

# **Inpatient Diabetes and Glycemic Control: A Call to Action Conference**

***Consensus Development Conference  
Conference Recommendations: Position Statement  
February 1, 2006***

## **INTRODUCTION**

Diabetes has reached epidemic proportions in the United States, affecting over 20 million individuals.<sup>1</sup> There also is a disproportionate increase in the number of people with diabetes in the hospital. Furthermore, for every two patients in the hospital with known diabetes, there may be an additional one with newly observed hyperglycemia.<sup>2,3</sup> Compelling evidence continues to accumulate to suggest that poorly controlled glucose levels are associated with increased morbidity and mortality, as well as with higher costs. In 2002, 4.9 million hospital discharges were associated with diabetes.<sup>4</sup> The cost of inpatient diabetes care is estimated at \$40 billion—the single largest component of direct medical costs for the disease.<sup>5</sup>

Until recently, glycemic control in hospitalized patients has not been a major therapeutic focus, partly because of a lack of published targets and guidelines for their care and partly because evidence demonstrating improved outcomes as the result of improved glycemia was only just emerging. In December 2003, the American Association of Clinical Endocrinologists (AACE) convened a two-day consensus conference, cosponsored or supported by nine other professional organizations, to review results of recent clinical trials and to explore the relationship, if any, between inpatient glycemic control and clinical outcomes. The conference brought together national and international experts, as well as several organizations concerned with clinical diabetes. Recommendations for the management of hyperglycemia were agreed upon and published.<sup>6</sup> The American Diabetes Association (ADA) supported an extensive technical review evaluating the relationships between glycemic control and its impact on hospital outcomes.<sup>7</sup> This review became the basis for the 2005 ADA Clinical Practice Guidelines.<sup>8</sup>

Notwithstanding national and local efforts, widespread implementation of improved glycemic control for inpatients has remained an elusive goal for many centers. Multiple institutional and attitudinal obstacles still exist to improved care—these barriers have created a significant and growing gap between what we know and what we do. For this reason, AACE and ADA have joined forces to plan and conduct this consensus conference (*Inpatient Diabetes and Glycemic Control: A Call to Action Conference*) with the goal of identifying strategies to overcome barriers and facilitate improvements in patient care.

To focus us in our considerations, the following questions were addressed:

## **Question 1. Does Improving Glycemic Control Improve Clinical Outcomes for Inpatients with Hyperglycemia?**

Epidemiologic and uncontrolled observational data have for many years associated acute and chronic hyperglycemia with adverse inpatient outcomes. More recently, interventional studies have linked reversal of hyperglycemia to better clinical outcomes in medical and surgical patients, especially in acute myocardial infarction, cardiac surgery, infection and critically ill patients.<sup>9-18</sup>

### ***Data Derived from Surgical and Medical Intensive Care Units***

- In a study of critically ill and mixed medical surgical intensive care unit (ICU) patients, the use of intensive insulin therapy to achieve arterial whole blood glucose levels of 80–110 mg/dL reduced mortality by 34%, sepsis by 46%, renal failure requiring dialysis by 41%, blood transfusion by 50%, and critical illness polyneuropathy by 44%.<sup>11</sup>
- *Note added in press:* Dr. Van den Berghe presented new data at the consensus conference regarding tight glycemic control in the medical ICU, findings that were published later in the week. Similar to her original investigation from the surgical ICU, patients who required prolonged (> 3 days) ICU stay, benefited significantly from the attainment of euglycemia vs. the conventionally-treated control group, with reduced mortality (52.5% vs. 43.0%, RRR=18.1%, p=0.009). In the entire cohort (an intent-to-treat analysis), there were improvements in several ICU-related morbidities (renal dysfunction, prolonged mechanical ventilation) but no significant reduction in mortality (40.0% vs. 37.3%; RRR=6.8%; p=0.33). Among the 433 patients who stayed in the ICU less than 3 days, mortality was 18.8% vs. 26.8% in the conventional and intensive groups, respectively. After adjustments for baseline characteristics, including APACHE-2 score, this difference was not statistically significant (p=0.41). While generally consistent with the surgical ICU data, the increased early mortality, although not statistically significant, will require further investigation, either through post-hoc analysis from this dataset or further studies in this area.<sup>19</sup>
- A study of 1600 patients admitted to a medical-surgical ICU evaluated outcomes associated with improved glycemic control. The insulin infusion group had improved blood glucose levels compared to a retrospective control group, 130.7 vs. 152.3 mg/dL, respectively (p<0.001). Those patients with reduced blood glucose levels had associated significant reductions in mortality and median length of ICU stay.<sup>13</sup>
- A recent meta-analysis of 35 clinical trials evaluating the effect of insulin therapy on mortality in hospitalized patients with critical illness found that insulin therapy decreased short term mortality by 15% in a variety of clinical settings.<sup>14</sup>

