8 mmol/l), using a high dose of a statin, is an option for high risk patients.
- Aggressive therapy of dyslipidemia will reduce the risk of CAD in patients with diabetes.
- Primary therapy should be directed first at lowering LDL levels.
 - The initial therapy should be to use statins; however, if this fails to reach the goal, then the addition of a resin or ezetimibe should be considered.
 - HDL cholesterol goals should be >40 mg/dL (1.0 mmol/l) in men and >50 mg/dL in women.
 - If the HDL is below those levels, a fibric acid such as fenofibrate might be used in patients with LDL cholesterol between 100 and 129 mg/dL.
- The initial therapy for hypertriglyceridemia is improved glycemic control.
 - Triglycerides should be lowered to <150 mg/dL (1.7 mmol/l).
 - Behavioral modification with weight loss, increased physical activity, and moderation of alcohol consumption can be useful in treating hypertriglyceridemia. See nutrition recommendations for medical nutrition therapy guidelines on pages 49-55.
 - Additional triglyceride lowering can be achieved with very high dose statins (for subjects with both high LDL and triglyceride levels) or fibric acid derivatives (gemfibrozil or fenofibrate).
- In some cases when goals are not achieved, combination lipid therapy may be initiated. Several options are available, but these combinations have not been evaluated in outcome studies for either CVD event reduction or safety.
 - The combination of statins with nicotinic acid and especially with gemfibrozil or fenofibrate has been associated with increased risk of myositis, although the risk of clinical myositis (as opposed to elevated creatinine phosphokinase levels) appears to be low.
 - The combination of statins with nicotinic acid is effective in modifying diabetic dyslipidemia (with the largest increases in HDL cholesterol levels), but the combination may worsen hyperglycemia and thus frequent monitoring of glucose levels is recommended to observe for this.
 - Other available combinations include statin and a resin, ezetimibe or Omega-3 polyunsaturated fatty acids.

C. Cardiac Disease

Screening

Screening protocols for hypertension and dyslipidemia are often indicators of coronary risk (see Hypertension and Dyslipidemia Sections). According to a Consensus Panel of the American Diabetes Association (ADA) and American College of Cardiology (ACC), stress testing should be performed for patients with diabetes who have any of the following:

- 1. Typical or atypical cardiac symptoms
- 2. Resting ECG suggestive of ischemia or infarction
- 3. Peripheral or carotid occlusive arterial disease
- 4. Sedentary lifestyle, age 35 or older, and plans to begin a vigorous exercise program

Positive screening is an indication for stress echocardiogram or nuclear stress test and/or cardiac catheterization. Referral to a cardiologist should be initiated.

There are no evidenced-based guidelines for screening the asymptomatic patient with diabetes for CAD.

Treatment

- 1. Aspirin at 81 mg/day or higher
- 2. Treat hypertension and dyslipidemia (see Hypertension and Dyslipidemia sections)
- 3. Aggressive treatment of diabetes
- 4. An ACE inhibitor should be considered in patients >55 years of age, with or without hypertension, who have another CVD risk factor (history of CVD, dyslipidemia, microalbumiuria or tobacco use)
- 5. Beta-blockers should be considered to reduce mortality in patients undergoing major surgery or with a prior myocardial infarction
- 6. Metformin use is contraindicated in patients with treated CHF
- 7. TZDs are associated with fluid retention and their use can be complicated by the development of CHF; caution in their use is advised

D. Peripheral Vascular Disease

Screening

Annually perform a comprehensive foot examination and provide self-care education for patients with diabetes to identify risk factors predictive of ulcers and amputations.

Routine foot examination is the most important means for assessing vascular insufficiency in the lower extremities of patients with diabetes. This should include the use of a monofilament, tuning fork, palpation, and a visual examination including the assessment of:

- Pallor or dependent rubor
- Loss of hair
- Atrophy of skin
- Cornification of the nails
- Fissures or ulcerations
- Temperature demarcation
- Venous-filling time
- Pulse

People with neuropathy should have a visual inspection of their feet at every visit with a health care professional.

Patients at risk should understand the implications of the loss of protective sensation; the importance of foot monitoring on a daily basis; the proper care of the foot, including nail and skin care; and the selection of appropriate foot wear.

Treatment

- Refer patients who smoke or who have prior lower extremity complications to foot care specialists for on-going preventive care and lifelong surveillance.
- Initial screening for peripheral arterial disease should include a history for claudication and an assessment of the pedal pulses. Consider obtaining an ankle-brachial index (ABI), as many patients with peripheral arterial disease (PAD) are asymptomatic.
- The following foot related risk conditions are associated with an increased risk of amputation:
 - Peripheral neuropathy with loss of protective sensation
 - Altered biomechanics in the presence of neuropathy
 - Evidence of increased pressure, such as erythema or hemorrhage under a callous
 - Bony deformity
 - Peripheral vascular disease with decreased or absent pedal pulses
 - A history of ulcers or amputation
 - Severe nail pathology
- Refer patients with significant claudication or a positive ABI to a vascular surgeon for further assessment and consider exercise, medications, and surgical options.
- People with neuropathy or evidence of increased plantar pressure may need to be managed with well-fitted walking shoes or athletic shoes.
- Hypertension, diabetes, and dyslipidemia must be treated vigorously.

Noninvasive vascular testing may include:

- Doppler systolic pressure measurements
- Ankle/brachial index
- Doppler waveform analysis
- Transcutaneous oxygen pressure
- Duplex color flow scanning
- Magnetic resonance angiography (MRA)

Any question of ischemia should necessitate a vascular consultation for the possible need for revascularization.

REFERENCE SECTION V

Aliskiren (Tekturna) for Hypertension. *The Medical Letter on Drugs and Therapeutics*. Issue 1258. 49:29-31. April 2007

American Association of Clinical Endocrinologists Medical Guidelines for the Management of Diabetes Mellitus. The AACE System of Intensive Diabetes Self-Managemement, 2002 Update. *Endocrine Practice.* 8:Supplement 1. January/February 2002

American College of Physicians PIER (Physicians Information and Education Resource). http://pier.acponlin.org

American Diabetes Association. Clinical Practice Recommendations. *Diabetes Care.* 30(Suppl. 1):S15-S16, S16-S17, S18-19, S22-S24. 2007

Aspirin for Primary Prevention of Cardiovascular Disease (Revisited). The Medical Letter on Drugs and Therapeutics. Issue 1258. 48:53. July 2006

Detection, Evaluation and Treatment of High Blood Cholesterol. Adult Treatment Panel III. National Cholesterol Education Program. National Heart, Lung and Blood Institute. National Institutes of Health. NIH Publication No. 01-2670. May 2001

Johnstone M, Veves A. Diabetes and Cardiovascular Disease. Totowa, NJ. Humana Press. 2nd Edition. 2005

Leahy J, Clark N, Cefalu W. Medical Management of Diabetes Mellitus. New York, NY. Marcel Dekker, Inc. 2000

VI: COMPLICATIONS: PREVENTION, SCREENING AND TREATMENT

A. Retinopathy

Definition

Diabetic retinopathy is a highly specific vascular complication of both type 1 and type 2 diabetes that is related in part to the duration of diabetes. It is estimated to be the most frequent cause of new blindness in adults 20-74 years of age. Intensive diabetes and hypertension management has been shown to prevent or delay the development of diabetic retinopathy.

General Recommendations

To prevent or slow the progression of diabetic retinopathy, optimal control of glucose and hypertension is essential. Screening and early detection of diabetic retinopathy offers the opportunity for treatment with laser photocoaugulation surgery, preventing or delaying visual loss.

Screening

- Patients with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 3-5 years after the onset of diabetes.
- In general, evaluation for diabetic eye disease is not necessary before 10 years of age. However, some evidence suggests that the pre-pubertal duration of diabetes may be important in the development of microvascular complications; therefore, clinical judgment should be used when applying these recommendations to individual pediatric patients.
- Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist once blood sugars are stabilized after the initial diagnosis.
- Subsequent examinations for both type 1 and type 2 patients with diabetes should be repeated annually by an ophthalmologist or optometrist. Examinations will be required more frequently if retinopathy is progressing or if symptoms of visual loss develop.
- When planning pregnancy, women with pre-existing diabetes should have a comprehensive eye examination and should be counseled on the risk of development and/or progression of diabetic retinopathy.
- Women with diabetes who become pregnant should have a comprehensive eye examination in the first trimester and close follow-up throughout pregnancy. This guideline does not apply to women who develop gestational diabetes, because such individuals are not at increased risk for diabetic retinopathy.

TABLE 14

Recommended Ophthalmologic Examination Schedule

| Patient Group | Recommended first examination | Minimum routine follow-up* |
|--|--|--|
| Type 1 diabetes | Within 3-5 years after diagnosis of diabetes once patient is age 10 years or older** | Yearly |
| Type 2 diabetes | At time of diagnosis of diabetes | Yearly |
| Pregnancy in pre- existing diabetes | Prior to conception and during first trimester | Physician discretion pending results of first trimester exam |

* Abnormal findings necessitate more frequent follow-up

** Some evidence suggests that the pre-pubertal duration of diabetes may be important in the development of microvascular complications; therefore, clinical judgment should be used when applying these recommendations to individual patients

Treatment

Optimal control of glucose and hypertension are essential in the prevention and treatment of diabetic retinopathy. Patients with any level of macular edema, severe nonproliferative diabetic retinopathy (NPDR), or any proliferative diabetic retinopathy (PDR), require the prompt care of an ophthalmologist. Referral to an ophthalmologist should not be delayed until PDR has developed in patients who are known to have severe nonproliferative diabetic retinopathy or more advanced retinopathy. (See Physical Activity Limitations in Section VII). Patients who experience permanent vision loss from diabetes despite treatment should be encouraged to pursue visual rehabilitation with an ophthalmologist or optometrist who is trained or experienced in low-vision care.

B. Nephropathy

Definition

Diabetic nephropathy occurs in 20-40% of patients with diabetes and is the single leading cause of endstage renal disease (ESRD). Persistent albuminuria in the range of 30-299 mg/24 hr (microalbuminuria) has been shown to be the earliest stage of diabetic nephropathy in type 1 diabetes and a marker for development of nephropathy in type 2 diabetes. Patients with microalbuminuria who progress to macroalbuminuria (>300 mg/24 hr) are likely to progress to ESRD over a period of years.

General Recommendations

To reduce the risk and/or slow the progression of nephropathy, optimize glucose and blood pressure control.

Screening

- Perform an annual test for the presence of microalbuminuria in:
 - Type 1 patients who have had diabetes >5 years
 - All type 2 patients starting at diagnosis
- Screening for microalbuminuria can be performed by three methods:
 - Measurement of the albumin-to-creatinine ratio in a random spot collection
 - 24 hr collection with creatinine, allowing the simultaneous measurement of creatinine clearance
 - Timed (e.g., 4 hr or overnight) collection
- The albumin-to-creatinine ratio in a random spot collection is recommended as screening in most patients because of convenience to patient and ease of obtaining sample; however, longer collections may be needed to confirm or further evaluate some patients

TABLE 15

Definitions of Abnormalities in Albumin Excretion

| Category | Spot Collection | 24 hr collection | Time Collection |
|------------------|--------------------|------------------|-----------------|
| | (µg/mg creatinine) | (mg/24 hr) | (µg/min) |
| Normal | <30 | <30 | <20 |
| Microalbuminuria | 30-299 | 30-299 | 20-199 |
| Macroalbuminuria | ≥300 | ≥300 | ≥200 |

Because of variability in urinary albumin excretion, two of three specimens collected within a 3 to 6 month period should be abnormal before considering a patient to have crossed one of these diagnostic thresholds. Exercise within 24 hours, infection, fever, congestive heart failure, marked hyperglycemia, marked hypertension, pyuria, and hematuria may elevate urinary albumin excretion over baseline values.

Serum creatinine should be measured annually for the estimation of glomerular filtration rate (GFR) in all adults with diabetes regardless of the degree of urine albumin excretion. The serum creatinine alone should not be used to measure kidney function but instead used to estimate the GFR and stage the level of chronic kidney disease. Estimated GFR calculations can be found at http://www.kidney.org/professionals/kdoqi/gfr_calculator.cfm .

| Stage | Description | GFR (mL/min per 1.73 m ² body surface area) |
|-------|---|---|
| 1 | Kidney damage* with normal or increased GFR | ≥90 |
| 2 | Kidney damage* with mildly decreased GFR | 60-89 |
| 3 | Moderately decreased GFR | 30-59 |
| 4 | Severely decreased GFR | 15-29 |
| 5 | Kidney failure | <15 or dialysis |

*Kidney damaged defined as abnormalities on pathologic, urine, blood, or imaging tests Source: *Diabetes Care*, Volume 30, Supplement 1, January 2007

Treatment

- In the treatment of albuminuria/nephropathy both ACE inhibitors and ARBs can be used:
- In hypertensive and nonhypertensive type 1 patients with any degree of albuminuria, ACE inhibitors have been shown to delay the progression of nephropathy.
- In hypertensive type 2 patients with microalbuminuria, ACE inhibitors and ARBs have been shown to delay the progression to macroalbuminuria.
- In patients with type 2 diabetes, hypertension, macroalbuminuria, and renal insufficiency (serum creatinine >1.5 mg/dL), ARBs have been shown to delay the progression of nephropathy.
- If one class is not tolerated, the other should be substituted.
- If ACE inhibitors, ARBs, or diuretics are used, monitor serum potassium levels for the development of hyperkalemia.
- Consider the use of non-DCCBs, ß-blockers, or diurectics in patients unable to tolerate ACE inhibitors or ARBs.
- See medical nutrition therapy guidelines (top of page 55).

End Stage Renal Disease

Consider referral to a nephrologist experienced in the care of diabetic renal disease when either the GFR has fallen to <60 mL/min per 1.73 m² or difficulties have occurred in the management of hypertension or hyperkalemia.

C. Neuropathy

Definition

Diabetic neuropathy is a common complication of diabetes mellitus. It is the most common form of neuropathy in the developed world and is responsible for up to 75% of nontraumatic amputations. Patients who develop autonomic neuropathy have a 25-50% mortality in the next 5 to 10 years. Diabetic neuropathy is a diverse group of syndromes that affect specific regions of the nervous system, either singly or combined. The primary types of diabetic neuropathy are sensorimotor and autonomic.

General Recommendations

Diabetic neuropathy should be suspected in all type 2 patients because many people have had the disease for several years before being diagnosed; and in type 1 patients who have had diabetes greater than 5 years. Early recognition and optimal glycemic control with intensive diabetes management is essential to reduce the risk or slow the progression of diabetic neuropathy.

Screening

Screening for distal symmetric polyneuropathy should be done at diagnosis and at least annually. Once a diagnosis has been established, inspection and evaluation of insensate feet should be done at every medical visit. Screening for autonomic neuropathy should be instituted in type 2 diabetes at diagnosis and in type 1 diabetes five years after diagnosis. Symptoms of autonomic neuropathy including dysfunction, neurovascular dysfunction and hypoglycemia unawareness should be carefully evaluated with every history and review of systems.

Sensorimotor Neuropathy

Diffuse Clinical Neuropathy - can be proximal or distal. Distal symmetric polyneuropathy (DPN) is the most commonly recognized form of diabetic neuropathy. Onset is often insidious and it may involve sensory or motor, small fibers or large fibers or both.

resting tachycardia, exercise intolerance, orthostatic hypotension, constipation, gastroparesis, erectile

TABLE 17

Neuropathy: Types, Findings, Screenings and Treatments

| Type | Typical Findings | Screening/Diagnostics | Treatment |
|---------------------|--|---|---|
| Mono- neuropathy | Acute onset; usually single nerve but can be multiple; self-limited; common nerves affected: C3, C6, ulnar, medial, peroneal | Abnormal sensory tests of vibration, touch or sensation of temperature Abnormal autonomic tests such as reduced heart rate variation with deep breathing, Vallsalva maneuver, and postural testing Abnormal electrodiagnostic tests with decreased nerve conduction velocity or amplitudes | Symptomatic, see Table 18 |
| Entrapment | Gradual onset; single nerves exposed to trauma; progressive; common nerves: median, ulnar, peroneal, and lateral plantar | Abnormal sensory tests of vibration, touch or sensation of temperature Abnormal autonomic tests such as reduced heart rate variation with deep breathing, Vallsalva maneuver, and postural testing Abnormal electrodiagnostic tests with decreased nerve conduction velocity or amplitudes | Rest, splints, medications and surgery, see Table 18 |
| Small Fiber | Burning and superficial pain with allodynia (perception that all stimuli are painful); reduced pain late in condition; defective warm temperature sensation; decreased sweating, dry skin, impaired vasomotion and blood flow, cold foot; reflexes and motor function intact; electrophysiologic silence; loss of cutaneous nerve fibers; increased risk for foot ulceration and infection | Reduced sensitivity to 10-g Semmes-Weinstein monofilament and pricking sensation using Waardenburg wheel Abnormalities in temperature sensation, neurovascular function, pain and autonomic function tests Abnormalities in vibration perception using a 128-Hz tuning fork | Symptomatic, see Table 18 |

| Туре | Typical Findings | Screening/Diagnostics | Treatment |
|-------------|---|---|------------------------------|
| Large Fiber | Impaired vibration perception and position sense; decreased tendon reflexes; deep-seated gnawing, dull, or crushing/cramp-like pain; sensory ataxia; small muscle wasting of feet; weakness of hands and feet; shortening of Achilles tendons; increased blood flow (hot foot); increased risk for diabetic neuroarthopathy (Charcot joint) | Reduced sensitivity to 10-g Semmes-Weinstein monofilament and pricking sensation using Waardenburg wheel Abnormalities in temperature sensation, neurovascular function, pain and autonomic function tests Abnormalities in vibration perception using a 128-Hz tuning fork | Symptomatic, see Table 18 |

Patients with peripheral neuropathy are at greater risk of foot infection, ulcers and amputation. The identification, examination, prevention and management of such patients will be discussed in the preventive foot care section (page 39).

Treatments

The goal of treatment is to achieve optimal glycemic control through intensive diabetes management. For pharmacological treatment of painful neuropathy see Table 18 below. Patients who do not respond to treatment should be referred to a health care specialist with experience in the management of neuropathy and chronic pain.

TABLE 18

| Distal S | ymmetric | Polyneuropathy | (DPN) | Treatments |
|----------|----------|----------------|-------|------------|
|----------|----------|----------------|-------|------------|

| Class | Examples | Typical doses* |
|---------------------------------|-----------------|---|
| Tricyclic drugs | Amitriptyline | 10-75 mg at bedtime |
| | Nortriptyline | 25-75 mg at bedtime |
| | Imipramine | 25-75 mg at bedtime |
| Anticonvulsants | Gabapentin | 300-1,200 mg three times per day |
| | Carbarnazepine | 200-400 mg three times per day |
| | Pregabalin | 100 mg three times per day |
| 5-hydroxytryptamine and | Duloxtine | 60-120 mg daily |
| norepinephrine uptake inhibitor | | |
| Substance P inhibitor | Capsaicin cream | 0.25-0.75% applied 3 to 4 times per day |

* Dose response may vary. Initial doses need to be low and titrated up.

Autonomic Neuropathy

Diabetic autonomic neuropathy can cause dysfunction of every system of the body. Autonomic neuropathy is often unrecognized because of its insidious onset and multisystem involvement. Patients who develop autonomic neuropathy have a 25-50% mortality in the next 5 to 10 years. Sudden death and silent myocardial ischemia have been attributed to cardiovascular autonomic neuropathy (CAN) in diabetes. Often autonomic neuropathy is not recognized until significant symptoms occur. It is rare (though not impossible) to find involvement of any other organ system in the absence of cardiovascular autonomic dysfunction. Therefore, tests for cardiac autonomic neuropathy can be used as a surrogate for the diagnosis of autonomic neuropathy of any system (see Table 20). Since many conditions affect the autonomic neuropathy rests with establishing the diagnosis and excluding other causes.

