## **Groups Unite to Cut Cardiac Risks From Diabetes**

BY KATE JOHNSON Montreal Bureau

iabetologists and cardiologists are joining forces to address the issue of cardiovascular disease in patients with diabetes.

In North America, new joint guidelines

from the American Heart Association (AHA) and the American Diabetes Association (ADA) focus on the primary prevention of cardiovascular disease in patients with diabetes (Circulation 2007;115:114-26: Diabates Care 20



26; Diabetes Care 2007;30:162-72).

"People with ... diabetes are at increased risk for [cardiovascular disease] and have worse outcomes after surviving a CVD event," wrote coauthor Dr. John Buse, director of the diabetes care center at the University of North Carolina at Chapel Hill, and his colleagues.

And in Europe, the European Association for the Study of Diabetes (EASD) and the European Society of Cardiology (ESC) have issued guidelines on diabetes, prediabetes and cardiovascular diseases (Eur. Heart J. 2007;28:88-136).

Although both the North American and European documents recognize the importance of harmonizing the approaches of cardiologists and diabetologists, they both also focus on specific and different aspects of the diabetes-cardiovascular disease dyad, making them potentially complementary documents. In both documents, special attention is placed on the early stages of disease development, but the European document focuses on the role of prediabetes in

It was an effort to hammer out the common ground in the few areas in which there were fairly nuanced differences. early cardiovascular dysfunction, whereas the North American document emphasizes primary prevention of cardiovascular disease in patients with overt diabetes.

DR. BUSE The importance of the ADA/AHA document is not so much its content, but

rather its existence, suggested Dr. Daniel Einhorn, medical director of the Scripps Whittier Institute for Diabetes, an endocrinologist at the University of California, San Diego, and a spokesperson for the American Association of Clinical Endocrinologists (AACE). "What is new here is that these two organizations are agreeing to a joint statement on primary prevention of cardiovascular disease in diabetes."

Cooperation between the ADA and AHA is, for both organizations, a hurdle crossed after some much publicized disagreement last year, acknowledged Dr. Buse in an interview. "This paper was an effort to get together and hammer out where the common ground is in the few areas where there were fairly nuanced differences in approach."

The main issue of contention between the ADA and AHA has been the debate over whether or not metabolic syndrome exists. In the joint statement, they have agreed to disagree: "The AHA and the [National Heart, Lung, and Blood Institute] have issued a statement on management of the metabolic syndrome and maintain that with regard to risk for CVD, the metabolic syndrome and type 2 diabetes can coexist in one person. The ADA, in contrast, contends that once type 2 diabetes is present, the metabolic syndrome no longer pertains because CVD risk factors characteristic of the metabolic syndrome are largely subsumed in the type 2 diabetes syndrome," they wrote.

Dr. Einhorn said that even with some opposing viewpoints, a single set of guidelines shared by cardiologists and endocrinologists serves not only to clarify clinical practice, but to justify a preventive approach.

"It is important for people in managed care environments to have some validation that it is important to do testing, to prescribe medications, and to follow up on these patients from a cardiovascular standpoint, even when they don't have any known cardiovascular disease yet. It offers some impetus in large medical group settings," he said.

More Aggressive Tactics Recommended

The new joint ADA/AHA guidelines "encourage more aggressive prevention and treatment of risk factors that lead to heart disease" in people with diabetes, according to a press release from the two organizations. "Patients with diabetes have twice the risk of incident myocardial infarction and stroke as that of the general population," they say. "Furthermore, large numbers of people with diabetes do not survive their first event, and if they do survive, their [mortality] over the subsequent months to years is generally greater than that of the general population. As many as 80% of patients with type 2 diabetes will develop and possibly die of macrovascular disease."

While continuing to encourage lifestyle changes—such as weight loss, improved nutrition, and physical activity—the joint statement also emphasizes the importance of medical interventions to manage lipids, blood pressure, and blood glucose in this population. The full text of the guidelines can be viewed at http://care.diabetesjournals.org/cgi/content/full/30/1/162.

## **Guidelines Target Hyperglycemic Crises in Adults Diabetics**

## BY MIRIAM E. TUCKER Senior Writer

The American Diabetes Association has issued a new consensus statement addressing the diagnosis, treatment, and prevention of diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults with diabetes.