### ***Data Derived from Patients with Acute Myocardial Infarction (AMI)***

- In patients with AMI, elevated glucose levels is a predictor of mortality in patients with and without diabetes.<sup>16-21</sup> In addition, elevated glucose levels were associated with larger infarct size in patients without a prior history of diabetes who were being treated with perfusion therapy for ST segment myocardial infarction (STEMI).<sup>20</sup>
- A meta-analysis of 15 studies of patients who were hospitalized for acute myocardial infarction reported that blood glucose levels in excess of 110 mg/dL were associated with proportionally greater mortality and increasing rates of congestive heart failure.<sup>22</sup>
- In the first Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) (DIGAMI) study, patients with acute MI received intravenous (IV) insulin therapy for 24 hours, followed by multiple daily injections for 3 months or longer had 29% reduction in mortality at one year and 28% at 3.4 years compared to the control group.<sup>15</sup>
- DIGAMI 2<sup>23</sup> was designed to compare three treatment strategies in patients with AMI: group 1 received acute insulin–glucose infusion followed by insulin-based long-term glucose control; group 2 received insulin–glucose infusion followed by standard glucose control; and group 3 received routine metabolic management according to local practice. Unfortunately this study did not reach recruitment goals and showed no treatment differences. Moreover, the primary treatment target of fasting blood glucose of 90-126 mg/dL for those in group 1 was never achieved. Fasting glucose levels (149 mg/dL) and hemoglobin A1C (6.8%) were similar among groups. Thus, if glycemia is predictive of outcomes, no differences would have been expected and none were observed.
- In CREATE-ECLA<sup>24</sup>, over 20,000 patients with STEMI were treated with a 24-hour glucose-insulin-potassium (GIK) infusion or placebo, irrespective of baseline glucose. GIK did not improve mortality; however, the relative hyperglycemia that did result in active therapy patients may have obscured any treatment benefit.

In these latter two studies, it is clear that insulin infusion *in the absence of glucose-lowering* has no effect on outcomes.

### ***Data Derived from the Cardiac Surgery Populations***

Hyperglycemia is an independent predictor of infection in patients with diabetes undergoing cardiac surgery.<sup>25</sup> Furthermore, hyperglycemia in the first 48 postoperative hours was associated with a twofold higher rate of surgical site infections among patients undergoing cardiothoracic surgery compared with surgical patients who were normoglycemic.<sup>17</sup>

Good glycemic control in patients undergoing cardiac surgery results in improved outcome. Furnary et al.<sup>10</sup> investigated the impact of continuous insulin infusions compared to the prior use of intermittent subcutaneous insulin injections in diabetic patients undergoing cardiac surgery. In patients treated with IV insulin during the perioperative period the risk of deep sternal wound infection was reduced by 57%. A subsequent analysis<sup>12</sup> reported that intensive glucose control

was associated with a 66% reduction in mortality; the lowest mortality was observed in patients with an average postoperative blood glucose <150 mg/dL.

### ***Hyperglycemia in Hospitalized Medical-Surgical Patients***

Observational studies suggest an association between hyperglycemia and poor clinical outcomes in general surgical and medical patients.