TABLE 19Autonomic Neuropathy: Types of Clinical Manifestations

| Туре | Clinical Manifestations |
|-----------------------|---|
| Cardiovascular | Tachycardia, exercise intolerance, cardiac denervation, painless myocardial infarction, orthostatic hypotension, heat intolerance, alterations in skin blood flow |
| Gastrointestinal | Esophageal dysfunction, gastroparesis diabeticorum [*] , diarrhea, constipation, fecal incontinence |
| Genitourinary | Erectile dysfunction, retrograde ejaculation, cystopathy, neurogentic bladder |
| Sweating disturbances | Areas of symmetrical anhydrosis, gustatory sweating |
| Metabolic | Hypoglycemia unawareness, hypoglycemia unresponsiveness |
| Pupillary | Decreased diameter of dark-adapted pupil, Argyll-Robertson-type pupil |

* See Gastroparesis, Section D, next page

TABLE 20

Diagnostic Tests of Cardiovascular Autonomic Neuropathy

| Test | Method/Parameters |
|---|---|
| Resting heart rate | >100 beats/min is abnormal. |
| Beat-to-beat heart rate variation (HRV) | With the patient at rest and supine (no overnight coffee or hypoglycemic episodes), breathing 6 breaths/min, heart rate monitored by EKG or ANSCORE device, a difference in heart rate of >15 beats/ min is normal and <10 beats/min is abnormal, R-R inspiration/R-R expiration >1.17. All indices of HRV are age-dependent. |
| Heart rate response to standing | During continuous EKG monitoring, the R-R interval is measured at beats 15 and 30 after standing. Normally, a tachycardia is followed by reflex bradycardia. The 30:15 ratio is normally >1.03. |
| Heart rate response to Valsalva maneuver | The patient forcibly exhales into the mouthpiece of a manometer to 40 mmHg for 15 seconds during EKG monitoring. Healthy subjects develop tachycardia and peripheral vasoconstriction during strain and an overshoot bradycardia and rise in blood pressure with release. The ratio of longest R-R/shortest R-R should be >1.2. |
| Systolic blood pressure response to standing | Systolic blood pressure is measured in the supine subject. The patient stands and the systolic blood pressure is measured after 2 min. Normal response is a fall of <10 mmHg, borderline is a fall of 10-29 mmHg, and abnormal is a fall of >30 mmHg with symptoms. |
| Diastolic blood pressure response to isometric exercise | The patient squeezes a hand grip dynamometer to establish a maximum. Grip is then squeezed at 30% maximum for 5 min. The normal response for diastolic blood pressure is a rise of >16 mmHg in the other arm. |
| EKG QT/QTc intervals | The QTc (corrected QT interval on EKG) should be <440 ms. |

Treatment

The most important issue in preventing and managing diabetic neuropathy is optimal glycemic control. Intensive diabetes management has been shown to significantly reduce the risk of developing neuropathy and also prevent further progression of neuropathy once it has developed. Specific treatments for autonomic neuropathy focus on symptom management. These treatments may not change the underlying pathology or course of the disease, but may improve the patient's quality of life.

D. Gastroparesis

Definition

Gastrointestinal symptoms are common in patients with diabetes. These arise from autonomic neuropathy affecting the gastrointestinal tract resulting in esophageal, stomach, small intestines and colon disorders. Gastrointestinal symptoms can include dysphagia, heartburn, nausea and vomiting, abdominal pain, constipation, diarrhea, and fecal incontinence.

Gastroparesis can be one of the most debilitating gastrointestinal complications of diabetes. It is estimated that approximately 25% of patients with diabetes have gastroparesis, although many patients with gastroparesis remain undiagnosed.

Gastroparesis results from gastric motility dysfunction that occurs as a consequence of impaired vagal nerve function. This results in impaired gastric emptying which causes the symptoms of esophageal reflux, and the other symptoms listed below.

General Recommendations

Routine glucose monitoring can assist in early recognition of gastroparesis. Maintain optimal glycemic control to prevent or delay the onset and progression of gastroparesis.

Screening

Gastroparesis is an under-recognized cause of erratic glucose control. Because gastric emptying is delayed, mealtime carbohydrate absorption is also delayed in the small intestines. Patients with gastroparesis, especially those on rapid acting pre-meal bolus insulin, may have early postprandial hypoglycemia with late postprandial hyperglycemia because of this mismatch between glucose absorption and insulin action. Unfortunately, even if the diagnosis of gastroparesis is made, often this effect is unpredictable and difficult to manage. Insulin pump therapy may be indicated to control hypoor hyperglycemia.

Symptoms

Typical symptoms may include the following, although keep in mind that many patients may have only some or none of these:

- Nausea/Vomiting
- Abdominal pain
- Bloating
- Early satiety
- Anorexia

Diagnostic Studies

When gastroparesis is suspected, other GI conditions must be ruled out, including gastritis and ulcer disease. Although esophagogastroduodenoscopy or barium series may suggest gastroparesis, especially if food is found retained in the stomach after an 8 to 12 hour fast, neither of these is sensitive enough to diagnose gastroparesis.

The gold standard evaluation of gastroparesis is nuclear medicine double-isotope scintigraphy. A radiolabeled meal is consumed which allows for measurement of gastric emptying. This test is used for diagnosis but can also be used to assess response to therapy.

Treatment

The most important initial therapy for gastroparesis is attaining excellent glycemic control. Hyperglycemia significantly interferes with gastric motility and improved glucose control can improve gastric motor dysfunction. Most patients with significant gastroparesis will require pharmacotherapy. There are a few options available to be considered:

Metoclopramide

A dopamine agonist is often the initial medication used to treat gastroparesis; however, effectiveness of this drug may wane over time. Some of these patients may respond to reintroduction after a

period of withdrawal. Side effects include drowsiness, lethargy, and depression. Extrapyramidal symptoms can also occur. This drug can reduce seizure threshold in patients with a seizure disorder.

Erythromycin

Increasing both liquid and solid emptying, erythromycin appears to be an effective alternative to more traditional forms of treatment, especially in patients where those treatments have failed. Its effectiveness also seems to diminish with time and there are concerns about antibiotic resistance problems with long term use.

Cisapride

This drug was once used commonly as a treatment for gastroparesis; however, because it has the potential to induce prolonged QT syndrome and therefore ventricular tachycardia, it has essentially been taken off the market except under special circumstances.

Domperidone

Not currently available in the United States, it is mentioned here because it is beginning to be used more frequently in patients with refractory gastroparesis. It seems to be more effective in patients who initially responded well to metoclopramide, but who could not continue because of side effects. It reportedly has less central nervous system side effects than metoclopramide and may have a longer duration of efficacy.

Other

There are several other pharmacologic agents under investigation, but they are not yet available in the United States. Nonpharmacologic treatment options are also currently being studied such as gastric pacing.

E. Preventive Foot Care

Risk identification

- Foot care risk identification and preventive management are essential for people with diabetes.
- The risk of ulcers or amputations is increased in people who have had diabetes >10 years, are male, have poor glucose control, or have cardiovascular, retinal, or renal complications.
- The following foot-related risk conditions are associated with an increased risk of amputation:
 - Peripheral neuropathy with loss of protective sensation
 - Altered biomechanics (in the presence of neuropathy)
 - Evidence of increased pressure (erythema, hemorrhage under a callus)
 - Bony deformity
 - Peripheral vascular disease (decreased or absent pedal pulses)
 - A history of ulcers or amputation
 - Severe nail pathology

Risk Assessment Guidelines

Risk Category 0 - No sensory loss, no deformity, palpable pulses, no history of ulcer: annual foot exam.

Risk Category 1 - Sensory loss, no deformity, palpable pulses, no history of ulcer: consider diabetic depth shoes, and biannual foot exam.

Risk Category 2 - Sensory loss, deformity, +/- palpable pulses, no history of ulcer: bimonthly foot exam, debridement of nails and callus, and depth shoes.

Risk Category 3 - Sensory loss, deformity, +/- palpable pulses, history of ulcer: at least bimonthly foot exam, debridement of nails and callus, depth shoes. This category often needs custom modified shoe inserts.

Foot Examination

- All individuals with diabetes should receive an annual comprehensive foot examination to identify high-risk foot conditions.
- This examination should include assessment of protective sensation, foot structure and biomechanics, vascular status, and skin integrity.
- People with one or more high-risk foot conditions should be evaluated more frequently for the development of additional risk factors.
- People with neuropathy should have a visual inspection of their feet at every visit with a health care professional.
- Evaluation of neurological status in the low-risk foot should include a quantitative somatosensory threshold test, using the Semmes-Weinstein 5.07 (10 gm) monofilament.
- Initial screening for peripheral vascular disease should include a history for claudication and an assessment of the pedal pulses.
- The skin should be assessed for integrity, especially between the toes and under the metatarsal heads.
- The presence of erythema, warmth, or callus formation may indicate areas of tissue damage with impending breakdown.
- Bony deformities, limitation in joint mobility, and problems with gait and balance should be assessed.

Prevention of High Risk Conditions

- Distal symmetric polyneuropathy is one of the most important predictors of ulcers and amputation.
- The development of neuropathy can be delayed significantly by maintaining glycemic levels to as near normal as possible.
- Tobacco cessation should be encouraged to reduce the risk of vascular disease complications.

Referral to Foot Care Specialist

• Patients with high risk conditions as outlined above should be referred to a podiatrist or other health care professional with experience and training in foot care.

Management of High Risk Conditions

- People with neuropathy or evidence of increased plantar pressure may be adequately managed with well-fitted walking shoes or athletic shoes.
- Patients should be educated on the implications of sensory loss and the ways to substitute other sensory modalities (hand palpation, visual inspection) for surveillance of early problems.
- People with evidence of increased plantar pressure (e.g., erythema, warmth, callus, or measured pressure) should use footwear that cushions and redistributes the pressure.
- Callus debridement with a scalpel can be performed by a foot care specialist or other health care professional with experience and training in foot care.
- People with bony deformities (e.g., hammertoes, prominent metatarsal heads, bunions) may need extra-wide shoes or depth shoes.
- People with extreme bony deformities (e.g., Charcot foot) that cannot be accommodated with commercial therapeutic footwear may need custom-molded shoes.
- People with symptoms of claudication should receive further vascular assessment.
- Exercise therapy and surgical options may be considered.
- People with a history of ulcers should be evaluated for the underlying pathology that led to the ulceration and be managed accordingly.
- Minor skin conditions such as dryness and tinea pedis should be treated to prevent the development of more serious conditions.

Patient Education

- Patients with diabetes and high-risk foot conditions should be educated regarding their risk factors and appropriate management.
- Patients at risk should understand the implications of the loss of protective sensation, the importance of foot monitoring on a daily basis, the proper care of the foot, including nail and skin care, and the selection of appropriate footwear.
- Patients with neuropathy should be advised to break in new shoes gradually to minimize the formation of blisters and ulcers.
- Patients with visual difficulties, physical constraints preventing movement, or cognitive problems that impair their ability to assess the condition of the foot and to institute appropriate responses will need other people, such as family members, to assist in their care.
- The patient's understanding of these issues and their physical ability to conduct proper foot surveillance and care should be assessed.
- Patients at low risk may also benefit from education on foot care and footwear.

F. Hypoglycemia

Hypoglycemia occurs from an excess of insulin in the blood and results in excessively low blood glucose levels. The level of glucose that produces symptoms of hypoglycemia varies from person to person and for the same person under different circumstances. Hypoglycemia may occur rapidly and might be associated with typical warning signs such as rapid heartbeat, perspiration, shakiness, anxiety, and hunger. When symptoms occur, corrective action can be taken by eating carbohydrates. A hypoglycemic reaction is not ordinarily associated with a loss of consciousness or a seizure. However, if warning signs are absent or ignored and the blood glucose level continues to fall, more severe hypoglycemia may lead to an alteration of mental function that proceeds to confusion, stupor, and finally to unconsciousness. Most individuals with diabetes never suffer such severe hypoglycemia. Those who experience recurrent episodes should be individually evaluated for occupational, recreational and lifestyle variances that may be precipitating hypoglycemia.

Hypoglycemia rarely occurs in people with diabetes who are only treated with medical nutrition therapy (MNT) and exercise and is rare in people treated with α -glucosidase inhibitors, biguanides, or thiazolidinediones. Except in elderly or chronically ill individuals or in association with prolonged fasting, severe hypoglycemia is unlikely to occur when appropriate doses of any oral glucose-lowering agents are used to manage blood glucose. Most people recognize the early warning signs of hypoglycemia and can quickly counteract them by eating. Thus, the proper use of systems that allow rapid and accurate self-monitoring of blood glucose levels can assist people in avoiding significant hypoglycemia. Thus, most people with diabetes can manage their condition in such a manner that there is a minimal risk of incapacitation from hypoglycemia.

REFERENCE SECTION VI

American Diabetes Association. Clinical Practice Recommendations. Standards of medical care in diabetes. *Diabetes Care.* 30(Suppl. 1):S14, S19-S23, S25. 2007

Aring A, Jones D, and Falko J. Evaluation and prevention of diabetic neuropathy. *American Family Physician*. 71(11):2123-2128. June 2005

Funnell MM. The Diabetes Attitudes, Wishes, and Needs (DAWN) Study. *Clinical Diabetes*. 24(4):154-155. October 2006

http://www.fda.gov/medwatch/safety.htm

Vinik A. *Diabetic Neuropathies*. Chapter 35. http://www.endotext.org/diabetes/diabetes28/diabetes28. htm. December 2002

Vinik AI, Erbas T, Pfeifer M, Feldman E, Stevens M, Russell J. Diabetic autonomic neuropathy. In: Porte D, Ellenberg M, Rifkin H, Sherwin RS, Baron A. *Ellenberg and Rifkin's Diabetes Mellitus*. 6th edition. New York, NY. McGraw-Hill. P789-804. 2002

Vinik AI, Maser RE, Mitchell BD, Freeman R. Diabetic autonomic neuropathy. *Diabetes Care.* 226:1553-1579. 2003

A. Aspirin Therapy

- Use aspirin therapy as a secondary prevention strategy in men and women with diabetes who have evidence of large vessel disease. This includes those with a history of myocardial infarction, vascular bypass procedure, stroke or transient ischemic attack, peripheral vascular disease, claudication, and/ or angina.
- In addition to treating the primary cardiovascular risk factor(s) identified, consider aspirin therapy as a primary prevention strategy in type 1 or type 2 diabetes; in particular, subjects with the following:
 - A family history of coronary heart disease
 - Tobacco use
 - Hypertension
 - Obesity
 - Albuminuria (micro or macro)
 - Dyslipidemia
 - Age >30 years
- Use enteric-coated aspirin in doses of 81-325 mg/day.
- In patients with severe CVD, clopidrogel can be used in conjunction with aspirin therapy.
- People with aspirin allergy, bleeding tendency, recent gastrointestinal bleeding, and clinically active hepatic disease are not candidates for aspirin therapy. Other antiplatelet agents may be an option for these patients.
- Use of aspirin has not been studied in individuals with diabetes who are under the age of 30 years.
- Aspirin therapy should not be recommended for patients under the age of 21 years because of the increased risk of Reye's syndrome associated with aspirin use.

B. Tobacco Cessation

Assessment of tobacco use and history

Systematic documentation of a history of tobacco use must be obtained from all adolescent and adult individuals with diabetes.

Counseling on tobacco prevention and cessation

- All health care providers should advise individuals with diabetes not to initiate use of tobacco.
- This advice should be consistently repeated to prevent smoking and other tobacco use among children and adolescents with diabetes under age 21 years.
- Among tobacco users, cessation counseling must be completed as a routine component of diabetes care.
- Every user of tobacco products should be urged to quit in a clear, strong, and personalized manner that describes the added risks of tobacco use and diabetes.
- Every tobacco user should be asked if he or she is willing to quit at this time:
 - If no, initiate brief and motivational discussion regarding the need to stop using tobacco, the risks of continued use, and encouragement to quit as well as support when ready.
 - If yes, assess preference for and initiate either minimal, brief, or intensive cessation counseling and offer pharmacological supplements as appropriate.
 - Refer to Wyoming Quitline, 1-866-WYO-QUIT or 1-866-996-7848 or www.wy.quitnet.com .

C. Immunization

Influenza

• Consistent with the recommendations of the Advisory Committee on Immunization Practices (ACIP), the influenza vaccine should be recommended every year for patients with diabetes, age 6 months and older, beginning each September.

- The ACIP recommends two doses of influenza vaccine administered at least 1 month apart (the last administered before December) for children <9 years of age who have never been vaccinated.
- Vaccination of health care workers and family of patients with diabetes may prevent person-toperson transmission.

Pneumococcal

- According to the ACIP, pneumococcal vaccination is indicated to reduce invasive disease from pneumococcus in people with diabetes.
- There is insufficient evidence to support revaccination of people with diabetes unless other special circumstances exist.
 - A one-time revaccination is recommended for individuals >64 years of age previously immunized when they were <65 years of age if the vaccine was administered more than 5 years prior.
 - Other indications for repeat vaccination potentially relevant to patients with diabetes include:
 - nephrotic syndrome
 - chronic renal disease
 - other immunocompromised states, such as post-organ transplantation.
- Pneumococcal vaccine may be administered with other vaccines (by a separate injection in another anatomic site) without an increase in side effects or decrease in efficacy.

D. Physical Activity/Exercise

Physical activity is one of the cornerstone management tools for diabetes. However, according to the U.S. Surgeon General, less than 30% of adults in the U.S. are currently achieving regular physical activity. This is also true of Wyoming residents. The current recommendations call for individuals to obtain 30-60 minutes of moderate to vigorous activity most days to help reduce the incidence of obesity, cardiovascular disease, and diabetes.

The benefits derived from activity for individuals with diabetes are improved insulin sensitivity; increased fibrinolysis; and decreased blood pressure, C-reactive protein, lipids, glucose levels, body fat and weight. There may also be a decrease in the need for exogenous insulin and oral medication. People often experience an improvement with symptoms associated with depression and stress.

Physical activity is a useful therapeutic tool in patients with, or at risk for, diabetes. However, like any therapy its effects must be thoroughly understood. This means that the diabetes health care team should understand how to analyze the risks and benefits of physical activity in a given patient.

Evaluation of the Patient Before Exercise

- Before increasing usual patterns of physical activity or an exercise program, the individual with diabetes should undergo a detailed medical evaluation with appropriate diagnostic studies.
- A careful medical history and physical examination should focus on the signs and symptoms of disease affecting the heart and blood vessels, eyes, kidneys, feet, and nervous system.

Cardiovascular System

- A graded exercise test is recommended if a patient, about to begin a moderate- to high-intensity physical activity program, is at high risk for underlying cardiovascular disease, based on one of the following criteria:
 - Age >35 years
 - Age >25 years and
 - Type 2 diabetes of >10 years duration
 - Type 1 diabetes of >15 years duration
 - Presence of any additional risk factor for coronary artery disease
 - Presence of microvascular disease (proliferative retinopathy or nephropathy, including microalbuminuria)
 - Peripheral vascular disease
 - Autonomic neuropathy

- In patients who exhibit nonspecific electrocardiogram (ECG) changes in response to exercise, or who have nonspecific ST and T wave changes on the resting ECG, alternative tests such as radionuclide stress testing may be performed.
- In patients planning to participate in low-intensity forms of physical activity (<60% of maximal heart rate) such as walking, the physician should use clinical judgment in deciding whether to recommend an exercise stress test.
- Patients with known coronary artery disease should undergo a supervised evaluation of the ischemic response to exercise, ischemic threshold, and the propensity to arrhythmia during exercise. In many cases, left ventricular systolic function at rest and in response to exercise should be assessed.

Peripheral Arterial Disease

- Evaluation of peripheral arterial disease (PAD) is based on signs and symptoms, including intermittent claudication, cold feet, decreased or absent pulses, atrophy of subcutaneous tissues and hair loss.
- Treatment for intermittent claudication is tobacco cessation and a supervised physical activity program.
- The presence of a dorsalis pedis and posterior tibial pulse does not rule out ischemic changes in the forefoot. If there is any question about blood flow to the forefoot and toes on physical examination, toe pressures as well as Doppler pressures at the ankle should be carried out.

Retinopathy

In patients who have active proliferative diabetic retinopathy (PDR), strenuous activity may precipitate vitreous hemorrhage or traction retinal detachment. These individuals should avoid anaerobic exercise and physical activity that involves straining, jarring, or Valsalva-like maneuvers.