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are the two most serious acute metabolic complications of diabetes. Mortality in DKA patients is less than 5% in experienced treatment centers, whereas HHS mortality remains high, at about 11%. The annual incidence rate for DKA ranges from 4.6 to 8 episodes per 1,000 patients with diabetes, with an estimated hospital cost exceeding \$1 billion a year, Dr. Abbas E. Kitabchi and his associates said (Diabetes Care 2006;29:2739-48).

Although most patients with DKA have autoimmune type 1 diabetes, patients with type 2 diabetes are also at risk during acute stress, such as that caused by trauma, surgery, or infection. Moreover, during the past decade, an increasing number of DKA cases without precipitating causes have been reported in individuals with type 2 diabetes, particularly those from minority groups.

Inadequate or inappropriate insulin therapy and infection are the two most common precipitating factors in the development of both DKA and HHS. Although HHS typically evolves over several days to weeks, the evolution of DKA in type 1 or type 2 diabetes tends to be much shorter. The classic picture of DKA includes a history of polyuria, polydipsia, weight loss, vomiting, abdominal pain, dehydration, weakness, mental status change, and coma. In HHS, the most common clinical presentation is altered sensorium, with signs of dehydration.

Initial laboratory evaluations of patients with suspected DKA or HHS should include the determination of plasma glucose; blood urea nitrogen; creatinine; serum ketones; electrolytes (with calculated anion gap); osmolality; urinalvsis and urine ketones by dipstick; initial arterial blood gases; and complete blood count with differential. If clinically indicated, an electrocardiogram; chest x-ray; and urine, sputum, or blood cultures should also be obtained, said Dr. Kitabchi, chief of the division of endocrinology, diabetes, and metabolism at the University of Tennessee, Memphis, and associates.

Patients with low-normal or low serum potassium concentration on admission have severe total-body potassium deficiency and require very careful cardiac monitoring and more vigorous potassium replacement, because treatment lowers potassium further and can provoke cardiac dysrhythmia, they said.

Successful treatment of DKA and HHS requires the correction of dehydration, hyperglycemia, and electrolyte imbalances, as well as the identification of comorbid precipitating events and—above all—frequent patient monitoring. Protocols for the management of both DKA and HHS are included in the document, which is available free online (http://care.diabetesjournals.org).

Initial fluid therapy is directed toward expansion of the intravascular and extravascular volume and restoration of renal perfusion. Successful progress with fluid replacement is judged by hemodynamic monitoring (improvement in blood pressure), measurement of fluid input and output, laboratory values, and clinical examination. Adequate rehydration with subsequent correction of the hyperosmolar state has been shown to result in a more robust response to lowdose insulin therapy.

Unless the episode of DKA is uncomplicated and mild or moderate, regular insulin by continuous intravenous infusion is the treatment of choice. However, recent data suggest that the use of subcutaneous rapid-acting insulin analogs in the management of patients with uncomplicated DKA could allow for treatment in general wards or emergency departments, thus avoiding admission to the intensive care unit. Direct measurement of β-hydroxybutyrate ( $\beta$ –OHB) in the blood is the preferred method for monitoring DKA, and has become more convenient with the recent development of bedside meters capable of measuring β–OHB in whole blood, they noted.

Criteria for resolution of DKA include glucose less than 200 mg/dL, serum bicarbonate greater than or equal to 18 mEq/L, and venous pH greater than 7.3. When a patient is able to eat, a multiple-dose schedule involving a combination of basal and premeal bolus insulins should be initiated as needed to control plasma glucose. To prevent hypokalemia, potassium replacement is started after serum levels drop to less than 5.3 mEq/L, assuming the presence of adequate urine output at 50 mL/hour.

The use of bicarbonate in DKA remains controversial. At a pH greater than 7.0, the administration of insulin blocks lipolysis and resolves ketoacidosis without any added bicarbonate. However, limited data do support the use of bicarbonate—along with potassium supplementation—in patients with pH values lower than 7.0, and particularly in those with levels lower than 6.9, for whom the risk for severe acidosis is elevated.

Routine use of phosphate is not indicated in the treatment of DKA or HHS; data suggest it provides no clinical benefit. However, careful phosphate replacement may be indicated in some patients with cardiac dysfunction, anemia, or respiratory depression in order to minimize the risks associated with hypophosphatemia.

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