- Pomposelli et al. found that single blood glucose level >220 mg/dL on the first postoperative day is a sensitive predictor of nosocomial infection.<sup>26</sup>
- A retrospective chart review of 1886 admissions by Umpierrez et al. reported an 18-fold increase in mortality in hyperglycemic patients without prior history of diabetes and a 2.5-fold increase in mortality in patients with known diabetes compared to controls.<sup>3</sup>
- A meta-analysis of 26 studies by Capes et al. identified an admission glucose > 110 mg/dL to be associated with increased mortality for patients who were hospitalized for acute stroke.<sup>27</sup>

Thus, the expansion of the database that has occurred since the first joint consensus conference on inpatient glycemic control is consistent with, and strengthens, our views regarding the importance of inpatient glycemic control.

## **Question 2. Is Cost a Barrier to Improved Inpatient Care?**

Cost is often perceived as a barrier to excellent inpatient glycemic control because achieving tight control safely and effectively requires efforts which appear to be relatively expensive, labor intensive and which require coordination of the services of many hospital divisions. It is more appropriate, however, to examine the cost-effectiveness of this care. Utilization of hospital services should be viewed as an investment, rather than an expense, since improved glycemic control actually results in cost savings as noted below. In 2002, direct inpatient costs for people with diabetes were \$40.3 billion.<sup>5</sup> Hyperglycemia itself has been shown to contribute to increasing length of stay and overall cost. It has been shown that for each 50 mg/dL increase in blood glucose in patients with diabetes undergoing CABG, there was an additional 0.76 day LOS (an incremental hospital cost of \$2824).<sup>28</sup> Hyperglycemia is an independent predictor of length of stay in trauma patients.<sup>29</sup>

Controlling hyperglycemia in patients with both previously diagnosed diabetes and newly discovered hyperglycemia in the hospital have been shown to be cost effective in many different settings:

- The use of a diabetes team consultation resulted in a 56% reduction in length of stay for a cost reduction of \$2353 per patient.<sup>30</sup>
- In cardiac surgical patients, implementation of intensive glycemic control using intravenous insulin protocols resulted in a substantial decrease in sternal wound

infections and subsequent decrease in both cost and length of stay when compared to historical data (Furnary, presentation AACE conf 2006).<sup>10</sup>

- Intensive insulin management protocol in the surgical ICU resulted in an improved medical outcomes with a reduction of ICU stay resulting in an estimated yearly cost savings of \$40,000 per ICU bed.<sup>11</sup> Although the cost of intensive treatment was nearly double the cost of the conventional treatment, the excess cost of intensive insulin therapy was more than offset by a 25% reduction of total hospitalization cost.<sup>31</sup>
- In North Carolina, Newton et al (presented AACE conf 2006) showed that in the MICU, intensive glycemic control resulted in a reduction of average blood sugar from 169 mg/dL to 123 mg/dL with a resultant reduction in catheter-related sepsis by 33.5%, thereby resulting in substantial cost savings. The same group reported that lowering the average blood sugar from 177 to 151 mg/dL was associated with a reduction in length of stay (LOS) from 6.01 to 5.75 days (-0.26 days), while there was no reduction in LOS in non-hyperglycemic patients during the same time interval. This reduced LOS enables the hospital to serve more patients/bed and generates further income from new patient DRGs. The “throughput value” calculated as incremental inpatient volume x revenue margin for this hospital was \$2.2 million per year (Ibid).
- At an academic medical center, financial cost-modeling analysis of the benefit of intensive diabetes management was performed in both critical care units and medical/surgical floors using a dedicated diabetes team approach. Substantial savings were possible based on better documentation, reduced length of stay and generation of new revenues. (Balcezak, AACE presentation 2006).
- The use of an intensified management protocol by a diabetes management team in Oklahoma resulted in correct coding and treatment of previously unrecognized hyperglycemic patients. Length of stay was reduced for both primary and secondary diagnoses, and readmission rates declined (Lawrence, presented at AACE conference 2006).