Considerations for Activity Limitation in Diabetic Retinopathy

| Level of Retinopathy | Acceptable Activities | Discouraged Activities | Ocular Reevaluation |
|-------------------------------|--|--|--|
| None | Dictated by medical status | Dictated by medical status | 12 months |
| Mild, nonproliferative | Dictated by medical status | Dictated by medical status | 6-12 months |
| Moderate, nonproliferative | Dictated by medical status | Activities that dramatically elevate blood pressure; power lifting, heavy valsalva | 4-6 months |
| Severe, nonproliferative | Dictated by medical status | Activities that substantially increase systolic blood pressure, valsalva maneuvers, and active jarring, boxing, heavy competitive sports | 2-4 months (may require laser surgery) |
| Proliferative | Low impact, cardiovascular conditioning, swimming, walking, low impact aerobics, stationary cycling, endurance exercises | Strenuous activities, valsalva maneuvers, pounding or jarring, weight lifting, jogging, high-impact aerobics, racquet sports, strenuous trumpet playing | 1-2 months (may require laser surgery) |

TABLE 21

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Nephropathy

- Specific physical activity recommendations have not been developed for patients with incipient microalbuminuria (>30 mg/24 hr albumin excretion) or overt nephropathy (>300 mg/24 hr).
- There is no clear reason to limit low-to-moderate-intensity forms of activity in patients with nephropathy, but high-intensity or strenuous physical activity should probably be discouraged in these individuals unless blood pressure is carefully monitored during exercise.

Neuropathy: peripheral

Peripheral neuropathy (PN) is an indication to limit weight-bearing exercise. Repetitive exercise on insensitive feet can ultimately lead to ulceration and fractures.

TABLE 22

| Exercises | for | Patients | with | Loss | of | Protective | Sensation |
|-----------|-----|----------|------|------|----|------------|-----------|
|-----------|-----|----------|------|------|----|------------|-----------|

| Contraindicated exercise | Recommended exercise |
|--------------------------|-----------------------------------|
| Treadmill | Swimming |
| Prolonged walking | Bicycling |
| Jogging | Rowing |
| Step exercises | Chair exercises |
| | Other non-weight-bearing exercise |
| | Resistant arm exercises |

Neuropathy: autonomic

- Autonomic neuropathy may limit an individual's physical activity capacity and increase the risk of an adverse cardiovascular event during physical activity.
- Resting or stress thallium myocardial scintigraphy is an appropriate noninvasive test for the presence and extent of macrovascular coronary artery disease in these individuals.
- Hypotension and hypertension after vigorous physical activity are more likely to develop in patients with autonomic neuropathy, particularly when starting a physical activity program.
- Because these individuals may have difficulty with thermoregulation, they should be advised to avoid physical activity in hot or cold environments and to be vigilant about adequate hydration.

Exercise and type 1 diabetes

People with type 1 diabetes are at greater risk to develop hypoglycemia during exercise. General guidelines that may prove helpful in preventing hypoglycemia can be summarized as follows:

- 1. Metabolic control before physical activity:
 - Avoid physical activity if fasting glucose levels are >250 mg/dL and ketosis is present, and use caution if glucose levels are >300 mg/dL and no ketosis is present
 - Ingest added carbohydrate if glucose levels are <100 mg/dL
- 2. Blood glucose monitoring before and after physical activity:
 - Identify when changes in insulin or food intake are necessary
 - Learn the glycemic response to different physical activity conditions
- 3. Food intake:
 - Consume added carbohydrate as needed to avoid hypoglycemia
 - Carbohydrate-based foods should be readily available during and after physical activity

General exercise recommendations

- Aerobic physical activity should be recommended, but taking precautionary measures for physical activity involving the feet is essential for many patients with diabetes.
 - The use of silica gel or air midsoles as well as polyester or blend (cotton-polyester) socks to prevent blisters and keep the feet dry is important for minimizing trauma to the feet.
 - Proper footwear is essential and must be emphasized for individuals with peripheral neuropathy.

- Individuals must be taught to monitor closely for blisters and other potential damage to their feet, both before and after physical activity.
- A diabetes identification bracelet or shoe tag should be clearly visible when exercising.
- Proper hydration is essential, as dehydration can affect blood glucose levels and heart function adversely. Adequate hydration prior to physical activity is recommended (e.g., 17 ounces of fluid consumed 2 hours before physical activity).
- Precautions should be taken when exercising in extremely hot or cold environments.
- Moderate weight training programs that utilize light weights and high repetitions can be used for maintaining or enhancing upper body strength in nearly all patients with diabetes.
- High-resistance exercise using weights may be acceptable in some individuals with diabetes. However, caution should be used in older individuals or those with long-standing diabetes.

Special population groups

Pregnancy

Women with pre-existing diabetes can exercise during pregnancy. Women on insulin may need to be continuously monitored and their insulin adjusted to normalize blood glucose levels. If the woman has vascular complications, the recommendations for any patient with vascular compromise should be followed.

Gestational diabetes is considered a state of insulin resistance. Exercise has been shown to improve blood glucose levels by improving peripheral resistance to insulin.

Recommendations from the American College of Obstetricians and Gynecologists for exercise in pregnancy include:

- Regular exercise (at least 3 times a week) is preferred to intermittent activity.
- Moderate exercise: one that doesn't cause fetal distress, low infant birth weight or uterine contractions.
 - Example: arm exercises in a sitting position, before a meal, using 2 lb. cans of food. Do this for 20 minutes 3 times a week. Discontinue if a contraction is felt. It is a good cardiovascular workout if the patient cannot sing "Row, row, row your boat . . . dream" all in one breath.
- Avoid the supine position after the first trimester. Prolonged periods of motionless standing should also be avoided.
- Since there is a decrease in available oxygen for aerobic activity during pregnancy, women should be encouraged to modify the intensity of their exercise according to maternal symptoms. They should stop exercising when fatigued and not exercise to exhaustion.
- Morphologic changes in pregnancy should serve as a relative contraindication to types of exercise in which loss of balance could be detrimental to maternal or fetal well being. Activity that involves the potential of even mild abdominal trauma should be avoided.
- Care should be taken to ensure adequate caloric intake to meet the needs of exercise and pregnancy.
- Women who exercise during the first trimester should be taught to augment heat dissipation by ensuring adequate hydration, appropriate clothing, and optimal environmental surroundings.
- Contraindications for exercising during pregnancy include:
 - Pregnancy-induced hypertension
 - Pre-term rupture of membrane
 - Pre-term labor during the prior or current pregnancy
 - Incompetent cervix
 - Persistent second to third trimester bleeding
 - Intrauterine growth retardation

Further guidelines on pregnancy, diabetes, and exercise can be found in *Guidelines for Exercise Testing* and *Prescription* from the American College of Sports Medicine; and *The Health Professional's Guide* to *Diabetes and Exercise* from the American Diabetes Association.

Children

Hypoglycemia is the most frequent problem associated with type 1 diabetes in children during exercise. This is due to an increase in insulin sensitivity and a decrease of glucagon stores. Hypoglycemia can be minimized by providing snacks before, during, and after the activity, depending upon the type of the activity and the timing of the insulin being used.

The physical needs of children should be assessed prior to implementing an exercise plan. The necessary adjustments of food intake and/or insulin adjustments must be made. Care should also be taken to assess the child's feelings about their disease and their willingness to address hypoglycemia in front of their peers.

Children with type 2 diabetes benefit from exercise similar to adults. Since these children are often overweight, they may need assistance with overcoming barriers that may exist for developing an exercise program (e.g., teasing, lack of support, lack of skills, etc.).

Exercise prescription

According to the American Heart Association, between 700-2000 calories/week should be expended for physical conditioning and health benefits. When planning an exercise program, individuals should be taught the FITT method: frequency, intensity, type, and time.

Frequency

Evidence indicates that little health benefits are derived when exercise is <2 days a week. The American College of Sports Medicine recommends exercise be performed at least 3 nonconsecutive days each week and ideally 5 days a week. Individuals trying to lose weight may need to complete 6-7 days a week until target weight is reached.

Intensity

Health care providers need to consider the intensity with which each person with diabetes should exercise. Special consideration should be given to those with known coronary artery disease, autonomic neuropathy and those receiving medications like ß-blockers. Based upon recommendations from the American College of Sports Medicine, the minimum training intensity for aerobic health benefits is 60% of the maximal heart rate, which can be estimated by the equation HRmax = 220 minus the individual's age. This also equates to a rating of perceived exertion (RPE) of 12 on the Borg 6-20 scale.

TABLE 23

Borg 6-20 Perceived Exertion Scale

| Rating of Perceived Exertion (RPE) | Verbal Description | Rating of Perceived Exertion (RPE) | Verbal Description |
|---------------------------------------|--------------------|---------------------------------------|--------------------|
| 6 | | 14 | |
| 7 | Very, very light | 15 | Hard |
| 8 | | 16 | |
| 9 | Very light | 17 | Very hard |
| 10 | | 18 | |
| 11 | Fairly light | 19 | Very, very hard |
| 12 | | 20 | |
| 13 | Somewhat hard | | |

Low to moderate intensity (60-80% maximum heart rate or RPE 12-13) activity is recommended for people with diabetes to receive the best health benefits. Individuals that were exercising at a high intensity prior to the diagnosis of diabetes should be able to continue with the activity, but may need some assistance in medication adjustments and with the signs and symptoms of hypo- and hyperglycemia.

Individuals participating in a resistance training program should complete 1-3 sets (one set equals 8-12 repetitions), at 60-80% of 1 repetition maximum. The individual lifting the maximum amount of weight possible, one time, with proper form determines a repetition maximum. This range may vary based upon the individual's goals and clinical status.

It is important that all individuals be instructed on how to properly warm up and cool down with each exercise session. This will help prevent cardiac and musculoskelatal injuries. A practical warm up and cool down can be completed by performing the activity at a lower intensity for 5 minutes. Stretching is also recommended to maintain flexibility.

Туре

Aerobic, resistant training, and flexibility activities provide the best overall health benefit. Each activity works together to develop lean body mass, improve cardiovascular function, promote weight loss/ maintenance, and improve or maintain range of motion and balance. Aerobic activities can include walking, jogging, swimming, cycling, dance, etc. Resistant activities may consist of weight machines, free weights and/or resistance bands.

An example of incorporating each activity into an exercise program would be walking Monday, Wednesday, and Friday, weight machine on Tuesday and Thursday, with stretching exercises at the end of each session for flexibility.

Time

Lower intensity activities will need to be performed longer to achieve the same health benefits of moderate to high intensity activities. Exercise sessions typically need be 20-60 minutes long. Individuals who are just starting to exercise should start out with less time and gradually increase the duration over time. Once a desired duration is reached, an individual can work on increasing the intensity.

Maintenance and Motivation

Fifty percent of the people who start an exercise program typically drop out within one year. Some specific steps that can be taken to lower drop out rates include:

- Ensure that the person has reasonable expectations at the start of the program.
- Have the new participant make a firm commitment to adhere to the program via a written contract.
- Start the exercise program at a comfortable level and progress gradually.
- Choose enjoyable activities that can be performed at a convenient time and location.
- Set realistic goals to ensure a gradual progression of exercise training.
- Review the person's performance on a regular basis and give them feedback about their progress.
- Reinforce positive changes in behavior via appropriate rewards.
- Use stimulus control strategies (e.g., write exercise time in appointment books) and cognitive strategies (e.g., have participants consider the pros and cons of exercise).
- Optimize social support from friends and relatives.
- Train in relapse prevention.

Individuals may also benefit from a referral to an exercise physiologist or physical therapist to help them learn how to start and maintain an exercise routine.

E. Medical Nutrition Therapy

Nutrition Recommendations

Medical nutrition therapy is one of the cornerstone treatments for diabetes. Recommendations have changed through the years for the most effective nutrition prescription for individuals with diabetes. Currently, there is not a "one size fits all diet." The "ADA" diets used over the years are not approved by the American Diabetes Association or the American Dietetics Association and should not be used; nor should blanket nutrition prescriptions that are not tailored to the individual. Since diabetes is a chronic disease, which changes as life experiences change, regular visits to a registered dietitian/certified diabetes educator (RD, CDE) are recommended to provide an ongoing nutrition plan specific to the individual with diabetes that will achieve optimal outcomes and goals.

The American Diabetes Association published Evidence Based Nutrition Principles and

Recommendations in 2002 with modifications published in 2004. Evidence is labeled alphabetically as A,B, C or E, with the most conclusive evidence having an A designation and the least clear evidence labeled C. Level E denotes evidence that is based upon clinical experience. The best available evidence must still take into account individual circumstances and preferences.

Goals of Medical Nutrition Therapy for Diabetes

- Achieve and maintain optimal metabolic outcomes including blood glucose levels in the normal or near normal range and lipoprotein profiles and blood pressure levels that reduce the risk for cardiovascular disease.
- Prevent and treat chronic complications associated with diabetes.
- Prevent and treat other health related disorders.
- Address individual nutritional needs based upon personal, cultural, and lifestyle choices, while respecting the individual's preferences and willingness to change.
- Encourage a healthy eating style that promotes the enjoyment of food, eating, and a healthy body image, while nourishing the body.

Goals for Specific Populations and Situations

- For youth with type 1 diabetes, integrate insulin regimens into usual eating and physical activity habits to provide adequate energy to ensure normal growth and development.
- For youth with type 2 diabetes, facilitate changes in eating and physical activity habits that reduce insulin resistance and improve metabolic status.
- For pregnant and lactating women, provide adequate energy and nutrients needed for optimal outcomes.
- For older adults, provide for the nutritional and psychosocial needs of an aging individual.
- For individuals treated with insulin or insulin secretagogues, provide self-management education for treatment and prevention of hypoglycemia, acute illnesses, and exercise-related blood glucose problems.
- For individuals at risk for diabetes, decrease risk by encouraging physical activity and promoting food choices that prevent weight gain and facilitate moderate weight loss.

Primary Prevention, Energy Balance and Obesity

Excess calories and body fat, especially centrally located, can increase insulin needs and insulin resistance. Individuals with type 1 diabetes should be encouraged to obtain and maintain a healthy body weight and healthy percentage of body fat.

Studies have shown that individuals who are overweight or obese, who lose 5-7% of their body weight, have improved blood pressure, glucose, and lipid levels. Individuals with type 2 diabetes who are overweight, or those at risk of developing type 2 diabetes, including those with metabolic syndrome and PCOS, should receive continued assistance in losing weight and maintaining a healthy body weight.

Recommendations

- In insulin-resistant individuals, reduced energy intake and modest weight loss improve insulin resistance and glycemia. Therefore weight loss is recommended for all overweight individuals at risk for diabetes. (A Level)
- Structured programs that emphasize lifestyle changes, modest decreased energy intake, physical activity (≥150 minutes/week), and regular participant contact have the best likelihood of producing long-term moderate weight loss (7% of body weight), and are recommended for people at risk of developing type 2 diabetes. (A Level)
- Exercise and behavior modification are most useful as adjuncts to other weight loss strategies. Exercise is helpful in maintenance of weight loss. (B Level)

- Weight loss medication in conjunction with lifestyle modification can be considered in the treatment of overweight and obese individuals with type 2 diabetes. (B Level)
- Bariatric surgery can be considered for individuals with a BMI ≥35 kg/m² and type 2 diabetes to help improve glycemia. Long-term studies on the benefit and risk of bariatric surgery on prediabetes and diabetes continue. (B Level)
- Low carbohydrate diets of <130 grams per day are not recommended since the long-term effects of these diets are unknown. Although these diets produce short-term weight loss, maintenance of weight loss is similar to low-fat diets and the impact on CVD risks is uncertain. (B Level)
- Individuals at risk for developing type 2 diabetes should be encouraged to consume the recommended amount of dietary fiber (14 gram/1000 calories). They should also be encouraged to eat foods containing whole grains. At least one-half of grain intake should be whole grain. (B Level)
- Data does not support consumption of alcohol to prevent type 2 diabetes. (B Level)
- Currently studies are inconsistent to support recommending a low glycemic load diet to reduce the risk for diabetes. However, low glycemic index foods that are rich in fiber and other nutrients are to be encouraged. (E Level)
- Some research has been conducted related to vitamin D and the prevention of type 1 diabetes, but currently no nutrition recommendations can be made for preventing type 1 diabetes. (E Level)
- The data for preventing the development of type 2 diabetes in children and adolescents is still insufficient, but an approach similar to preventing the disease in adults is reasonable providing that nutritional needs for normal growth and development are maintained. (E Level)

Secondary Prevention - Macronutrients and Diabetes

There continues to be controversy in the medical and nutrition fields concerning the correct distribution of carbohydrate, protein, and fat in an individual's diet. All metabolic parameters, goals, individual preferences, and lifestyle habits should be considered when developing an eating plan. The individual with diabetes should be included in the decision-making process.

Carbohydrates

Carbohydrates include all sugars, starches, and fiber. Carbohydrates are a primary fuel for the body and should be included in the diet of a person with diabetes. Pattern management, food records, metabolic control, and other health conditions should be used to help individuals with diabetes determine the appropriate amount and type of carbohydrate that is best for their goals.

Recommendations

- The total amount of carbohydrate in meals or snacks is important in determining the overall effect on blood glucose levels. (A Level)
- Sucrose containing foods can be included in the diet of an individual with diabetes but they must be included in the total carbohydrate content for the meal or snack, or covered with appropriate medication. (A Level)
- Non-nutritive sweeteners have proven to be safe when consumed within the acceptable daily intake levels established by the FDA. (A Level)
- Individuals receiving intensive insulin management should adjust pre-meal insulin doses based on the carbohydrate content of meals. (A Level)
- The glycemic index and load may provide a slight additional benefit over that observed when just total carbohydrate is considered. (B Level)
- As with the general public, increased consumption of dietary fiber is encouraged. (B Level)
- Foods containing carbohydrate from whole grains, fruits, vegetables, and low-fat milk should be included in a healthy diet. (B Level)
- Individuals receiving fixed daily insulin doses should try to be consistent in day-to-day carbohydrate intake. (C Level)
- Low carbohydrate diets of <130 grams/day are not recommended for the management of diabetes. (E Level)

Protein

Protein intake in the United States usually accounts for 15-20% of the total caloric intake. This amount of protein intake does not appear to be associated with the development of diabetic nephropathy. However, long-term effects of consuming >20% of energy as protein on the development of nephropathy has not been determined.

Protein requirements can be higher in individuals with type 2 diabetes who have moderate glycemic control due to an increase in protein turnover. In individuals with type 1 diabetes being treated with conventional insulin therapy, studies have demonstrated an increase in protein catabolism. Since most individuals consume at least 50% more protein than what is needed, people with diabetes appear to be protected against protein malnutrition when consuming a typical diet.

Recommendations

- Ingested protein, in individuals with type 2 diabetes, can increase insulin response without increasing plasma glucose concentrations. Thus, protein should not be used to treat hypoglycemia or prevent nocturnal hypoglycemia. (A Level)
- For people with diabetes and normal renal function, there is insufficient evidence to suggest that usual protein intake (15-20%) should be modified. (E Level)
- Currently, high-protein, low-carbohydrate diets are being recommended by some health care providers. Short-term studies have shown these diets can promote weight loss and improve glycemia. However, long-term studies have not been conducted to determine if the weight loss persists, the long-term impact on LDL cholesterol, long-term glycemic control, or any links with other disorders or diseases. (E Level)

Fat

The primary dietary fat goal for individuals with diabetes is to limit saturated fat and dietary cholesterol due to the negative impact these dietary lipids exhibit on serum lipid levels. Recommendations for total cholesterol and saturated fat intake are consistent with the American Heart Association recommendations.

Diets low in total fat (<10% of energy) and high in carbohydrates increase postprandial blood glucose levels, triglycerides and may decrease HDL when compared to isocaloric high monounsaturated fat diets. However, high-monounsaturated fat diets have not been shown to improve fasting plasma glucose or A1c values. Polyunsaturated fats, when substituted for saturated fats, lower total and LDL cholesterol but not as well as monounsaturated fats. Care should be taken to adjust intake of monounsaturated fats with the individual's total energy needs.

Trans-fatty acids can impact serum lipid levels similar to saturated fats. They can also lower HDL levels in the blood and should be limited.

Recommendations

- Less than 7% of energy intake should be derived from saturated fats. (A Level)
- Dietary cholesterol should be <200 mg/day. (A Level)
- Two or more servings of fish per week (except commercially fried fish) provide omega-3 fatty acids and are recommended. (B Level)
- Trans-fatty acids should be limited. (E Level)

Micronutrients

Individuals with diabetes who are able and willing to improve their diet through wise food choices by incorporating a wide variety of foods from all the basic food groups will most likely meet their micronutrient needs. Classic vitamin deficiencies like scurvy, pellagra, or beriberi are typically not seen in the U.S. However, suboptimal intake of some vitamins due to the inability and/or unwillingness to improve one's diet, or poor glycemic control can increase the risk for chronic diseases or complications. Likewise excessive intake of micronutrients in the form of supplements can also lead to imbalances and toxicity. Each person with diabetes should be assessed to determine if they might benefit from extra supplementation. Special population groups like vegetarians, elderly, pregnant or lactating women may benefit from a multivitamin/mineral supplement.