It can be seen therefore that optimizing glycemic management is not only medically effective, saving lives and reducing morbidity, but is also cost-effective to health care systems.

### **Question 3: Has Inpatient Diabetes Management Become a Quality and Safety Concern?**

#### **Quality**

Inpatient management of hyperglycemia and avoidance of hypoglycemia have become important measures of the quality of healthcare afforded to hospitalized patients. Translation of the evidence regarding glycemic management that has been derived from multiple clinical trials into performance metrics will be useful in inpatient settings throughout the country. Performance measures will be important tools for widespread assessment and benchmarking of quality of care

and will be a key driver for improvement of quality. Development of performance measures will require agreed upon definitions of quality based on translation of available evidence into valid, feasible, reproducible and actionable performance metrics for both internal quality improvement and external accountability.

- A compendium of tested tools and strategies is needed to assist sites as they implement programs for glycemic control at their sites. Conference co-sponsors commit to develop a website, accessible through multiple co-sponsoring organizations, that contains a guidebook to implementation with a collection of protocols, standing orders, and other educational tools to assist in the implementation of tested programs for improved glycemic control.
- The National Diabetes Quality Alliance is encouraged to develop performance measures for inpatient management of hyperglycemia in people with and without diabetes. The development of measures that can be used internally by medical centers/hospitals for quality improvement along with the development of measures robust enough for use for external accountability are recommended. This consensus conference also encourages the Alliance to submit the measures to the National Quality Forum for the approval process, which then establishes these measures as standards for the nation.
- When available, we encourage purchasers, payers, and accreditors to adopt nationally standardized measures for use in their publicly reported measure sets (e.g. ORYX), their disease management accreditation programs (e.g. the new JCAHO-ADA Advanced Disease Management Certification), and their pay-for-performance programs (e.g. CMS demonstrations and publicly reported measure sets as part of the CMS Hospital Compare program).

### **Safety**

Both under-and over-treatment of hyperglycemia are safety issues in the hospitalized patient. Unrecognized and untreated hyperglycemia is an “error of omission” as hyperglycemia creates an unsafe setting for the treatment of illness and disease. Undertreatment may occur due to failure to treat significant hyperglycemia or by inappropriately holding insulin doses. The fear of hypoglycemia is a barrier to adequate care and yet the risk of hypoglycemia may actually be reduced by a policy of intensive glucose management. On the other hand, overtreatment of hyperglycemia leading to hypoglycemia remains a significant safety issue. JCAHO considers insulin to be one of the 5 highest risk medicines in the inpatient setting. To improve safety, medication errors must be documented, analyzed and tracked. A systems approach to analyzing hospital processes is essential and a “culture of safety” must exist that is embraced by all parties.

Some of the common sources of errors that threaten patient safety include:

- Lack of coordination between feeding and medication administration leading to mistiming of insulin action
- Lack of sufficient frequency in blood glucose monitoring
- Orders not clearly or uniformly written
- Failure to recognize changes in insulin requirements due to advanced age, renal failure, liver disease, change in clinical status, steroid use or interruption/changes in feeding.

A systems approach to reducing errors in insulin therapy in the inpatient setting has recently been described.<sup>32</sup> Strategies to reduce medical errors that can lead to safety issues include the use of:

- Electronic Medical Record (EMR)
- Computerized Physician Order Entry
- Checklists
- Written protocols
- Improved communication between caregivers, especially in transitions of care, including discharge

Avoiding the common sources of errors and implementing systems to detect them can improve patient safety and enhance quality of care.