Deficiencies of certain minerals, such as potassium, magnesium, zinc and chromium may aggravate carbohydrate intolerance. Potassium and magnesium deficiencies are easy to detect and supplementation can be added. Chromium and zinc deficiencies are harder to determine. Some studies have shown benefit with chromium supplementation, others have not.

Vanadium salts are being explored to determine if they have a role in blood glucose control. Since significant evidence for efficacy has not been established and there is an increase risk of toxicity, no current recommendations exist.

Recommendations

- There is no concise evidence of the benefit from vitamin and mineral supplementation in people with diabetes who do not have deficiencies. Exceptions include folate for prevention of birth defects and calcium for the prevention of bone disease. (A Level)
- Routine supplementation with antioxidants is not currently recommended due to uncertainties related to long-term use. (A Level)

Alcohol

Alcohol recommendations for people with diabetes are the same as the general public. If people do not currently drink, they are not advised to start. However, if an individual chooses to drink, moderation is recommended.

Alcohol can have hypoglycemic and hyperglycemic effects in people with diabetes. Studies have shown that moderate amounts of alcohol ingested with food had no acute effect on blood glucose or insulin levels.

Recommendations

- If individuals choose to drink alcohol, daily intake should be limited to one drink for adult women and two drinks for adult men. One drink is defined as 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of distilled spirits. (B Level)
- To reduce risk of hypoglycemia, alcohol should be consumed with food, especially at night. (E Level)

Special Populations and Conditions

Type 1 Diabetes

- Insulin therapy should be integrated into the individual's nutrition and physical activity pattern. (E Level)
- Insulin doses can be adjusted for planned exercise; however, for unplanned exercise, extra carbohydrate may be needed. (E Level)

Type 2 Diabetes

- Individuals should be encouraged to adopt lifestyle habits that reduce the intake of calories, saturated and trans fatty acids, cholesterol, and sodium, while increasing physical activity. (E Level)
- Blood glucose monitoring is helpful to determine whether adjustments with food and activity will be adequate to obtain targeted goals, or if medication is also needed. (E Level)

Pregnancy and Lactation with Diabetes

Nutrition requirements during pregnancy and lactation are similar for women with and without diabetes. Carbohydrate amount and distribution should be based upon the clinical outcomes, hunger, glucose levels, weight gain and ketone levels; but a minimum of 175 grams per day should be ingested. Carbohydrate intake in the morning should be limited to 15-45 grams due to increased insulin resistance at this time. A meal plan with 3 meals and 3 snacks can help prevent hyperglycemia and hypoglycemia and control postprandial blood glucose levels. Some women are unable to eat this often, but need to be counseled about avoiding more than 10 hours from bedtime to breakfast to prevent ketone production.

TABLE 24

| | - | | | | | |
|------------|-------------|-------------|-------|----------|------|----------|
| Nutrient I | Needs Durin | g Pregnancy | and L | actation | with | Diabetes |

| Nutrient | Pre-conception | Pregnancy | Lactation |
|--------------|--|---|--------------------------------|
| Calories | Individualized based on wt goals: 30 kcal/kg normal weight 25 kcal/kg overweight 20 kcal/kg obese | + 300 after week 13 | +500 for duration of lactation |
| Protein | 12-20% of calories | 20-25% of calories | Same as pregnancy |
| Carbohydrate | Individualized | 40-45% GDM 40-50% Others | Individualized |
| Fat | Individualized | 30-40%, emphasize monounsaturated fats | Individualized |
| Folic Acid | 400 mcg | 800 mcg | 400 mcg |
| Iron | 15-18 mg | 27 mg | 15-18 mg |

- Gestational diabetes is a risk factor for developing type 2 diabetes so postnatal counseling should focus on lifestyle modifications aimed at reducing weight and increasing physical activity. (A Level)
- Patients should be counseled to avoid ketonemia from ketoacidosis. Starvation ketosis should be avoided. (C Level)
- MNT for gestational diabetes focuses on food choices for appropriate weight gain, normoglycemia, and absence of ketones. (E Level)
- In some women with gestational diabetes, modest energy and carbohydrate restriction may be appropriate. (E Level)

Older Adults with Diabetes

- Energy requirements for older adults are less than for younger adults. Obese older adults may benefit from a moderate energy restriction and an increase in physical activity. (E Level)
- A multivitamin once a day may be beneficial. (C Level)

Cardiovascular Disease

- In normotensive and hypertensive individuals, sodium intake should be reduced to 2300 mg/day. A diet high in fruits, vegetables, and low-fat dairy products lowers blood pressure. (A Level)
- Obtain an A1c as close to target as possible without significant hypoglycemia. (B Level)
- A modest amount of weight loss beneficially affects blood pressure. (C Level)
- If patients also have symptomatic heart failure, dietary sodium should be <2000 mg/day. (C Level)
- Patients may reduce their risk for CVD if a diet high in fruits, vegetables, whole grains, and nuts is maintained. (C Level)

Microvascular

- In individuals with microalbuminuria and overt nephropathy, a reduction of protein to 0.8-1.0 gm per kg body weight per day may slow the progression of nephropathy and improve renal function. (B Level)
- MNT that reduces risk factors for CVD may also improve microvascular complications. (C Level)

Hypoglycemia

- Ingesting 15-20 grams of glucose is the preferred treatment, although any form of carbohydrate that includes glucose may be used. (A Level)
- Patients should respond to hypoglycemia treatment within 10-20 minutes. Additional treatment may be necessary so a repeat test of blood glucose within 60 minutes should be performed. (B Level)

Acute Illness

- Insulin and oral hypoglycemic agents should be continued. (A Level)
- It is important to drink adequate fluids, ingest carbohydrates, and test blood glucose and ketones during acute illness. (B Level)

Patients in Acute Care Facilities

- A menu planning system that utilizes consistent carbohydrate content of meals should be considered by medical care facilities. (E Level)
- Improving the care of patients with diabetes during and after hospitalizations can occur with an interdisciplinary team, implementing MNT and providing timely disease specific discharge planning. (E Level)

Patients in Long-Term Care Facilities

- Undernutrition in the institutionalized elderly is a concern and caution should be exercised when prescribing weight loss diets. (B Level)
- Residents should be served a regular menu with a consistent carbohydrate amount. (C Level)
- "No concentrated sweets" or "no sugar added" diets have no basis and should not be prescribed. (E Level)
- An interdisciplinary team should be utilized to integrate MNT into the overall diabetes management. (E Level)

Disordered Eating

Individuals with diabetes, PCOS, or pre-diabetes, especially woman, are at an increased risk for eating disorders and disordered eating practices that meet the DSM-IV diagnostic criteria. The treatment for these diseases can foster an environment for the development of disordered eating due to the emphasis placed on food, activity, metabolic control and weight. Common practices include insulin omission, binge eating, purging, severe food restrictions, and dieting. There is an increase in complications associated with eating disorders. Individuals should be screened based upon the DSM-IV criteria.

Since recovery from an eating disorder can take years, a referral to a mental health professional trained in eating disorders is necessary. Regular communication is needed between the health care team members to provide the best treatment outcomes for the individual.

Health care professionals need to encourage a healthy eating style when counseling individuals with diabetes, pre-diabetes, or PCOS. Emphasis should be placed on achieving health. Morality judgments (good versus bad) attached to food choices, weight, or metabolic parameters do not have a place in achieving medical nutrition therapy goals.

Summary

Medical nutrition therapy needs to be individualized. Monitoring of metabolic parameters and quality of life issues are necessary to assess when changes in therapy are needed and to ensure successful outcomes. Access to ongoing nutrition self-management training needs to be available to all individuals with diabetes.

F. Oral Health

Individuals with diabetes are at risk for oral health complications including:

- Caries
- Periodontal disease
- Xerostomia
- Oral candidiasis
- Lichen planus
- Infection and delayed healing
- Taste impairment

Dental infections may be a contributing factor for uncontrolled blood glucose. Dental care, blood glucose control, proper nutrition, and absence of tobacco use are needed to prevent oral health complications.

Individuals with diabetes should be encouraged to brush teeth twice a day with fluoride toothpaste and clean between the teeth with floss or an inter-dental cleaner at least once a day. They should be seen by a dental care specialist twice a year for cleaning and an oral health exam. Individuals with dentures should obtain an oral health exam yearly. Follow-up may be more frequent if any complications are identified. Medication adjustments may be needed if an infection is present or surgery is needed.

REFERENCE SECTION VII

American Diabetes Association. Clinical Practice Recommendations. *Diabetes Care*. 30(Suppl. 1):S48-S61. 2007

American Diabetes Association. Evidence-Based Nutrition Principles and Recommendations for the Treatment and Prevention of Diabetes and Related Complications. *Diabetes Care*. 26:S51-S61. 2003

Goodwin RD, et al. Diabetes and eating disorders in primary care. International Journal of Eating Disorders. 33:85-91. 2003

Herpertz S, et al. Comorbidity of diabetes mellitus and eating disorders: a follow-up study. J. Psychosomatic Research. 51:673-678. 2001

Neumark-Sztainer D, et al. Weight control practices and disordered eating behaviors among adolescent females and males with type 1 diabetes: associations with sociodemographics, weight concerns, familial factors, and metabolic outcomes. *Diabetes Care*. 25:1289-1296. 2002

Rodin G, et al. Eating disorders in young woman with type 1 diabetes mellitus. *J Psychosomatic Research*. 53:943-949. 2002

Ruderman N, Devlin J. American Diabetes Association. The Health Professional's Guide to Diabetes and Exercise. Alexandria, VA. Pages 70-88. 1995

www.cdc.gov/nip/recs/menus/vaccines.htm. 2007

VIII. PRE-DIABETES, METABOLIC SYNDROME, AND PREVENTION OF TYPE 2 DIABETES

A. Pre-diabetes

Type 2 diabetes is increasing in epidemic proportions in the U.S. and throughout the world. The complications resulting from diabetes can result in significant morbidity and mortality. Individuals with type 2 diabetes are at a significantly higher risk for coronary heart disease, peripheral vascular disease, stroke, as well as preventable blindness, end stage renal disease and non-traumatic amputation. They often have other comorbidities such as hypertension, dyslipidemia, and obesity. The term pre-diabetes refers to the intermediate metabolic states between normal and diabetic glucose homeostasis. It consists of two distinct states: 1) impaired fasting glucose or IFG (fasting BG between 100 and 125 mg/ dL) and 2) impaired glucose tolerance or IGT (BG between 140-199 mg/dL 2 hours after 75 mg glucose load). Pre-diabetes can be thought of as an early stage of diabetes because a high proportion of these individuals develop the disease.

TABLE 25

Risk Factors for Development of Type 2 Diabetes

- 1. Age >45 years
- 2. Overweight defined as BMI >25 kg/m² (may not be correct for all ethnic groups)
- 3. Family history of diabetes (i.e., parents or siblings with diabetes)
- 4. Habitual physical inactivity
- 5. Race/ethnicity (e.g., African-Americans, Hispanic-Americans, American Indians, Asian-Americans, and Pacific Islanders)
- 6. Previously identified IFG or IGT
- 7. History of gestational diabetes mellitus or delivery of a baby weighing >9 lbs
- 8. Hypertension (>140/90 mmHg in adults)
- HDL cholesterol ≤ 35 mg/dL (0.90 mmol/l) and/or a triglyceride level >250 mg/dL (2.82 mmol/l)
- 10. Polycystic ovary syndrome
- 11. History of vascular disease
- 12. Signs of insulin resistance, metabolic syndrome or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia)

It is recommended that individuals with two or more of above risk factors be screened for diabetes.

B. Metabolic Syndrome

This is a condition that is usually associated with obesity, particularly visceral obesity, insulin resistance and type 2 diabetes. Individuals with metabolic syndrome are also at higher risk for developing atherosclerotic cardiovascular disease. Metabolic syndrome has also been variously called syndrome X, insulin resistance syndrome and cardiac dysmetabolic syndrome.

Various organizations, including the Adult Treatment Panel III (ATP III), the American Association of Clinical Endocrinologists (AACE), and the World Health Organization (WHO), have proposed different sets of criteria for diagnosis of metabolic syndrome. Perhaps the most commonly used criteria are the ones proposed by the Adult Treatment Panel III (ATP III), which require an individual to have three of the following five conditions to be diagnosed with metabolic syndrome:

- Abdominal obesity, defined as a waist circumference in men >102 cm (40 in) and in women >88 cm (35 inches)
- Serum triglycerides ≥150 mg/dL (1.7 mmol/l) or drug treatment for elevated triglycerides
- Serum HDL cholesterol >40 mg/dL (1 mmol/l) in men and <50 mg/dL (1.3 mmol/l) in women or drug treatment for low HDL cholesterol
- Blood pressure >130/85 mmHG or drug treatment for elevated blood pressure
- Fasting plasma glucose (FPG) ≥110 mg/dL (6.1 mmol/l) or drug treatment for elevated blood glucose.

C. Recommendations to Prevent or Delay Type 2 Diabetes

Individuals at high risk for developing diabetes need to become aware of the benefits of weight loss and following a carbohydrate-controlled diet and participating in regular physical activity.

At the present time, no pharmacologic intervention is proven to be effective in prevention of type 2 diabetes; however, individuals with both impaired fasting glucose and impaired glucose intolerance may benefit from metformin therapy.

REFERENCE SECTION VIII

AACE Medical Guidelines for Clinical Practice for the Management of Diabetes Mellitus. *Endocrine Practice.* 13(Suppl 1):3-66. May/June 2007

IX. DIABETES DURING PREGNANCY

TABLE 26

| A. Ouler Reference Guide for the Gale of Diabeles Defore & During Treghan | A. C | Ouick Reference | Guide for the | Care of Diabetes | Before & Durin | g Pregnancy |
|---|------|------------------------|---------------|------------------|----------------|-------------|
|---|------|------------------------|---------------|------------------|----------------|-------------|

| When | Procedure/Test | Action or Goal |
|--------------------------|--|---|
| Prepartum | A1c monthly 24 hr urine creatine clearance & microalbumin each quarter Eye exam baseline and as indicated TSH (in type 1) Cardiac assessment if DM >10 years | A1c at least ≤7.0% |
| Prepartum & during PG | SMBG: preprandial, 1-2 hr post prandial, at bedtime, and 3 AM | Fasting BG* 60-90, or 1 hr post prandial <120 mg/dL |
| Prepartum & during PG | Diet: 40% carbohydrate, 20% protein, 40% fat Grams of carbohydrates = 10% of calorie level 3 meals plus bedtime snack Breakfast low in carbohydrates Self-management Training Calorie Level: <90% of DBW 36-40 calories/kg/day 90-120% of DBW 30 calories/kg/day 120-150% of DBW 24 calories/kg/day >150% of DBW 12-18 calories/kg/day (DBW = 110 lb. + 5 lb/inch over 5 ft., ±10% for large/small frame) | Reduce hyperglycemia and triglycerides |
| Prepartum & during PG | Insulin therapy (See Tables 28 and 29): AM PM Dinner Bedtime N/R N/R N/R R N N/H H H N H H H Lantus (Class C) Or Insulin Pump Give 1 unit for every 10 grams of carbohydrate ¹ Correcting dose: point drop in glucose for one extra unit = 1500÷total daily dose of insulin ¹ | Prepartum: A1c at least ≤7.0% During pregnancy: A1c ≤6.0% Fasting BG 60-90, or 1 hr post prandial <120 mg/dL |
| Monthly during PG | A1c | A1c ≤6.0% |
| During PG | Blood Pressure | Treat hypertension with Aldomet or Hydralazine (see below) |

1 This ratio is a starting point; this adjustment often needs to be individualized

* BG throughout these Recommendations means plasma or serum glucose. For a discussion on the ways of measuring glucose in the blood and their differences, see the Appendix, page 93.

Full Clinical Recommendations available on American Diabetes Association website: www.diabetes.org

- Insulin requirements may decline in 1st trimester and increase in 2nd and 3rd trimester.
- Statins should be discontinued and not taken during pregnancy.
- ACE inhibitors, beta blockers and diuretics should be avoided.
- ARBs are category C in the first trimester of pregnancy (maternal benefit may outweigh fetal risk in certain situations). Later in pregnancy, they are category D and should generally be discontinued before delivery.
- None of the oral anti-diabetic medicines are FDA approved for pregnancy. There is not sufficient data to establish their safety in pregnancy. There is one study using glyburide which seems to show that it is as effective and safe as insulin (see references).

TABLE 27

B. Quick Reference Guide for the Care of Gestational Diabetes

| When | | Who | Pro | ocedure/T | lest | | Action or Goal | | |
|--|------------------------|-----------------------------------|------------------|---|-------------|--------------------------------------|---|--|--|
| 24-28 weeks or sooner | S | Each PG woman | GC | GCT* | | | If 1 hr value >130-140 mg/dL, then do OGTT | | |
| 24–28 weeks or sooner | S | GCT positive or high risk ◊ | 100 | 100 gm OGTT‡ | | | OGTT positive, then treat for GDM | | |
| OGTT Posi | tive | Those with positive OGTT | Tea t Ver | Teach diet, SMBG, and self- management Verify vitamins & folic acid supplementation | | | Fasting BG 60-90, or 1 hr post prandial <120 mg/dL | | |
| Diagnosed | GDM | All GDM | Die Car Ch | Diet: 25 calories/kg actual wt/day Carbohydrates: 35–40% of calories Check first AM urine ketones | | ual wt/day of calories ketones | Reduce hyperglycemia and triglycerides | | |
| If glucose go exceeded aft wk of diet th | oals er 1 herapy | All GDM | Sta mg >14 | Start insulin if fasting BG >95 mg/dL, or 1 hr post prandial >140 mg/dL | | BG ≻95 randial | Fasting BG 60-90, or 1 hr post prandial <120 mg/dL | | |
| Monthly | | All GDM | A1 | A1c | | | A1c ≤6.0% | | |
| 6 weeks pos partum and every 3 year | st- l then rs | All GDM | Fas | Fasting BG or OGTT | | | Rule out non-gestational diabetes | | |
| Ι | Dose | Fasting 1 | hr | <u>2 hr</u> | <u>3 hr</u> | <u>Result</u> | | | |
| *GCT 5 | 50 gm | 1 | 30-140 | | | positive i | f exceeded | | |
| ‡OGTT 1 | 00 gm | 95 1 | 80 | 155 | 140 | positive i or exceed | f 2 values met ed | | |

◊ High risk includes obesity; history of GDM, diabetes in first degree relative, history of poor pregnancy outcome, and higher risk ethnic groups; if urine ketones positive, check later in day; if positive, then carbohydrates may need to be increased

Full Clinical Recommendations available on American Diabetes Association website: www.diabetes.org

C. Screening, Diagnosis and Treatment of Gestational Diabetes (GDM)

Who and when

- Risk of GDM should be assessed at first prenatal visit.
- Test as soon as feasible if markedly obese, previous GDM, glycosuria, or strong family history of diabetes.
- EVERY pregnant woman should be tested by 24-28 weeks of gestation.

Testing

- A glucose challenge test (GCT) is done:
 - 50 gm of glucose is given orally regardless of time of day or prandial state.
 - A positive test is a plasma glucose of >130-140 mg/dL one hour later.
 - If the GCT is positive, then an OGTT is done.
- Oral Glucose Tolerance Test (OGTT):
 - Do after fasting for 8-14 hr; do in the morning; diet and physical activity unrestricted for 3 days. Remain seated during the test. No tobacco use during the test.
 - 100 gm OGTT is most commonly used and the most well validated. Test is positive if at least 2 plasma glucose values are met or exceeded: fasting ≥95 mg/dL; 1 hr ≥180 mg/dL; 2 hr ≥155 mg/dL; 3 hr ≥140 mg/dL.
- May go directly to the OGTT in high risk individuals or populations.