#### **Question 4: What are the Systematic Barriers and Challenges to Improved Hyperglycemia Management?**

Many of the changes needed to improve the management of the inpatient with hyperglycemia involve changes to culture, long standing practice patterns, processes of care and work flow habits. Competing priorities and limited resources can present a major barrier to the institutional support that is essential to a successful improvement effort. Other organizational barriers are outlined below. These include:

- Incremental nursing time and effort needed can be a burden on nursing systems. The current national nursing shortage magnified by inadequate support systems may make this situation more difficult. Nurses are essential to successfully implement protocols, order sets, more intensive glucose monitoring, and educational programs targeting enhanced glycemic control.
- Skepticism about the benefits of good inpatient glycemic control remains a barrier to rapid adoption of attempts to implement change, in spite of the preponderance of evidence suggesting it is beneficial. This may be exacerbated by a general resistance to change.
- Fear of hypoglycemia is a major barrier to efforts to improve glycemic control.

- Inadequate knowledge and understanding of diabetes, hyperglycemia, and its management also represents a barrier. Educational programs for providers and inpatients are time consuming.
- Lack of integrated information systems that allow tracking and trending of glycemic control and hypoglycemia metrics are a challenge for implementing glycemic management programs. Improvement teams are faced with the task of devising regular reports to summarize and trend parameters describing glycemic control or hypoglycemia rates in the absence of standardized methods to do so.
- Diabetes and hyperglycemia are prevalent on all services in the hospital, requiring broad educational efforts, and process change. Patients frequently move across a spectrum of care providers and geographic locations during a single inpatient stay, entailing multiple hand-offs, communication challenges, and opportunities for error. The complexity of the task of achieving safe hand-offs and consistency in the approach across this spectrum of care is a significant challenge. A lack of ownership for hyperglycemia contributes to the challenges of glycemic control since most patients are admitted for reasons other than hyperglycemia.<sup>33</sup>

### **Question 5. What are Effective Strategies for Achieving Improved Diabetes Management in Hospitalized Patients?**

Successful implementation of a program to improve glycemic control in the inpatient setting should include the following components:<sup>34</sup>

1. An appropriate level of administrative support
2. Formation of a multidisciplinary steering committee to drive the development of initiatives
3. Assessment of current processes, quality of care, and barriers to practice change
4. Development and implementation of interventions including standardized order sets, protocols, policies and algorithms with associated educational programs
5. Metrics for evaluation

*Administrative support:* In order to improve glucose control in the hospital, the management of patients with diabetes and/or hyperglycemia must become an institutional priority. This involves enlisting administrative support for the long-term investment of both time and resources from multiple individuals and departments. The most salient means of demonstrating this commitment is through the establishment of a multidisciplinary steering committee that is empowered to develop and guide processes for improving glycemic control in the hospital. Supporting data are available for the financial and clinical benefits of these programs.

*Multidisciplinary steering committee:* A multidisciplinary *steering committee* should be charged with assessing and monitoring the quality of glycemic management within the institution. Members of this team should include all key

stakeholders, ideally including medical staff, nursing and case management, pharmacy, nutrition services, dietary, laboratory, quality improvement and information systems personnel, and administration.

*Assessment of current processes, quality of care, and barriers to practice change:* This step involves an investigation of current practices and policies and how these impact glycemic control. Hospitals should systematically track glucose data to assess the quality of care delivered. Personnel from Information Systems and other departments can help identify data sources to obtain information for accurate assessment of glycemic control prior to and following implementation of specific protocols. Identification of organizational structure, culture, and resources will help guide the plan for protocol development and approach to implementation.

*Development and implementation of interventions:* Protocols/algorithms and order sets should be developed to guide the management of hyperglycemia and hypoglycemia throughout the hospital. An educational effort for both staff and patients with ongoing assessment of efficacy and safety is essential. In order to achieve any set target reliably, a standardized protocol is necessary.

The best intravenous insulin protocols take into account several factors, including the current and previous blood glucose levels (and, therefore, the rate of change), and the current infusion rate. The intensive approach to glucose control with insulin infusion mandates frequent blood glucose determinations, usually on an hourly basis. There are several published insulin protocols available.<sup>35-38</sup> The exact protocol is probably less important than its presence in an institution, adaptation to the individual hospital, adequate buy-in from key local opinion leaders and implementation staff, and its ultimate validation.