Treatment

- Diet (see nutrition recommendations for MNT related to pregnancy and diabetes on page 54)
- Patient monitoring
- Insulin, if necessary
- Office monitoring
- Exercise
- Although oral anti-diabetic agents are not recommended during pregnancy, at least one study suggests that glyburide may be considered during the later part of pregnancy

Patient monitoring

- Fingerstick blood glucose four times daily: fasting and 1-2 hrs after each meal
- Blood glucose goals: fasting 60-90 mg/dL; 1 hr post prandial <120 mg/dL

TABLE 28

Gestational Diabetes: Insulin (if diet fails)

| Breakfast | Lunch | Supper | Bedtime |
|------------------|------------------|------------------|----------|
| 70/30 | Regular | 70/30 | none |
| NPH/Regular | Regular | Regular | NPH |
| NPH/Humalog* | Humalog/Novolog* | Humalog/Novolog* | NPH |
| Humalog/Novolog* | Humalog/Novolog* | Humalog/Novolog* | Lantus** |

* NPH and Regular are preferred insulins in GDM, but if BG is not controlled, then Humalog/ Novalog can be used

** Class C - The safety of Lantus is controversial, because of the theoretical risk of stimulating the IGF-1 receptor in the fetus. This risk should be weighed against the benefit of tight glucose control not achieved by other insulins.

Office monitoring

Test A1c monthly - Goal: 4-6% (in the normal range)

Exercise

See exercise guidelines for recommendations related to pregnancy and exercise

Post-partum

- Women who have had GDM have a 40-60% chance of developing type 2 diabetes.
- This chance decreases to 25% if the woman becomes lean and fit after delivery.
- The chance of developing type 2 diabetes increases with more marked hyperglycemia, obesity, GDM diagnosed before 24 weeks or previous GDM.
- Fasting BG or OGTT should be done 6 weeks after delivery and every 3 years thereafter.
- If IFG or IGT diagnosed, then the patient should be tested yearly.

D. Management of the Patient with Diabetes Before and After Conception

1. Pre-conception care

Involve the diabetologist, internist, family practice physician, obstetrician, diabetes educator, dietician and social worker when available and where appropriate. The care should include:

- Patient education about the interaction of diabetes, pregnancy and family planning
- Education in diabetes self-management skills
- Physician directed care and testing
- Counseling by a mental health professional when indicated to reduce stress and improve adherence to treatment plan.

2. Pre-conception goals

- Use of appropriate meal plan
- Self-monitoring of blood glucose
- Self-administration and self-adjustment of insulin
- Treatment of hypoglycemia (by patient and family)
- Exercise
- Development of techniques to reduce stress and cope with denial
- A1c of <1% above the normal range (e.g., <7%)

3. Initial visit

History

- Duration and type of diabetes
- Acute complications history (infections, DKA, hypoglycemia)
- Chronic complications (retinopathy, nephropathy, hypertension, vascular disease, autonomic and peripheral neuropathy)
- Diabetes management (insulin regimen, prior or current oral agents, SMBG regimen and results, diet and exercise)
- Concomitant medical conditions (especially thyroid disease in type 1 diabetes)
- Menstrual/pregnancy history and contraceptive use
- Support system including family and work environment
- Physical examination
 - Blood pressure
 - Dilated retinal exam by an ophthalmologist or other eye specialist knowledgeable about diabetic eye disease
 - Cardiovascular exam for evidence of cardiac or peripheral vascular disease; if positive, screening tests for coronary artery disease should be done before attempting pregnancy
 - Neurological exam including exam for signs of autonomic neuropathy

Laboratory examination

- A1c
- Serum creatinine
- 24 hr urine for total protein or albumin (>190 mg/24 hr carries increased risk for hypertensive problems during pregnancy; >400 mg/24 hr carries increase risk for intrauterine growth retardation later in pregnancy)
- Serum TSH in the type 1 patients because of the 5-10% co-incidence of hypo- or hyperthyroidism
- Other tests as indicated

Management plan

- Counseling about:
 - Risk and prevention of congenital anomalies
 - Fetal and neonatal complications of maternal diabetes
 - Effects of pregnancy on maternal diabetic complications
 - Risks of obstetrical complications which occur more frequently in diabetic pregnancies (especially hypertensive)
 - The need for effective contraception until diabetes is well controlled
- The cost benefit relationship between preconception care and the prevention of malformations
 - Finger stick blood glucose 4-6 times a day: preprandial, 1-2 hr post prandial, bedtime, 3:00 AM
 - Goals: fasting or before meals: 60-90 mg/dL; 1 hr post prandial: <120 mg/dL
- A1c
 - Measure every month
 - Goal: <1% above upper limit of normal (e.g., <7%)
 - It is safe for patient to get pregnant once A1c goal is achieved and maintained
 - Modify treatment plan if A1c goal is not reached in a few months

Exercise

See exercise guidelines for recommendations related to pregnancy and exercise, page 47.

Diet

See nutrition recommendations for medical nutrition therapy related to pregnancy and diabetes, page 54.

• Insulin program - for type 1 and type 2 diabetes, see table below.

TABLE 29

Pregnant Patient with Diabetes: Insulin (type 1 and if diet fails in type 2)

| Breakfast | Lunch | Supper | Bedtime | | | |
|--------------------|------------------------------|------------------|----------------------|--|--|--|
| 70/30 | Regular | 70/30 | none | | | |
| NPH/Regular | Regular | Regular | NPH | | | |
| NPH/Humalog* | 'H/Humalog* Humalog/Novolog* | | NPH | | | |
| Humalog/Novolog* | Humalog/Novolog* | Humalog/Novolog* | Lantus ^{**} | | | |
| Or an insulin pump | | | | | | |

* NPH and Regular are preferred insulins during pregnancy, but if BG is not controlled, then Humalog/Novalog can be used

** Class C - The safety of Lantus is controversial, because of the theoretical risk of stimulating the IGF-1 receptor in the fetus. This risk should be weighed against the benefit of tight glucose control not achieved by other insulins.

4. Special considerations

Hypoglycemia

- Attempts to achieve normal glycemic control increase the risk of severe hypoglycemia.
- Frequent, unexplained severe hypoglycemia may be due to hypoglycemia unawareness, insulin dose errors or excess alcohol intake.
- There is no solid evidence that severe hypoglycemia is an independent risk to the developing human embryo.
- There is a risk to the mother; the patient and her family should be included in education about the management of hypoglycemia.

Retinopathy

- Diabetic retinopathy may accelerate during pregnancy; therefore, better control should be attained gradually, if possible.
- A baseline dilated eye exam should be done before conception and repeat exams done during the pregnancy as indicated.

Hypertension

- Hypertension is a frequent complication or concomitant disorder, especially in type 2 diabetes.
- ACE inhibitors, beta blockers and diuretics should be avoided during pregnancy.
- Aldomet and Hydralazine are known to be safe in pregnancy.
- ARBs are category C in the first trimester of pregnancy (maternal benefit may outweigh fetal risk in certain situations). Later in pregnancy, they are category D and should generally be discontinued before delivery.

Nephropathy

- Serum creatinine >3 mg/dL, creatinine clearance <50 mL/minute, or urine protein >300 mg/24 hr is associated with a significant risk of worsening maternal renal function and a higher risk for morbidity and mortality of the infant.
- A urine protein >190 mg/24 hr before or early in pregnancy is associated with an increase likelihood of pregnancy-induced hypertension.

Neuropathy

- Gastroparesis is a relative contraindication to pregnancy.
- Urinary retention or orthostatic hypotension may complicate the management of diabetes in pregnancy.
- Compartment syndromes, such as carpal tunnel syndrome, may be exacerbated by pregnancy.

Coronary Artery Disease

- Clinically proven, but untreated cardiovascular disease is associated with up to a 50% maternal mortality.
- The increased cardiovascular demands of gestation are more likely to be tolerated if treatment results in normal exercise tolerance.

REFERENCE SECTION IX

American College of Obstetricians and Gynecologists (ACOG). Clinical Management Guidelines for Obstetrician-Gynecologists. *ACOG Practice Bulletin*. Number 30. Gestational Diabetes. 2001

American Diabetes Association. Clinical Practice Recommendations. *Diabetes Care.* 30(Suppl 1):S26-S27, S46-S47. 2007

American Diabetes Association. Medical Management of Pregnancy Complicated by Diabetes. Third Edition. Clinical Education Series. 2000

Jovanovic-Peterson. Glucose metabolism and its disorders during pregnancy. *Endocrine Practice*. 2(2):118-143. 1996

Langer O, et. al. A Comparison of Glyburide and Insulin in Women with Gestational Diabetes Mellitus. *The New England Journal of Medicine*. 343:1134-1138. 2000
X. DIABETES CARE IN THE HOSPITAL

A. Guidelines for Hospitalization

The decision to hospitalize a patient for diabetes must be individualized. The following criteria serve as general indications for hospitalizing patients for reasons related to diabetes:

- Life-threatening, acute metabolic complications of diabetes (diabetic ketoacidosis, hyperglycemic hyperosmolar state, or hypoglycemia with neuroglycopenia).
- Newly diagnosed diabetes in children and adolescents.
- Substantial and chronic poor metabolic control that necessitates close monitoring of the patient to determine the etiology of the control problem, with subsequent modification of therapy.
- Severe chronic complications of diabetes that require intensive treatment or other severe conditions unrelated to diabetes that significantly affect its control or are complicated by diabetes.

Glycemic Goals for Hospitalized Patients

Inpatient diabetes management has been the focus of attention in the past few years and several highly-acclaimed studies have demonstrated important benefits in tighter glycemic control in hospital patients. These benefits are more apparent in acutely ill patients in the ICU settings. In August 2006, the American College of Endocrinology and the American Diabetes Association published a consensus report on inpatient diabetes and glycemic control. However, the optimal glycemic goals in non-critical patients are not well established. The following glycemic goals present generally recommended targets for hospitalized patients:

Glycemic goals in the intensive care setting:

- **80-110** mg/dL (4.4-6.1 mmol/l) all the time.
- Glycemic goals in the non-critical setting:
 - <110 mg/dL (6.1 mmol/l) pre-prandial</pre>
 - <180 mg/dL (10.0 mmol/l) maximal.</p>

Values above 180 mg/dL (10 mmol/l) are an indication to monitor glucose levels more frequently to determine the direction of any glucose trend and the need for more intensive intervention. Achieving these targets may require consultation with a diabetes specialist.

The occurrence of significant hyperglycemia in the hospital requires close follow-up after discharge. In those with previously diagnosed diabetes and an elevated A1c on hospital admission, revision of the pre-admission diabetes therapy is required to establish glycemic control. In those without previously diagnosed diabetes, the differentiation between hospital-related hyperglycemia and undiagnosed diabetes requires follow-up testing (Fasting BG*, 2-hour OGTT) once metabolically stable.

Glycemic Goals for Pregnant Inpatients

Separate upper-limit targets (Table 30) have been developed to address the increased risk of poor outcomes caused by hyperglycemia in pregnancy.

^{*} BG throughout these Recommendations means plasma or serum glucose. For a discussion on the ways of measuring glucose in the blood and their differences, see the Appendix, page 93.

TABLE 30

Glycemic Goals for Pregnant Inpatients

| | ADA | | AACE | | | | |
|--------------------------|--------------|-------------------|--------------------|------------------|-------------------|--|--|
| Prenatal | | | Prenatal | | | | |
| $\leq 100 \text{ mg/dL}$ | (5.6 mmol/1) | preprandial | 60-90 mg/dL | (3.3-5.0 mmol/1) | preprandial | | |
| $\leq 120 \text{ mg/dL}$ | (6.7 mmol/l) | 1 hr postprandial | <120 mg/dL | (6.7 mmol/1) | 1 hr postprandial | | |
| Labor and Delivery | | | Labor and Delivery | | | | |
| $\leq 100 \text{ mg/dL}$ | (5.6 mmol/l) | | 70-90 mg/dL | (3.9-5.0 mmol/1) | | | |

Again, if these targets are unable to be achieved, then consultation with a diabetes specialist should be considered.

B. Hospital Barriers to Excellent Glycemic Control

There are several reasons why patients with diabetes often do not have excellent glycemic control when hospitalized:

- Infection, fevers, glucocorticoid therapy, surgical trauma, and general medical stress may make diabetes control challenging.
- Decreased physical activity (especially in a previously active patient) can result in worsening hyperglycemia.
- Subcutaneous insulin absorption may be erratic in acutely ill patients.
- Patients often lose individual control of their diabetes and are unable to utilize self-management techniques when the responsibility is taken over by the health care team.
- Interruptions in meals and medication doses due to hospital diagnostic and therapeutic procedures.

C. Common Errors in Inpatient Glucose Management

- Admission Orders: All too frequently no change in a patient's diabetes regimen is made or it is stopped completely upon hospitalization. Modification of the outpatient diabetes treatment is generally necessary after hospitalization.
- Use of "Sliding Scales:" Frequently patients will be managed on a nonphysiologic sliding scale, without scheduled basal and pre-meal insulin, resulting in wide glycemic excursions.
- Under utilization of insulin drip: IV insulin is an effective tool in attaining excellent glycemic control and should be considered in the majority of inpatient diabetes cases.

Recommendations

Diet: Diet should always be individualized based on a patient's medical status and concurrent illness. Consultation by a dietitian or diabetes educator while an inpatient should be considered.

Glucose monitoring: Patients should have blood glucose testing at least four times a day upon admission. This may be continued or reduced depending on the glycemic control and medical status of the individual patient. More frequent testing (every 1 or 2 hours) is indicated for more seriously ill patients and/or those on IV insulin.

Glycemic control: Poor glycemic control can result in many complications such as infection and poor wound healing. Glycemic goals should be individualized for each patient.

D. Inpatient Pharmacotherapeutic and Insulin Recommendations

General Recommendations

- Inpatient diabetes regimens should be reassessed frequently.
- Patients with type 1 diabetes will require some insulin at all times, even when fasting, to prevent ketoacidosis.
- The use of sliding scales should be minimized. The use of sliding scale insulin alone should be completely avoided in all type 1 and in many insulin-requiring type 2 patients. These patients are better managed with scheduled dose basal and prandial insulin. A supplementation/correction scale may then be added at the discretion of the clinician to address hyperglycemia.
- If optimal glycemic control is not attained, consultation with diabetes specialist should be considered.

Specific Recommendations

Type 2 patient usually treated with oral medications who IS NOT eating:

- Consider stopping insulin secretagogues (sulfonyureas, etc.) to avoid hypoglycemia. Addition of long-acting insulin can be considered in those patients with glycemic excursions or persistent hyperglycemia on short acting insulin alone.
- Metformin is frequently recommended to be stopped upon hospitalization because of concerns about altered renal function in an acutely ill patient. It should definitely be held in patients who are perioperative, scheduled to have radiocontrast studies, have evidence of or are at high risk for renal, hepatic, or cardiac dysfunction or dehydration.
- Thiazolidinediones may be continued for a short time, unless there are cardiac (acute CHF) or hepatic problems.

Type 2 patient usually treated with oral medications who IS eating:

- Insulin secretagogues (sulfonyureas, etc.) may be continued but attention should be paid to increased risks of hypoglycemia in a hospital patient with decreased oral intake or gastrointestinal absorption.
- Metformin should be held for same reasons as outlined above.
- Thiazolidinediones may be continued unless there are cardiac (acute CHF) or hepatic problems.
- Always consider adding insulin for those unable to attain optimal glycemic control on oral medications alone.

Type 1 or insulin-requiring type 2 patient:

- Strongly consider using an intravenous insulin infusion.
- Another less desirable option can be subcutaneous long-acting insulin with a scheduled rapid-acting insulin for meals and supplemental insulin for hyperglycemia.
- IV 5% dextrose should be utilized to prevent hypoglycemia.
- Blood glucose should be checked no less frequently than every 6 hours.
- Insulin-requiring type 2 patients who are fasting can sometimes be managed with correction scales of short/rapid-acting insulin alone, but addition of scheduled long-acting insulin to this regimen should always be considered in those with glycemic excursions or persistent hyperglycemia.

1. Sample Intravenous Insulin Infusion Orders (not intended for management of DKA)

General Guidelines

- Discontinue all subcutaneous insulin and/or oral anti-diabetes medications.
- Standard drip: 50 units of Regular insulin in 50 mL of 0.9% NaCl.
- Insulin infusion should be stopped 2-3 hours after subcutaneous insulin has been resumed. Contact physician for orders.
- Surgical patients who have received oral anti-diabetes medication within the previous 24 hours should start the infusion when BG is above 120 mg/dL. Post-operative patients require hourly BG monitoring until the infusion protocol is initiated.
- All other patients should start when BG is above 70 mg/dL.
- Most patients require 5-10 gm of glucose per hour (D5 @ 100-200 mL/hr) or equivalent continuous TPN or enteral feeding.

D _____ at ____ mL/hr

- D5NS + _____ mEq Kcl/L at _____ mL/hr
- $\square D5^{1/2}NS + \underline{\qquad} mEq Kcl/L at \underline{\qquad} mL/hr$

Initiating the Infusion

Blood glucose (BG) Goal Range = 80-180^{*} mg/dL or _____. No patient should be initiated on Algorithm 3 or 4 unless discussed with physician.

- Algorithm 1: Start here for MOST patients.
- Algorithm 2: Start here for patients receiving above 80 units/day of insulin as an outpatient. Move to this one for patients not controlled with Algorithm 1 or patients on glucocorticoids.
- Algorithm 3: Move to this one for patients not controlled with Algorithm 2.
- Algorithm 4: Move to this one for patients not controlled with Algorithm 3.
- Move up one algorithm: If the patient is above goal range AND the BG does not decrease by at least 60 mg/dL within 1 hour.
- Move down one algorithm: When BG is under 70 mg/dL for 2 consecutive checks.
- Move down one algorithm: If nutritional therapy (TPN or tube feedings) is discontinued or reduced by 50% or more.
- A Move down one algorithm: If BG decreases greater than 80 mg/dL within 1 hour.
- * Maintain drip rate when goal is obtained

| Algorithm 1 | | Algorithm 2 | | Algorithm 3 | | Algorithm 4 | | | | |
|--|----------|-------------|----------|-------------|----------|-------------|--------------|--|--|--|
| BG | Units/Hr | BG | Units/Hr | BG | Units/Hr | BG | Units/Hr | | | |
| Under 60 = See next page for treatment | | | | | | | | | | |
| Under 70 | Off | Under 70 | Off | Under 70 | Off | Under 70 | Off | | | |
| 70-109 | 0.2 | 70-109 | 0.5 | 70-109 | 1 | 70-109 | 1.5 | | | |
| 110-119 | 0.5 | 110-119 | 1 | 110-119 | 2 | 110-119 | 3 | | | |
| 120-149 | 1 | 120-149 | 1.5 | 120-149 | 3 | 120-149 | 5 | | | |
| 150-179 | 1.5 | 150-179 | 2 | 150-179 | 4 | 150-179 | 7 | | | |
| 180-209 | 2 | 180-209 | 3 | 180-209 | 5 | 180-209 | 9 | | | |
| 210-239 | 2 | 210-239 | 4 | 210-239 | 6 | 210-239 | 12 | | | |
| 240-269 | 3 | 240-269 | 5 | 240-269 | 8 | 240-269 | 16 | | | |
| 270-299 | 3 | 270-299 | 6 | 270-299 | 10 | 270-299 | 20 | | | |
| 300-329 | 4 | 300-329 | 7 | 300-329 | 12 | 300-329 | 24 | | | |
| 330-359 | 4 | 330-359 | 8 | 330-359 | 14 | 330-359 | 28 | | | |
| ≥360 | 6 | ≥360 | 12 | ≥360 | 16 | continued | l on next pa | | | |

1. Sample Intravenous Insulin Infusion Orders - Continued

Patient Monitoring

- Check BG every hour until it is within goal range for 4 consecutive hours, then decrease to every 2 hours for 4 hours. If the BG remains within the goal range, decrease monitoring to every 4 hours.
- If the patient is eating, hourly BG monitoring is necessary for at least 3 hours after a meal.
- Hourly monitoring may be needed for critically ill or perioperative patients even if the BG is stable and within the goal range.
- Monitor every 30 minutes for BG between 60-70 mg/dL.

Treatment of Hypoglycemia (BG under 60 mg/dL)

- Stop insulin drip AND:
 - If awake and taking PO, give 4 ounces of juice or non-diet soda. If not taking PO, give 25 mL (1/2 amp) D₅₀ IV push.
 - If NOT awake, give 50 mL (1 amp) of D₅₀ IV push.
- Recheck BG every 20 minutes and repeat 25 mL of D₅₀ IV until BG is above 60 mg/dL.
- Restart insulin drip one Algorithm lower once BG is above 70 mg/dL on 2 consecutive checks.

When to Notify the Physician

- For any BG decrease more than 50% in 1 hour.
- For any BG increase greater than 100 mg/dL in 1 hour.
- For any BG above 360 mg/dL.
- For hypoglycemia that has not resolved within 20 minutes of giving 50 mL of D₅₀ (make sure insulin drip is stopped).

Patients usually on an insulin pump as an outpatient:

- Patients who are hospitalized for minor procedures and who will be awake and alert for the entire hospitalization may be permitted to continue to self manage their diabetes and use their insulin pump while in the hospital.
- Patients who are acutely ill, not awake and alert, or otherwise unable or unwilling to self manage their insulin pumps during hospitalization should be converted to IV insulin.
- Also, if glycemic goals are not being reached during hospitalization, then the pump should be discontinued and alternative insulin regimen begun. Consultation with a diabetes educator or certified pump trainer should be considered to troubleshoot the pump.

Perioperative Recommendations:

- Blood glucose should be checked every 1 to 2 hours before, during and after surgery or procedure.
- Sliding scales alone should be avoided because of greater risk of glycemic excursions.

Perioperative type 1 diabetes:

- Preferred: Begin IV insulin drip.
- A less desirable option is to give a long-acting insulin with supplemental doses of rapid-acting insulin.

Perioperative type 2 diabetes:

- Hold oral hypoglycemic agents the day of procedure and resume when the patient is eating again.
- Metformin should be held for 48 hours until normal renal function is assured.
- Thiazolidinediones may be continued (except for the other reasons noted above); however, missing a few doses in a patient who must be kept NPO would not negatively affect blood glucose control.
- Insulin-requiring type 2 patients may be treated similarly to type 1 patients.

Intravenous Insulin Infusion Recommendations:

- The use of intravenous insulin therapy is strongly recommended in the following groups of patients:
 - Critical illness
 - Prolonged NPO status
 - Perioperative period
 - After organ transplant
 - Total parenteral nutrition therapy
 - Blood glucose exacerbated by high-dose glucocorticoid therapy
 - Stroke
 - Labor and delivery
 - As a dose-finding strategy prior to conversion to subcutaneous insulin therapy
 - Other illnesses requiring prompt glucose control

Intravenous insulin therapy should always be used in certain settings such as diabetic ketoacidosis and hyperglycemic hyperosmolar state.

E: Hypoglycemia: Treatment of Adults and Children Older than 1 Year of Age

Recognition of hypoglycemia in the patient with diabetes:

- Patient has a diagnosis of diabetes.
- Patient is on a medication that can cause hypoglycemia (insulin or insulin secretagogues).
- One or more symptoms of hypoglycemia are present: shakiness, hunger, irritability, altered level of consciousness, headache, sweats, and cool skin.
- A stat bedside blood glucose should be done (patient may perform his/her own bedside blood glucose).
- Hypoglycemic treatment should begin when bedside blood glucose is lower than 70 mg/dL.

Treatment of the CONSCIOUS patient with hypoglycemia:

- 15/15 rule: Give a 15 gm carbohydrate oral feeding of one of the following:
 - 8 oz of low fat/nonfat milk
 - 4 oz of any juice WITHOUT ADDED SUGAR
 - 4 oz of regular soda pop
 - 1 tube of glucose gel
 - 3 glucose tablets.
- Wait 15 minutes. Recheck bedside blood glucose. If still less than 70 mg/dL, feed a second 15 gm carbohydrate feeding.
- Wait 15 minutes. Recheck bedside blood glucose. Notify physician of event if not resolved after 30 gm of carbohydrate.
- If meal is not to be served for over an hour, give patient a snack of 30-45 gm carbohydrate. Consider sandwich, cheese and crackers, or other snack that incorporates carbohydrates with fat and protein.
- Troubleshoot for cause. Too much medication, extra activity, medication taken/given at wrong time or delay in meal are common reasons for hypoglycemic events. Prevent reoccurrence and educate patient as needed.

Treatment of the UNCONSCIOUS patient with hypoglycemia:

- Call for bedside glucose in the patient with known diabetes.
- Stop IV insulin if present.
- Treat hypoglycemia and call physician.
- Consider IV placement if one not present.

- 1/2 to 1 ampule of Dextrose 50% solution IV per orders, or 1 amp of glucagon IM per orders. Glucagon takes 20 minutes to raise blood glucose and for patient to regain consciousness. Nausea and vomiting are common side effects or glucagon.
- Recheck blood glucose. If glucagon was given, the possibility of continued hypoglycemia is present for 24 hours and the patient may need extra carbohydrate intake. Test blood glucose every four hours and feed as necessary to keep blood glucose readings greater than 80 mg/dL.
- Troubleshoot for cause.

Prevention of Hypoglycemia

Prevention of hypoglycemia requires diligent monitoring of blood glucose, proper dosing of medications, regular meal planning and close monitoring during and after exercise. Sick day management includes increased fluid intake and frequent blood glucose monitoring with meals and at bedtime. Monitoring urine for ketones (if on insulin) is an essential tool of diabetes management.

Education: Hospital admission should be viewed as an opportunity to reassess a patient's selfmanagement and other skills. Patients who have never received diabetes education, who lack knowledge of these skills or who need a review of diabetes self-management, should be considered for consultation by the diabetes education team or specialist prior to being discharged from the hospital.

Discharge Planning: Ideally, the outpatient regimen should be begun prior to the patient being discharged. Patients should be made aware of any changes in this regimen. Appropriate follow-up should be arranged and patients should be instructed on how to proceed if there are any diabetes related issues or problems that arise after discharge.

F. Diabetic Ketoacidosis (DKA)

Definition

- Absolute or relative insulin deficiency with consequent hyperglycemia and accumulation of ketones in the blood resulting in a metabolic acidosis of the anion gap type.
- Criteria: glucose >250 mg/dL; arterial pH <7.35; bicarbonate <15; positive serum ketones; anion gap >10.

Pathogenesis

- Reduction in the net effective action of circulating insulin.
- Elevation of counter-regulatory hormones: glucagon, catecholamines, cortisol and growth hormone.
- Increased hepatic and renal glucose production and impaired glucose utilization in peripheral tissues.
- Hyperglycemia and parallel changes in the osmolality of the extracellular space.
- Release of free fatty acids into the circulation from fat tissue leading to unrestrained hepatic fatty acid oxidation to ketone bodies with resulting ketonemia and metabolic acidosis.
- Loss of water, sodium, potassium and other electrolytes.

Precipitating Factors

- The precipitating factor is identifiable in 80% of the cases:
 - Infection: 30-40%
 - Cessation of insulin: 15-20%
 - Myocardial infarction, pancreatitis, stroke, alcohol abuse, drugs, trauma, other: 10-15%
 - No cause identified: 20-25%
- Special:
 - Drugs: corticosteroids, thiazides, sympathomimetic agents
 - Young patients: psychological problems, fear of weight gain

Presentation

- History: polyuria, polydipsia, polyphagia, weight loss, vomiting, abdominal pain, clouded sensorium.
- Physical examination: poor skin turgor, Kussmaul breathing, tachycardia, hypotension, altered mental status, shock, coma, normothermic or hypothermic because of peripheral vasodilation.

Laboratory

- Initial lab
 - Complete blood count, blood glucose, BUN, serum creatinine, serum ketones, electrolytes (calculate anion gap), osmolality, urinalysis, urine ketones, arterial blood gasses, magnesium, calcium, phosphorus and chest x-ray.
- Additional lab
 - EKG: if severely ill, has history of heart disease or over age 40.
 - Cultures (if indicated): urine, blood, throat, sputum, vagina, wound, spinal fluid or stool.
- Comments
 - Leukocytosis may be proportional to ketosis and not indicative of infection.
 - Hyponatremia can be due to flux of water from the intracellular space or falsely lowered by severe hypertriglyceridemia.
 - Serum potassium should be initially elevated due to extracellular shift caused by insulin deficiency, hypertonicity and acidemia; if initial serum potassium is not elevated, the patient may have severe total-body potassium deficiency and require cardiac monitoring and more vigorous potassium replacement.
 - If patient is stuporous or comatose and calculated effective or measured serum osmolality is not 320 or greater, then another cause for the mental status change needs to be looked for (calculated effective serum osmolality = 2 x serum sodium plus serum glucose divided by 18).
 - "Corrected" serum sodium helps assess dehydration:
 - "Corrected" [Na+] = [Na+] + 1.6 x blood glucose minus 100 divided by 100.
 - An elevated corrected serum sodium indicates a greater free water deficit and intracellular dehydration.
 - As glucose is lowered with insulin, patients with a high corrected serum sodium will need larger quantities of normal saline to preserve intravascular volume before hypotonic fluids can be safely used.

Differential Diagnosis

- Starvation ketosis bicarbonate usually not lower than 18 mEq/L
- Alcoholic ketoacidosis glucose elevation mild (rarely >250 mg/dL)
- Lactic acidosis elevated blood lactate
- Salicylate ingestion elevated serum salicylate
- Ethylene glycol ingestion calcium oxalate and hippurate crystals in the urine
- Methanol ingestion elevated blood methanol
- Chronic renal failure usually a hyperchloremic acidosis

Treatment

- Successful treatment:
 - Correction of dehydration, hyperglycemia and electrolyte imbalance.
 - Identification and treatment of comorbid conditions.
 - Frequent patient monitoring: electrolytes, blood glucose, BUN, creatinine, osmolality and venous pH should be measured every 2-4 hours.
 - Caution should be used in measuring ketones during therapy. Beta-hydroxybutyrate is the strongest and most prevalent ketoacid in DKA. During therapy it is converted back to acetoacetic acid and so measuring ketones by the nitroprusside method may be misleading.
 - Criteria for the resolution of DKA are: blood glucose <200 mg/dL; serum bicarbonate >18 mEq/L; and venous pH >7.30.

Fluid therapy

- In the absence of cardiac compromise, give normal saline at the rate of 15-20 mL per kg body weight per hour (1 to 1.5 L for the average adult).
- Subsequent hydration depends on state of hydration, electrolyte levels and urinary output.
- Half normal saline is indicated at 4-14 mL per kg per hour if corrected serum sodium is normal or high; give normal saline at the same rate if corrected serum sodium is low.
- Once urine output is established, the IV should include 20-30 mEq/L potassium until the patient is stable and can tolerate oral potassium.
- Fluid replacement should correct estimated deficits within the first 24 hours.

Insulin treatment

- Once hydration and, if needed, potassium replacement has started, a bolus of regular insulin at 0.15 units/kg (total 8-12 units for average adult) can be given and a continuous insulin infusion begun.
- The continuous insulin infusion should be at the rate of 0.1 units per kg per hour (5 to 9 units per hour in the average adult).
 - Usually add insulin in concentration of 10% or more (e.g., more than 100 units per 1,000 cc).Mix well.
 - Discard the first 50 cc through the tubing before beginning the infusion.
- Plasma glucose should decline at a rate of 50-75 mg/dL per hour.
- If plasma glucose has not fallen by 50 mg/dL in the first hour, and hydration status is acceptable, insulin infusion rate may be doubled every hour until the above rate of decline is achieved.
- When plasma glucose of 250 mg/dL is reached, insulin infusion rate may be decreased to 0.05-0.1 u/kg/hr (3-6 u/hr in average adult) and dextrose added to the IV fluids to maintain the above plasma glucose until the acidosis is resolved.
- To prevent rebound acidosis and ketosis again, IV insulin can be continued for a full additional 24 hours before going back to subcutaneous insulin; there should always be at least 2 hours of overlap between initiation of subcutaneous insulin and cessation of IV insulin.
- Potassium
 - Insulin treatment, volume expansion, and correction of acidosis decrease what is usually an elevated serum potassium to start with.
 - Potassium replacement is begun when serum potassium falls below 5.5 mEq/L, assuming there is an adequate urine output.
- Bicarbonate
 - At a pH of 7.0 or greater, fluid, insulin, and electrolytes resolve the ketoacidosis without the need for bicarbonate.
 - Prospective randomized studies done when the arterial pH is between 6.9 and 7.1 have failed to show either benefit or harm from bicarbonate therapy.
 - There are no prospective randomized studies of the use of bicarbonate in DKA when the pH is <6.9.
 - Given that severe acidosis may lead to myriad adverse vascular events, the following guidelines may be followed:
 - If the arterial pH is <6.9, 100 mmol bicarbonate may be given in 400 mL IV fluid over a 2 hour period.
 - If the arterial pH is 6.9 7.0, 50 mmol bicarbonate may be given in 200 mL IV fluid over a 1 hour period.
 - The arterial pH should be re-measured every 2 hours and the above therapy repeated until the arterial pH is 7.0.

Phosphate

- Despite whole body phosphate deficits in DKA, which are in the range of 1.0 mmol per kg body weight, serum phosphate levels are often normal or increased at presentation.
- Serum phosphate decreases with insulin treatment.
- Prospective randomized studies have failed to show any clinical benefit from phosphate therapy in DKA.

• Overzealous phosphate treatment can cause severe hypocalcemia. Nevertheless, careful phosphate replacement may be indicated in the presence of cardiac dysfunction, anemia, respiratory depression or the presence of a serum phosphate <1.0. In that case, 10-30 mEq/L potassium phosphate may be added to IV fluids.

Complications of DKA

- Hypoglycemia from over-corrected insulin therapy
- Hypokalemia due to insulin and bicarbonate therapy and under-corrected potassium replacement
- Hyperglycemia due to discontinuance of IV insulin treatment without adequate overlapping subcutaneous insulin treatment; subcutaneous regular insulin and IV insulin should overlap by at least 2 hr
- Cerebral edema
 - Seen in 0.7-1.0% of children with DKA and has been reported in young adults in their 20's
 - If present, is frequently fatal
 - Preventive measures that might decrease the risk are:
 - Gradual replacement of sodium and water in patients who are hyperosmolar (maximal reduction in osmolality 3 mosm/kg/hr)
 - $\circ\,$ The addition of dextrose to the IV once the plasma glucose reaches 250 mg/dL
- Non-cardiogenic pulmonary edema

Prevention of DKA

Educating the patient and family members on self-management training, recognition of potential DKA, and self-management of sick care may help prevent DKA. Self-management skills need to be combined with access to medical care and effective communication with health care provider.

G. Non-Ketotic Hyperosmolar Hyperglycemic State (HHS) in Adults

Definition

- Absolute or relative insulin deficiency with consequent severe hyperglycemia resulting in profound dehydration and electrolyte imbalance.
- Criteria: glucose >600 mg/dL; arterial pH >7.30; bicarbonate >15; trace or small serum ketones; effective serum osmolality >320; variable anion gap; stupor or coma.

Pathogenesis

- Reduction in the net effective action of circulating insulin.
- Elevation of counter-regulatory hormones: glucagon, catecholamines, cortisol and growth hormone.
- Increased hepatic and renal glucose production and impaired glucose utilization in peripheral tissues.
- Severe hyperglycemia and parallel changes in the osmolality of the extracellular space.
- Loss of water, sodium, potassium and other electrolytes.

Precipitating Factors

- Infection
- Cessation of insulin or oral medications
- Myocardial infarction, pancreatitis, stroke, alcohol abuse, drugs, trauma
- Drugs such as corticosteroids, thiazides, sympathomimetic agents

Presentation

- History: polyuria, polydipsia, polyphagia, weight loss, vomiting, clouded sensorium or coma
- Physical examination: poor skin turgor, tachycardia, hypotension, altered mental status, shock, coma, normothermic or hypothermic because of peripheral vasodilation in spite of infection

Laboratory

 Initial lab: Complete blood count, blood glucose, BUN, serum creatinine, serum ketones, electrolytes (calculate anion gap), osmolality, urinalysis, urine ketones, arterial blood gasses, magnesium, calcium, phosphorus and chest x-ray

Additional lab

- EKG: if severely ill, has history of heart disease or over age 40
- Cultures (if indicated): urine, blood, throat, sputum, vagina, wound, spinal fluid or stool

Comments

- Leukocytosis may be proportional to ketosis and not indicative of infection.
- Hyponatremia can be due to flux of water from the intracellular space or falsely lowered by severe hypertriglyceridemia.
- Serum potassium should be initially elevated due to extracellular shift caused by insulin deficiency, hypertonicity and acidemia. If initial serum potassium is not elevated, the patient may have severe total-body potassium deficiency and require cardiac monitoring and more vigorous potassium replacement.
- If patient is stuporous or comatose and calculated effective or measured serum osmolality is not 320 or greater, then another cause for the mental status change needs to be looked for (calculated effective serum osmolality = 2 x serum sodium plus serum glucose divided by 18).
- "Corrected" serum sodium helps assess dehydration:
 - "Corrected" [Na+] = [Na+] + 1.6 x blood glucose minus 100 divided by 100.
 - An elevated corrected serum sodium indicates a greater free water deficit and intracellular dehydration.
 - As glucose is lowered with insulin, patients with a high corrected serum sodium will need larger quantities of normal saline to preserve intravascular volume before hypotonic fluids can be safely used.

Differential Diagnosis

- Starvation ketosis bicarbonate usually not lower than 18 mEq/L
- Alcoholic ketoacidosis glucose elevation mild (rarely >250 mg/dL)
- Lactic acidosis elevated blood lactate
- Salicylate ingestion elevated serum salicylate
- Ethylene glycol ingestion calcium oxalate and hippurate crystals in the urine
- Methanol ingestion elevated blood methanol
- Chronic renal failure usually a hyperchloremic acidosis

Treatment

- Successful treatment:
 - Correction of dehydration, hyperglycemia and electrolyte imbalance.
 - Identification and treatment of comorbid conditions.
 - Frequent patient monitoring: electrolytes, blood glucose, BUN, creatinine, osmolality and venous pH should be measured every 2 4 hours.

Fluid therapy:

- In the absence of cardiac compromise, give normal saline at the rate of 15-20 mL per kg body weight per hour (1 to 1.5 L for the average adult).
- Subsequent hydration depends on state of hydration, electrolyte levels and urinary output.
- Half normal saline is indicated at 4-14 mL per kg per hour if corrected serum sodium is normal or high; give normal saline at the same rate if corrected serum sodium is low.
- Once urine output is established, the IV should include 20-30 mEq/L potassium until the patient is stable and can tolerate oral potassium.
- Fluid replacement should correct estimated deficits within the first 24 hours.

Insulin treatment:

• Once hydration and, if needed, potassium replacement has started, a bolus of regular insulin at 0.15 units/kg (total 8-12 units for average adult) can be given and a continuous insulin infusion begun.

- The continuous insulin infusion should be at the rate of 0.1 unit per kg per hour (5 to 9 units per hour in the average adult).
 - Usually add insulin in concentration of 10% or more (e.g., more than 100 units per 1,000 cc).
 - Mix well.
 - Discard the first 50 cc through the tubing before beginning the infusion.
- Plasma glucose should decline at a rate of 50-75 mg/dL per hour. If plasma glucose has not fallen by 50 mg/dL in the first hour, and hydration status is acceptable, then insulin infusion rate may be doubled every hour until the above rate of decline is achieved.
- When plasma glucose of 300 mg/dL is reached, insulin infusion rate may be decreased to 0.05-0.1 u/kg/hr (3-6 u/hr in average adult) and dextrose added to the IV fluids to maintain the above plasma glucose until the obtundation and hyperosmolarity is resolved.
- To prevent rebound hyperglycemia, IV insulin can be continued for a full, additional 24 hours before going back to subcutaneous insulin or oral agents.

Potassium

- Insulin treatment and volume expansion decrease what is usually an elevated serum potassium level.
- Potassium replacement is begun when serum potassium falls below 5.5 mEq/L, assuming an adequate urine output.
- Insulin treatment should be delayed until serum potassium is >3.3 mEq/L to avoid cardiac arrhythmias, cardiac arrest or respiratory muscle weakness.
- Bicarbonate: usually not necessary unless the HHS is accompanied by lactic acidosis.

Complications of HHS

- Hypoglycemia due to over-corrected insulin therapy
- Hypokalemia due to insulin therapy and under-corrected potassium replacement
- Hyperglycemia due to discontinuance of IV insulin treatment without adequate overlapping subcutaneous insulin or oral agent treatment; to avoid hyperglycemia, subcutaneous regular insulin and IV insulin should overlap by at least 2 hrs
- Non-cardiogenic pulmonary edema

Prevention

Educating the patient and family members on self-management training, recognition of potential DKA, and self-management of sick care may help prevent DKA. Self-management skills need to be combined with access to medical care and effective communication with health care provider.