It is expected that with tight glycemic control there will be an increase in frequency of hypoglycemia, which, in this setting, is typically rapidly diagnosed, mild, transient and not clearly associated with any adverse outcomes. The benefit of intravenous insulin infusion in critically ill patients, where intensive monitoring is available, far outweighs any potential risk. If a protocol does not appear to be working in a specific patient, then urgent input is necessary from a clinician with expertise in diabetes management. Standardization across the institution should be considered for practical and logistical reasons. Lastly, the important transition to subcutaneous insulin must be an integral part of any insulin infusion protocol.

In the initial implementation of an insulin infusion protocol, it is important to educate all staff as to the importance of tight glycemic control in critically ill patients and to also engage them in the process. Specifically, those implementing the protocol should be asked to help troubleshoot when specific concerns arise. Pre-printed algorithms or computerized systems and adequate technical support should be available. During the early phase, appropriate expert

support should be readily available. Protocols should be periodically reviewed to ensure they continue to meet the needs of the hospital and its patients.

Many non-critically ill patients may benefit from intensive management similar that of the ICU setting. Some institutions have successfully implemented insulin infusion safely on general wards with modifications, including intensive staff education and adequate staff support. Without these, however, intensive insulin infusion becomes difficult and potentially dangerous in this setting. An alternative approach to IV insulin therapy is physiologic subcutaneous insulin therapy, which may be the most practical method for achieving glycemic control outside of the ICU. Targets should be individualized for patients with significant co-morbidities, particularly if life expectancy is reduced and in those at risk for hypoglycemia (elderly, liver and renal failure, malnourished, cognitively impaired).

Several approaches to antihyperglycemic therapy have been proposed for general hospital wards. It is generally agreed that, in many circumstances oral agents are not appropriate for in-hospital use. In stable patients who are eating, they may be used, but only after careful consideration of the anticipated stability in the patient's nutritional status and the potential for any adverse effects. There is widespread agreement that the traditional regular insulin "sliding scale" particularly when used as the sole form of insulin therapy should be abandoned as the standard of care. This "retroactive" form of insulin replacement is inherently illogical and has been associated with increased glycemic excursions. Moreover, in certain settings, such as the patient with type 1 diabetes, it is potentially very dangerous.

Instead, standardized order sets promoting the use of scheduled insulin therapy should be utilized. Basal replacement insulin therapy (i.e. NPH, glargine, detemir) is advised, with nutritional/prandial short/rapid-acting insulin (i.e. regular, aspart, lispro, glulisine). Additional "correction insulin" added to the short/rapid-acting insulin (same type) is also widely employed. Examples of this method are available in the literature.<sup>39</sup> Provisions for special patient circumstances including NPO status, parenteral and enteral nutrition and steroid therapy should be addressed by algorithms and educational efforts. Protocols should suggest starting dose and adjustment strategies. Aggressive and frequent dosing changes are necessary to achieve control during hospitalizations.

One intervention that may be considered to facilitate control of hyperglycemia is a specific glycemic management clinical team. The timely consultation of such teams has been demonstrated to improve quality, reduce length of stay and lower costs. These teams offer subspecialty assistance in those patients who do not achieve adequate control on protocols alone. Whether the team focuses on every hyperglycemic patient, or simply those not quickly achieving targets, is best decided based on local culture and needs.

Hypoglycemia remains a major impediment to achieving glucose control. Appropriate standardized treatment protocols that addresses mild, moderate, and severe hypoglycemia should be automatic part of all order sets for patients treated with insulin or insulin secretagogues. With these protocols in place, and with the recognition that most hypoglycemia is mild, transient, and easily treated, implementation of appropriate glycemic control is achievable.

Medical nutrition therapy is another integral part of inpatient hyperglycemia management. A nutritional plan outlined by a registered dietitian and a meal plan focusing on consistent carbohydrate consumption is suggested. Given the caloric requirements of sick patients, adequacy of nutritional intake always needs to be ensured. Restriction of calories is *not* the appropriate way to control glucose; instead adequate insulin therapy should be administered.