REFERENCE SECTION X

AACE Medical Guidelines for Clinical Practice for the Management of Diabetes Mellitus. *Endocrine Practice.* 13(Suppl 1):3-66. May/June 2007

American Diabetes Association. Clinical Practice Recommendations. Standards of medical care for patients with diabetes mellitus. *Diabetes Care*. 30(Suppl 1):S4-S34. 2007

DeFronzo R. Diabetic ketoacidosis. Diabetes Reviews. 2(2):209-238. 1994

Hirsch, I. Insulin in the Hospital Setting. Adelphi publishing. New York, NY. 2003

Van den Berghe G, et al. Intensive insulin therapy in critically ill patients. *The New England Journal of Medicine*. 345(19):1359-1367. 2001

Van den Berghe, G et al. Intensive insulin therapy in Medical ICU. *The New England Journal of Medicine*. 354(5):449-461. 2006

XI. DIABETES SELF-MANAGEMENT AND THE DIABETES HEALTH CARE TEAM

Diabetes Self-Management

Diabetes is a chronic, lifelong disease. Individuals with diabetes are asked to test their blood glucose levels 1–8 times a day, exercise, choose a healthy diet, take their medication properly, see their health care team on a regular basis, manage their stress level, and deal with every other aspect of life. Juggling all these tasks can be difficult. The health care team often labels people with diabetes 'noncompliant' when they do not perform these tasks to the preference of the team. Rather, it may be that the treatment regimen has not been tailored to the individual's lifestyle.

Multiple studies have been done to determine the importance of self-monitoring blood glucose (SMBG). Most studies find that SMBG is necessary in insulin dependent diabetes patients with a recommendation of SMBG three or four times per day. For diabetes patients not using insulin, study results are less clear.

For type 2 diabetes patients, not on insulin therapy, there is inconclusive evidence of the benefits of SMBG. There appears to be little to no difference in A1c levels as a result of SMBG. Other concerns raised were cost of supplies for SMBG, correct technique, and patient satisfaction. However, these studies did not evaluate SMBG as a tool to assist the patient in understanding the effect of diet, exercise and stress on blood glucose and as a means for more autonomous participation in diabetes care. One study shows a positive benefit to SMBG in making dietary changes based on blood glucose readings. For some individuals, SMBG may be the feedback needed to make behavioral changes to improve their health.

Diabetes Self-Management Training (DSMT) allows individuals with diabetes to be active members of their health care team. DSMT allows individuals to learn how to incorporate disease management into their lifestyle. DSMT includes:

- Describing the disease process and treatment options
- Incorporating appropriate nutritional management
- Incorporating physical activity into lifestyle
- Utilizing medications for therapeutic effectiveness
- Monitoring blood glucose, urine ketones (when appropriate), and using the results to improve control
- Preventing, detecting, and treating acute complications
- Preventing, detecting, and treating chronic complications
- Goal setting to promote health and problem solving for daily living
- Integrating psychosocial adjustments to daily life
- Promoting pre-conception care, management during pregnancy, and gestational diabetes management.

The American Diabetes Association (ADA) provides a baseline framework by which DSMT should be conducted. The State of Wyoming has a number of ADA recognized DSMT programs. Medicare and most insurance companies reimburse for DSMT if provided at ADA recognized sites.

The Diabetes Health Care Team

The patient directs the health care team and each member of the team provides a particular focus to the education and management process. Diabetes self-management skills are taught by a multidisciplinary team, which may consist of:

- Health Care Providers
- Registered Nurse/CDE

- Registered Dietitian/CDE
- Exercise Specialist
- Behaviorist
- Podiatrist
- Pharmacist
- Eye care specialist
- Dentist
- Other health care professionals

Regular communication between the multidisciplinary professionals helps to provide a coordination of care to optimize the best training and management plan for the individual with diabetes. Individuals with diabetes should receive training when they are first diagnosed based on a needs assessment. Since self-management is ongoing, they should also receive, at the minimum, an annual assessment of self-management skills.

REFERENCE SECTION XI

American Diabetes Association. National Standards for Diabetes Self-Management Education. *Diabetes Care*. 30(Suppl. 1):S96-S103. 2007

American Diabetes Association. Standards of Care in Diabetes 2007. *Diabetes Care*. 30 (Suppl. 1):S9. 2007

Davis W, Bruce D, Davis T. Is Self-Monitoring of Blood Glucose Appropriate for All Type 2 Diabetic Patients? The Fremantle Diabetes Study. *Diabetes Care*. 29:1764-1770. 2006

Franciosi M, Pellegrini F, De Berardis G, Belfiglio M, Cavalier D, Di Nardo B, Greenfield S, Kaplan S, Sacco M, Tognoni G, Valentini M, Nicoluucci A. The Impact of Blood Glucose Self-Monitoring on Metabolic Control and Quality of Life in Type 2 Diabetic Patients: An urgent need for better educational strategies. *Diabetes Care*. 24:1870-1877. 2001

Harris M. Frequency of Blood Glucose Monitoring in Relation to Glycemic Control in Patients with Type 2 Diabetes. *Diabetes Care*. 24:979-982. 2001

O'Riordan M, Barclay L. Self-Monitoring of Blood Glucose Does Not Improve HbA1c Levels in Patients With Non-Insulin Treated Diabetes. *Medscape Medical News*. 2007

Supporting Effective Education (SEED). Module 1: Clinical Overview of Diabetes Management. Health Learning Systems. Wayne, New Jersey. 2001

Ulrich S, Siebolds M, Mertes G. Meal-Related Structured Self-Monitoring of Blood Glucose: Effect on diabetes control in non-insulin treated type 2 diabetic patients. *Diabetes Care*. 25:1928-1932. 2002

Welschen L, Bloemendal E, Nijpels G, Dekker J, Heine R., Stalman W, Bouter L. Self-Monitoring of Blood Glucose in Patients With Type 2 Diabetes Who Are Not Using Insulin: A systematic review. *Diabetes Care*. 28:1510-1517. 2005

XII. ASSOCIATED DISORDERS

A. Autoimmune Disorders

Patients with type 1 diabetes have a greater incidence of autoimmune disorders including thyroid disorders, celiac disease, adrenal insufficiency, and polyglandular disorders. Thyroid disorders and celiac disease are the most common. It is recommended that close to the time patients are diagnosed with diabetes, thyroid function and thyroid antibody tests are performed as a baseline. Repeat screening annually of thyroid function tests is suggested.

1. Celiac Disease

Screening for the disease should be considered close to the time patients are diagnosed with diabetes, and repeated if clinically indicated. Celiac disease is usually asymptomatic.

- Symptoms:
 - recurring abdominal bloating and pain
 - chronic diarrhea and/or constipation
 - weight loss
 - steatorrhea
 - unexplained anemia
 - flatulence
 - osteopenia/osteoporosis
 - behavior changes/depression
 - muscle cramps
 - fatigue
 - delayed growth
 - failure to thrive in infants
 - bone or joint pain
 - seizures
 - tingling numbness in the legs (from nerve damage)
 - aphthous ulcers
 - dermatitis herpetiformis
 - tooth discoloration or loss of enamel
 - missed menstrual periods (often because of excessive weight loss)
- Laboratory screening:
 - IgA anti-tissue transglutaminase antibody, IgA endomysial antibody and a serum IgA should be obtained (patient must not be on a gluten free diet at the time of the blood draw).
 - Refer for small bowel biopsy if blood tests positive or if high degree of suspicion.
- Diagnosis:
 - Diagnosis must be confirmed by resolving symptoms on a gluten free diet.

2. Other Autoimmune/Endocrine Conditions

In addition to celiac disease, type 1 diabetes is also not infrequently encountered with other autoimmune mediated disorders. The possibility of these comorbidities should be considered in every patient with type 1 diabetes.

2a. Addison's Disease

- Adrenal insufficiency can occur alone or along with other autoimmune endocrinologic disorders including type 1 diabetes.
- Symptoms can include weight loss, fatigue, hyperpigmentation, hypotension, gastrointestinal symptoms (anorexia, nausea and vomiting, and abdominal pain), hypoglycemia and electrolyte abnormalities (hyponatremia and hyperkalemia); onset is often insidious and non-specific.

- Unrecognized adrenal insufficiency could be catastrophic; therefore, patients with type 1 diabetes who also exhibit some or all of the above symptoms should be considered for evaluation of adrenal function.
- Although a significantly abnormal serum cortisol level could be useful, the gold standard for assessment of adrenal function is a stimulation test with an adrenocorticotropic (ACTH) analogue (Cosyntropin) and measuring a serum ACTH level on a blood sample drawn before the Cosyntropin is given.
- Treatment is replacement of steroid deficiencies; those clinicians who are unfamiliar with this should refer to appropriate specialist.

2b. Thyroid Disorders

- Autoimmune thyroid dysfunction can result in either hypothyroidism or hyperthyroidism. It is commonly seen in diabetes, both because of shared underlying autoimmune pathophysiology, and also because there is a high prevalence in the general population.
- Depending on the thyroid abnormality and severity of disease, symptoms can range from vague and nonspecific to very significant and obvious.
- Measurement of serum T4 and TSH should be performed at the time of diagnosis of diabetes and subsequently as necessary in appropriate individuals; further evaluation and/or treatment depends on the underlying abnormality.

2c. Other Autoimmune Disorders

- There are other autoimmune mediated disorders occasionally found with type 1 diabetes either in specific autoimmune polyendocrine syndromes or sporadically.
- These can include not only thyroid disease, adrenal insufficiency, and celiac disease as described above, but also, hypogonadism, hypopituitarism, vitiligo, pernicious anemia, autoimmune hepatitis, hypoparathyroidism, alopecia, myasthenia gravis, and chronic mucocutaneous candidiasis.

B. Other Associated Disorders

Just as autoimmune disorders are found in greater frequency in type 1 diabetes, there are some disorders that are found with greater frequency in patients with type 2 diabetes. Three of these disorders (hemochromatosis, polycystic ovarian syndrome, and depression) are mentioned here.

1. Hemochromatosis

- Hereditary hemochromatosis is the most common autosomal recessive disorder affecting individuals of northern European descent.
- In the general U.S. population its prevalence approaches 1 in 400. Patients with type 2 diabetes have been shown to have higher risk of having hemochromatosis than the general population.
- Hemochromatosis results from inappropriate absorption and deposition of dietary iron that can result in the development of hepatic and nonhepatic end-organ injury, leading to liver cirrhosis, hepatocellular carcinoma, diabetes, pituitary dysfunction, arthritis, skin pigmentation, and cardiac diseases.

Clinical Presentation

- In patients who are symptomatic, the most common presenting features of hemochromatosis are weakness, lethargy, arthralgias, abdominal pain, and impotence; these patients may also have a mild increase in their serum aminotransferase.
- Most patients with hemochromatosis are asymptomatic for many years.
- The frequency of diabetes as an initial presenting symptom has become less common because of more extensive population screening.

Screening

- Consider screening for positive family history or unexplained liver transaminase levels.
- Measure fasting serum transferrin and serum ferritin.
- If saturation is >45%, refer to gastroenterologist for consideration of genetic testing and/or liver biopsy.
- Other family members should be screened if diagnosis of hemochromatosis is established.

Treatment

• Consult a specialist trained in hemochromatosis.

2. Polycystic Ovarian Syndrome (PCOS)

- Polycystic ovarian syndrome is a syndrome of chronic anovulation and hyperandrogenism that affects 5% to 10% of pre-menopausal women; its association with insulin resistance has led to increased recognition of its importance.
- PCOS is the leading hormonally related cause of infertility.
- PCOS is a major risk factor for type 2 diabetes and is one of the factors in the AACE criteria for diagnosis of metabolic syndrome.
- Overall prevalence rates of glucose intolerance and type 2 diabetes have been reported to be as high as 40% in several studies of women with PCOS.

Clinical Presentation

- Women with PCOS often first present with complaints of menstrual irregularities.
- Oligomenorrhea and hirustism are often common early symptoms, but other complaints can also include: infertility, amenorrhea, dysfunctional uterine bleeding, acne, alopecia, and seborrhea.
- Central abdominal obesity is common in women with PCOS, but it does not occur in all patients. Thus, a lack of central abdominal obesity does not rule out PCOS.
- Acanthosis nigricans from insulin resistance is also a common finding, especially in obese PCOS women.
- Family history may also include infertility, menstrual irregularities, early type 2 diabetes, hypertension, and dyslipidemia.

Diagnosis

- The diagnostic criteria for PCOS are hyperandrogenism and chronic anovulation in pre-menopausal women in the absence of other endocrinologic etiologies.
- Although most women with PCOS will have polycystic ovaries on ultrasound, this finding is neither specific nor required to make the diagnosis; ultrasound is not recommended in a diagnostic work up unless there are other specific reasons to do so.
- The initial screening recommended in women with chronic anovulation and hyperandrogenism includes: b-HCG to rule out pregnancy, and then a 0700-0900 hr serum prolactin, TSH, total and free testosterone, dehydroepiandrosterone sulfate (DHEAS), and 17-hydroxyprogesterone (17-OHP).
- Abnormal prolactin or TSH requires disease-specific evaluation.
- Moderately elevated total and free testosterone and/or dehydroepiandrosterone sulfate (DHEAS) suggests PCOS.
- Very significantly elevated testosterone (>150 ng/dl) and/or DHEAS (>700 ug/dl) means that ovarian or adrenal neoplasms must be ruled out.
- Elevated 17-OHP (>300 ng/dl) suggests possibility of congenital adrenal hyperplasia-non-classic adrenal 21-hydroxylase deficiency and in this case a referral to an endocrinologic specialist should be considered.
- An elevated leutenizing hormone/follicle stimulating hormone ratio can suggest PCOS, but because of the pulsate secretion of leutenizing hormone, single measurements are insensitive.
- Approximately half of the siblings of women with PCOS also have the condition, even without clinical symptoms; therefore, diagnostic testing of these at risk individuals should be considered.

Therapy for PCOS

- Lifestyle modification including caloric restriction and increased physical activity should be considered the first-line therapy. As little as 7-10% weight loss has been associated with return of regular ovulatory cycles and improvement of insulin sensitivity.
- Because of the association with insulin resistance and metabolic syndrome, all women who have been diagnosed with PCOS should be screened for dyslipidemia, hypertension, and impaired glucose tolerance/type 2 diabetes.
- Because fasting BG* has been reported to fail to detect type 2 diabetes in up to 50% of PCOS patients who are later confirmed to have diabetes by OGTT, it is recommended that a 75 gm OGTT be considered in women with PCOS in which impaired glucose tolerance/type 2 diabetes is suspected.

• There are several pharmacologic options available, each directed at the different physiologic abnormalities that occur in PCOS.

- Metformin: Metformin has been used with some success in women with PCOS. It has been found to reduce serum insulin levels and decrease androgen levels. There are more studies available regarding the use of metformin in PCOS than the currently available thiazolidinediones because this product has been available for a longer period of time.
- Thiazolidinediones (TZDs): Most of the studies available for this group are with Troglitazone, a product no longer available. Some clinicians prefer TZDs over metformin because of their potent insulin sensitizing effects as well as successful clinical experience. However, the results of ongoing research with the two newer TZDs (Rosiglitazone and Pioglitazone) in PCOS are still pending.
- Oral contraceptives: Menstrual problems include some of the symptoms that are often most concerning for women with PCOS. Appropriate use of oral contraceptives can be one tool to help restore cyclic menstrual bleeding.
- **Spironalactone:** This drug has been used for its antiandrogenic properties that can lessen the symptoms of hyperandrogenism. It is not without side effects, however.
- Referral to a specialist with experience in PCOS may be considered for any PCOS patients in which the diagnosis or management is unclear or in those experiencing difficulty with infertility or other issues.

3. Depression

Definition

Depression has been shown to increase morbidity and mortality of many health conditions including diabetes. Multiple studies conclude that diabetes doubles the chance of depression. One study concluded that diabetes causes multiple psychosocial problems and that these issues are barriers to achieving adequate glycemic control and interfere with self-management behaviors. Many studies suggest our current health care systems are poorly equipped to handle and support chronic illness care. Effective treatment of depression can improve clinical outcomes and quality of life.

General Recommendations

Preliminary assessment of psychological and social status should be included as part of the medical management of diabetes. Psychosocial screening should include assessing attitudes about illness, expectations for medical management and outcomes, affect/mood, general and diabetes-related quality of life, resources (financial, social and emotional), and psychiatric history. Screening for psychosocial problems such as depression is needed especially when adherence to treatment regimen is poor.

Screening

Self-reported symptoms and/or scales such as the Beck Depression Inventory or the Center for Epidemiologic Studies-Depression Scale can be used to screen for depression.

^{*} BG throughout these Recommendations means plasma or serum glucose. For a discussion on the ways of measuring glucose in the blood and their differences, see the Appendix, page 93.

Symptoms of Depression:

- Persistent sad, anxious, or "empty" mood
- Feelings of hopelessness, pessimism
- Feelings of guilt, worthlessness, helplessness
- Loss of interest or pleasure in hobbies and activities that were once enjoyed, including sex
- Decreased energy, fatigue, being "slowed down"
- Difficulty concentrating, remembering, making decisions
- Insomnia, early-morning awakening, or oversleeping
- Appetite and/or weight changes
- Thoughts of death or suicide, or suicide attempt
- Restlessness, irritability

If five or more of these symptoms are present every day for at least two weeks and interfere with routine daily activities such as work, self-care, and childcare or social life, seek evaluation and treatment for depression.

Treatments

Psychotherapy and/or pharmacotherapy may be required for patients diagnosed with depression. The following resources are listed to obtain further information on depression and treatments: http://health.nih.gov/result.asp/183 http://www.psych.org/psych_pract/

http://www.fpnotebook.com/PSYCh5.htm

Metabolic Syndrome

Metabolic syndrome is a common associated disorder of diabetes. For information on the metabolic syndrome, refer to page 57.

REFERENCE SECTION XII

American College of Physicians PIER (Physicians Information and Education Resource). http://pier.acponline.org

Arbor A. Depression. National Guideline Clearinghouse. University of Michigan Health System. P20. October 2005

Kriensen C, Dunaif A. Diabetes and polycystic ovarian syndrome (Chapter 41). In *Medical Management of Diabetes Mellitus.* Clark NG, Cefalu W, Leahy JL. CRC Press. New York, NY. 2000

XIII. EMERGENCY AND DISASTER PREPAREDNESS IN DIABETES

People with diabetes or any other chronic disease should always be prepared for emergencies. In Wyoming, weather conditions can change drastically in only minutes. Emergencies can arise affecting the nation, the state, a community, or local families without notice.

To lessen the impact emergencies can have on health, advise patients with diabetes to prepare the following items ahead of time: an insulated cooler for injectable medications; extra insulin; insulin syringes; needles; a meter; extra batteries for the meter, extra test strips; lancets; glucose containing foods, instant glucose gel or tabs; glucagon; other oral medications; and pump supplies and batteries to last for a week or more. All these items are critically important to diabetes self-management care.

Advise all patients to carry a list of medications. Note prescription numbers since many chain pharmacies may be able to fill medications in another part of the country. Local pharmacies may not be available during disasters. A list of pertinent medical conditions should be readily available so health care workers will be able to triage care if necessary. Copies of medically relevant lab tests or x-rays should also be considered.

Advise patients to make or buy a disaster kit with first aid supplies. Remind them to have enough food and water in the emergency kit to last at least 3 days. The emergency kit should be reviewed and replenished at least twice a year.

For more information on emergency and disaster preparedness in diabetes, refer to the Centers for Disease Control and Prevention website at http://www.cdc.gov/diabetes/news/docs/hurricanes.htm#1.

REFERENCE SECTION XIII

American Diabetes Association. Clinical Practice Recommendations. Standards of medical care in diabetes. *Diabetes Care*. 30(Suppl 1):S33. 2007

XIV. DIABETES CARE IN THE SCHOOL SETTING

About one in every 400-600 children and adolescents have type 1 diabetes. The majority of these young people attend school and need knowledgeable school staff to provide a safe learning environment. Under federal laws protecting people with disabilities, students with diabetes cannot be discriminated against and schools must make reasonable accommodations to meet the special needs of students with diabetes.

A brief summary of diabetes (for school personnel reading this section)

Insulin is a hormone produced by the pancreas that helps the body convert food into energy called glucose. In people with diabetes, either the pancreas does not make insulin or the body cannot use the insulin properly. When the body lacks insulin or cannot use it properly, glucose (the body's main energy source) builds up in the body instead of being used for energy. High blood glucose levels over time cause damage to the eyes, kidneys, nerves, heart, and blood vessels. People with type 1 diabetes do not produce insulin and must receive insulin through injections or insulin pumps. Type 2 diabetes is more common in adults, although it is now being diagnosed in school-aged children. Type 2 diabetes occurs when the body loses its ability to produce sufficient amounts of insulin. Some people with type 2 diabetes can control their disease with diet and exercise alone, while others also need medications and insulin. All people with diabetes need to balance their food, medications, and physical activity levels to keep blood glucose levels as close to normal as possible.

Hypoglycemia (low blood glucose) is the most common immediate health problem for students with diabetes. It occurs when the body gets too much insulin, too little food, a delayed meal, or more than the usual amount of exercise. Symptoms include sweating, light-headedness, confusion, drowsiness, irritability, and tremors. Students suffering from hypoglycemia need to ingest carbohydrates promptly. If a student suffering from hypoglycemia is not able to eat a source of carbohydrates, glucagon must be administered. A student suffering from a hypoglycemic episode should not be left unsupervised until blood glucose values return to the normal range.

Hyperglycemia (high blood glucose) occurs when the body gets too little insulin, too much food or too little exercise. It can also be caused by stress or an illness such as a cold. Common symptoms are thirst, frequent urination, and blurry vision. If untreated, ketones can build up in the body and cause nausea and vomiting. High levels of ketones in the blood or urine require immediate medical attention. Students on insulin pumps may be at a higher risk for developing ketones.

Diabetes Management Plan

Several studies have linked blood glucose control with decreasing the impact of diabetes complications. To reach the goal of controlled blood glucose, parents, health care providers, and school personnel should work together to develop an individualized plan for each student with diabetes, such as the 504 plan. The American Diabetes Association (ADA) offers a sample diabetes management plan for use in a school or day care setting. The individualized plan should be updated with any change in regimen treatment and should be reviewed at least once a year.

The diabetes management plan must be individualized for each student. Potential topics for the plan include the following:

- Frequency of blood glucose monitoring
- Insulin administration or pump management
- Content, amount, and timing of meals and snacks
- Plan for treating hypoglycemia (including the administration of glucagon)
- Plan for treating hyperglycemia
- Plan for checking for ketones and responding to results
- Plan for meeting the student's psycho-social needs (i.e., support groups).

Studies have shown the majority of school personnel have inadequate training for understanding diabetes. School training plans should be implemented and include school administrators, coaches, nurses, teachers, bus drivers, secretaries and other adults with direct links to students. Care of students with diabetes should extend to all school-sponsored events including transportation on the school bus, field trips, and extracurricular activities.

Division of responsibilities

Students

Self-care tasks must be individualized and based on the child's unique developmental time frame. By age 8, most children are able to perform their own fingersticks. By high school, most students can administer insulin without supervision (although many students master this skill much earlier).

Parents

Parents should supply, maintain, and provide for safe disposal of all supplies and equipment for blood glucose monitoring, insulin administration, and ketone testing. In addition, parents should supply emergency telephone numbers, a schedule for meals and snacks, an emergency glucagon kit, a source of glucose, and a plan for contacting health care providers.

School

To meet the needs of students with diabetes, school officials should do the following:

- Train school personnel on diabetes and diabetes care so that an adult and a trained back-up adult can perform fingersticks for blood glucose monitoring and know how to treat readings out of range, administer insulin, test for ketones and respond to results.
- Provide a private location (if requested) for blood glucose monitoring and insulin administration, along with a storage area for diabetes supplies.
- Provide immediate accessibility for the treatment of hypoglycemia by a trained adult, including when necessary, the administration of glucagon.
- Grant students permission to eat a snack anywhere to control blood glucose levels.
- Know the student's schedule for meals and snacks and provide nutrition information on meals served at school.
- Develop an individualized health care plan for each student (such as a 504 plan).

Resources

Several excellent resources are available to help schools provide the needed care for their students with diabetes. The following resources are available from the ADA:

- Diabetes Care Tasks at School: What Key Personnel Need to Know (training modules in a *Power Point* slide format, free download from the ADA website).
- Children with Diabetes: Information for School and Child Care Providers (brochure).

The National Diabetes Education Program (NDEP) is a partnership of the National Institutes of Health, the Centers for Disease Control and Prevention, and more than 200 public and private organizations. NDEP offers the following resource for schools:

• A comprehensive guide designed to empower school personnel, parents, and students to create a safe learning environment and equal access to educational opportunities for all children with diabetes: http://ndep.nih.gov/diabetes/pubs/Youth_NDEPSchoolGuide.pdf.

The National Association of School Nurses offers a program on diabetes for school nurses. The program is called H.A.N.D.S. To learn more the program, visit their website at www.nasn.org.

REFERENCE SECTION XIV

American Diabetes Association. Clinical Practice Recommendations. *Diabetes Care*. 30(Suppl 1):S31, S66-S73. 2007

NDEP Website. http://ndep.nih.gov. Web pages on resources for school personnel. 2007

XV. DIABETES MANAGEMENT IN LONG TERM CARE SETTINGS

About one-fourth of individuals admitted to long term care (LTC) settings have diabetes. More than 80% of these persons also have cardiovascular disease or hypertension and 60% have two or more chronic conditions in addition to diabetes. Costs associated with LTC are burdensome. Increased A1c values of LTC clients cause up to a 30% increase in care costs for this select group of clients.

Literature about the care of diabetes in LTC settings is scarce. Most of the research is over 20 years old and pre-dates the current therapy modalities. The general goals are similar to care for any patient with diabetes; prevent acute metabolic decompensation and decrease morbidity and mortality from long term complications.

In 2003, the American Geriatric Society (AGS) published guidelines for the improvement of care of the older person with diabetes. In 2004, the American Diabetes Association (ADA) first mentioned the care of the geriatric population in relationship to diabetes. While the ADA recognized that softer treatment goals could be indicated for the older adult, separate treatment guidelines were not recommended for the institutionalized adult. There is no consensus about any one set of glycemic targets that apply to all elderly patients.

Four overriding themes come from the AGS published guidelines:

- 1. Individualize care and education.
- 2. Aggressively prevent and manage cardiovascular risk factors.
- 3. Stress glycemic control as an element of preventing and managing microvascular complications.
- 4. Screen for and treat those geriatric syndromes that are more common in older patients with diabetes, including depression, cognitive impairment, urinary incontinence, falls, pain, and polypharmacopia.

Three factors are primary foci for the care of the older adult with diabetes:

- 1. The elimination of symptoms of uncontrolled hyperglycemia (like polyuria, nocturia, vision disturbances, and weakness) and avoiding treatment related hypoglycemia.
- 2. Individualization of care, taking into account the patient's longevity, personalized glucose goals, financial resources, and life situation.
- 3. Attention to nonglycemic risk factors that contribute to cardiovascular mortality, namely blood pressure, dyslipidemia, tobacco use, and physical inactivity.

A1c testing

In higher functioning adults, the treatment goals of diabetes remain as established for the general population. The AGS guidelines recommend a treatment goal of A1c of $\leq 8.0\%$ for selected older persons with diabetes who are unable to achieve the more stringent goals, or who are less likely to benefit from a lower A1c. There are no data to support different targets in older adults and further research is needed.

Self-Monitoring Blood Glucose (SMBG)

Because A1c measurements do not address the extremes of hypo- or hyperglycemia, the AGS guidelines indicate the SMBG may be useful. SMBG allows rational adjustment of therapy to prevent hyperglycemia that may cause polyuria, blurred vision, abnormal sensation, or volume depletion and these symptoms can cause a decrease in quality of life while contributing to the risk of falls, urinary dysfunction and possible cognitive decline.

REFERENCE SECTION XV

American Diabetes Association. Clinical Practice Recommendations. Standards of medical care in diabetes. *Diabetes Care*. 30(Suppl 1):S27. 2007

California Healthcare Foundation/American Geriatrics Society Panel on Improving Care of Elders with Diabetes. Guidelines for improving the care of older persons with diabetes mellitus. *Journal of American Geriatric Society*. 51:S265-S280. 2003

Holt RM, Schwartz FL, Shubrook DO. Diabetes guidelines in extended care facilities. *Diabetes Care*. 30:1454-1459. 2007

Olson DE, Norris SL. Diabetes in older adults. Overview of AGS guidelines for the treatment of diabetes mellitus in geriatric populations. *Geriatrics*. 59(4):18-24. 2004

Rizvi AA. Management of diabetes in older adults. *The American Journal of the Medical Sciences*. 333(1):35-47. 2007

Zarowitz BJ. Management of Diabetes Mellitus in older persons. Geriatric Nursing. 27(2):77-82. 2006

Zarowitz BJ, Tangalos EG, Hollenack K, O'Shea T. The Application of evidence-based principles of care in older persons: Management of Diabetes Mellitus. *Journal of American Medical Directors Association*. 7(4):234-240. 2006

XVI. DIABETES MANAGEMENT IN CORRECTIONAL INSTITUTIONS

For the complete set of the 2007 American Diabetes Association's (ADA) Clinical Practice Recommendations for Diabetes Management in Correctional Institutions, visit the ADA web page at: http://care.diabetesjournals.org/cgi/content/full/28/suppl_1/s4.

Recommendations

- Individuals with a diagnosis of diabetes should have a complete medical history and undergo an intake physical examination by a licensed health care professional in a timely manner (see Initial Evaluation on page 8).
- Insulin treated inmates should have a BG* determination within 1-2 hours of arrival.
- Medications and MNT should be continued without interruption upon entry into the correctional environment.
- Correctional staff should be trained in the recognition, treatment, and appropriate referral for hypo- and hyperglycemia.
- Correctional staff should also be trained to recognize signs and symptoms of serious metabolic decompensation and to immediately refer the individual for appropriate medical care.
- Institutions should implement a policy of requiring staff to notify a physician of all BG results outside of a specified range as determined by the treating physician.
- Identify individuals with type 1 diabetes who are at high risk for DKA.
- Test each woman of childbearing age who has diabetes for pregnancy.
- Test any pregnant inmate for GDM at appropriate times during the pregnancy (see Screening, Diagnosis and Treatment of GDM on page 60).
- Refer any inmate who is pregnant and has diabetes or GDM for appropriate consultative care.
- In the correctional setting, policies and procedures should be developed and implemented to enable BG monitoring to occur at the frequency necessitated by each individual's glycemic control and diabetes regimen.
- Include diabetes information in correctional staff educational programs.
- For all interinstitutional transfers, complete a medical transfer summary to be transferred with the inmate.
- Diabetes supplies and medications should accompany the inmate during transfer.
- Begin discharge planning with adequate lead time to insure continuity of care and facilitate entry into community diabetes care.
- Individuals should be evaluated for diabetes risk factors at the intake physical, tested as indicated and evaluated at appropriate times thereafter (see Table 1 on page 4).

REFERENCE SECTION XVI

American Diabetes Association. Clinical Practice Recommendations. *Diabetes Care*. 30(Suppl. 1):S32-S33, S77-S84. 2007

Correctional Institutions

^{*} BG throughout these Recommendations means plasma or serum glucose. For a discussion on the ways of measuring glucose in the blood and their differences, see the Appendix, page 93.

XVII. COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM)

The National Center for Complementary and Alternative Medicine (NCCAM) at the National Institutes of Health (NIH) defines CAM as "a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine. Complementary medicine is often used in conjunction with conventional medicine, and alternative medicine is used in place of conventional medicine" (http://nccam.nih.gov/health/whatiscam/). CAM incorporates a variety of therapies and modalities.

Types of complementary and alternative medicine include the following:

- Manipulative and body-based therapies (e.g., acupressure, Alexander technique, chiropractic medicine, Feldenkrais method, massage therapy, neuromuscular therapy, osteopathy, reflexology, rolfing).
- Alternate systems of medical practice (e.g., acupuncture, ayurveda, community-based practices, environmental medicine, homeopathy, Native American medicine, naturopathic medicine, past life therapy, Shamanism, Tibetan medicine, traditional Oriental/Chinese medicine).
- Biological therapies (e.g., antioxidants, cell treatments, changes in lifestyle, chelation, diet, megavitamins, metabolic therapy, botanicals and herbs, nutritional supplements).
- Energy medicine (e.g., blue light treatment and artificial lighting, electroacupuncture, electrostimulation and neuromagnetic stimulation, magnetic therapy, magnetoresonance spectroscopy devices, reiki, therapeutic touch).
- Mind/body interventions (e.g., art therapy, aromatherapy, biofeedback, dance therapy, humor, hypnotherapy, meditation, music therapy, prayer, psychotherapy, relaxation, support groups, yoga).

There is much about health and healing that we do not yet know. Some evidence is available to support the use of some CAM therapies, for certain conditions. However, for the majority of such therapies the evidence is limited or lacking. The NIH funds multiple centers for CAM research in an effort to provide evidence or refute claims of various therapies.

Complementary and Alternative Medicine Use in Diabetes

Egede et al. (2002) showed that individuals with diabetes were 1.6 times more likely to use CAM than individuals without diabetes. Among people with diabetes, older age (\geq 65 years old) and higher education were independently associated with CAM use. Bell et al. (2006) further showed that CAM use was higher for people with diabetes than those without the disease. Female gender, higher education, western U.S. residence and having at least two chronic conditions were associated with a greater use of CAM. Except for diet-based therapies, most CAM use by people with diabetes was related to non-diabetes conditions. According to Garrow and Egede (2006), 48% of adults with diabetes use some form of CAM and the use of CAM appears to be associated with increased use of preventive services, emergency care, and primary care visits. Thus CAM use may not be a barrier toward using allopathic medicine in adults with diabetes. The most common CAM therapies used were nutritional and lifestyle advice, prayer, herbal remedies, massage, and mind-body techniques.

Health Care Team and Complementary and Alternative Medicine

The health care team has a responsibility to be aware of all forms of therapies that patients are using. It is important to try to understand different approaches to health and help patients in making informed and safe choices. Patients will often not tell about CAM therapies they use. It is up to the health care team to ask about CAM as part of the history taking process. Points to keep in mind in order to discuss CAM effectively with patients:

- Ask about use; be specific about the different therapies.
- Avoid dismissing CAM, which may discourage the patient from discussing the actual use; patients can be concerned about the response from the health care team.

- Understand the rationale for the health care choices the patient makes as this may provide insight into the health goals for the patient.
- Be aware of and explain to patients that information on the Internet is varied and can be unreliable.
- Be prepared to discuss the different therapies including risks and benefits.

A common misconception is that a "natural" product will be safe. Encourage patients to obtain information about a particular therapy regarding efficacy, safety and potential harmful effects. Determine where biological therapies were purchased (over-the-counter, from a naturopath, etc.). Determine if Good Manufacturing Practices (GMP) were used to make a product. The GMP label is used by the FDA and European Union as a label that is recognized worldwide for the control and management of manufacturing and quality control testing of foods and pharmaceutical products.

It is well known that there is a lack of reliable science-based information about nontraditional therapies and their effect on the human condition. It is difficult for the health care provider to be knowledgeable in all aspects of CAM. Thus, education and an open mind will benefit health care providers in learning more in assisting their patient to best practices.

Resources

For further information on CAM, visit the following websites:

NCCAM - http://nccam.nih.gov/

The Diabetes Unit to NCCAM - http://nccam.nih.gov/research/intramural/diabetes-unit.htm

National Institutes of Health Office for Dietary Supplements - http://ods.od.nih.gov/index.aspx

U.S. Food and Drug Administration Center for Food Safety and Applied Nutrition: Overview of Dietary Supplements - http://www.cfsan.fda.gov/~dms/supplmnt.html

The University of Michigan Integrative Medicine Program - http://www.med.umich.edu/umim/ research/cam.htm

Columbia University Rosenthal Center for CAM - http://www.rosenthal.hs.columbia.edu/

Purdue University and University of Alabama-Birmingham Botanicals Research Center - http://www.cfs.purdue.edu/fn/bot/

University of Arizona Program of Integrative Medicine - http://www.integrativemedicine.arizona.edu/index.html

North Carolina Consortium on Natural Medicines - http://www.naturalmedicinesofnc.org/

Facts and Comparisons: The Review of Natural Products - http://www.factsandcomparisons.com/ Products/index.aspx?id=1053

Herbal Medicine: Expanded Commission E Monographs - http://abc.herbalgram.org/site/ PageServer

Natural Medicine Comprehensive Database - http://www.naturaldatabase.com/ (S(neqhonixjia3ep55jr2jppzj))/home.aspx?cs=&s=ND

The Center for Mind-Body Medicine - http://www.cmbm.org/

American Nutraceutical Association - http://www.ana-jana.org/index.cfm?cfid=809349&cftoken=354 54439

REFERENCE SECTION XVII

Bell RA, Suerken CK, Grywacz JG, Lang W, Quandt SA, Arcury TA. Complementary and alternative medicine use among adults with diabetes in the United States. *Alternative Therapies*. 12(5):16-21. 2006

Egede LE, Ye X, Zheng D, Silverstein MD. The prevalence and pattern of complementary and alternative medicine use in individuals with diabetes. *Diabetes Care*. 25(2):324-329. 2002

Garrow D, Egede LE. Association between complementary and alternative medicine use, preventive care practices, and use of conventional medical services among adults with diabetes. *Diabetes Care*. 29(1):15-19. 2006

Payne C. Complementary and integrative medicine: emerging therapies for diabetes. Part 1. *Diabetes Spectrum*. 14(3):129-131. 2001

Shane-McWorter L. Botanical dietary supplements and the treatment of diabetes: what is the evidence? *Current Diabetes Reports*. 5(5):391-398. 2005

Yeh GY, Eisenberg DM, Davis RB, Phillips RS. Use of complementary and alternative medicine among persons with diabetes mellitus: results of a national survey. *Am J Pub Health*. 92(10):1648-1652. 2002

Appendix

APPENDIX

Blood Glucose Meters

For a current list of available blood glucose meters, including approximate purchase price, approximate cost of strips, size, weight, altitude limit (some cannot be used above 7000 feet), temperature operating range (some cannot be used below 55 degrees), and toll-free phone number for the manufacturer, visit the following website:

http://www.diabeteshealth.com/media/pdfs/Blood-Glucose-Meter-Reference-Guide-060707.pdf

Insulin Pumps

For a current list of available insulin pumps, including size, weight, battery life, pumps usability with water, and number of button pushes needed to program certain features, visit this website: http://www.diabeteshealth.com/media/pdfs/Insulin-Pump-Reference-Guide-040507-R1.pdf

Continuous Blood Glucose Monitoring

The FDA approved a 7-day continuous glucose monitoring system in 2007. A 3-day version of the device was approved by the FDA in 2006. While a BG test records a person's glucose level at a snapshot in time, the continuous glucose monitoring system measures glucose levels every 5 minutes throughout a 7-day period. This additional information can be used to detect trends and patterns that could not be captured by BG test measurements alone, such as patterns of glucose levels overnight and between meals. A disposable sensor is placed just below the skin and must be replaced weekly. The sensor can be programmed for an alarm to signal when a patient's glucose levels reach a pre-set low or pre-set high. Use of continuous blood glucose monitoring readings are not recommended for treatment decisions related to meal intake or hyperglycemia. BG tests are still needed to decide when additional insulin is needed.

For information on the continuous blood glucose monitoring system (also known as glucose sensor), visit the following website:

http://diabetes.webmd.com/continuous-glucose-monitoring

Measuring Blood Glucose

Their are three ways to measure the glucose level on blood in the laboratory: on whole blood, on plasma, and on serum. Measurement of glucose levels in plasma or serum are approximately equivalent. Results of measuring glucose levels on whole blood will be 12-15% lower if the hematocrit is normal. Most fingerstick blood glucose meters give a result which is equivalent to a laboratory whole blood glucose measurement. Some meters arithmetically add 12-15% to make their answer equivalent to the laboratory plasma or serum glucose. Any laboratory whole blood glucose measurement or any fingerstick blood sugar will be falsely high in anemia and falsely low with a high hemoglobin/ hematocrit.