Diabetes self-management education is an important component to the management of the patient with hyperglycemia. Self-management knowledge and skills should be assessed and appropriate interventions provided by individuals trained in diabetes care. Survival skills education should be delivered in the inpatient setting with followup education and self-management support scheduled as needed after discharge.

A1C measurement on admission can be useful for the assessment of preadmission diabetes control and to assist in guiding transition to outpatient management.

A smooth inpatient-to-outpatient transition is critical. Appropriate discharge planning with identification of subsequent management plans and follow-up should be explicit. Goal-directed glycemic management in the hospital will serve as a model for the patient's self-directed care upon discharge. Importantly, even when intensive regimens are used in the hospital, the ultimate discharge regimen must take into account the motivations and capacities of the patient. However, his/her anticipated compliance as an outpatient should not dissuade aggressive inpatient control, especially during prolonged hospitalizations.

Metrics for Evaluation: A system to track hospital glucose data in an ongoing basis should be in place to assess the quality of care delivered. This will drive the continuous improvement of processes and protocols for glycemic management.

## **Question 6:      Diagnosis and Management of Patients Identified with Hyperglycemia in the Hospital**

Patients with hyperglycemia fall into one of three categories: previously diagnosed diabetes, unrecognized diabetes, or hyperglycemia related to

hospitalization. This problem is relatively large. For example, almost 70% of patients with their first myocardial infarction have either impaired glucose tolerance or undiagnosed diabetes.<sup>41</sup> The severity of hyperglycemia is variable and may be an indicator of prognosis.

Unfortunately, newly noted hyperglycemia as well as established diabetes, are frequently ignored in the hospital, with patients often discharged without a plan for evaluation and management of these conditions. This clearly is detrimental to the patient, because such a diagnosis may represent an opportunity to institute a plan for long-term glycemic control, which if initiated early, may lead to prevention of complications. Multiple studies have demonstrated that in-hospital mortality is particularly high in those patients who have newly discovered hyperglycemia. Furthermore over 50% of patients admitted with acute coronary syndromes have an abnormality of glucose metabolism.<sup>41</sup> Hemoglobin A1C is a long-term indicator of glycemic status and also predicts mortality in patients with myocardial infarction who are not known to have diabetes.<sup>42</sup> Chaudhuri et al<sup>43</sup> demonstrated the effects of insulin in patients with a myocardial infarction who did not have diabetes. Insulin infusion led to lower elevations of markers of inflammation and myocardial damage.

The principles of glucose management in patients with newly detected hyperglycemia remain the same as that for patients with established diabetes.

The discharge plan for those with newly recognized glucose abnormalities must emphasize a plan to evaluate the etiology of the hyperglycemia. Many of these individuals will indeed have diabetes or at the very least, pre-diabetes, which requires, at the very least, ongoing observation. Pre-diabetes also presents an opportunity for evidence-based prevention of diabetes, and such interventions may also prevent cardiovascular events. A clear care plan should be developed for short- and long-term testing, survival skills education, follow-up, and management.

## **Question 7: What are the Areas Needing Further Research?**

Questions and Issues to Address:

1. Which is the central mechanism(s) underlying the development and exacerbation of hyperglycemia in the hospitalized patient? Is it:
  - Counter-regulatory hormones
  - Increased hepatic glucose production
  - 
  - Decreased glucose utilization (peripheral insulin resistance)
  - Diminished tissue perfusion
  - Peripheral insulin resistance
  - What of the role of increased circulating free fatty acids?

- The role of inflammation (i.e. cytokines)?
- 
- 2. By what mechanisms does hyperglycemia produce harm?
  - Metabolic
  - Glucosamine
  - Polyol pathways
  - Hexose monophosphate (HMP) shunt
  - Glycation products and their reactive products
  - Oxidative stress
  - Inflammatory (i.e. cytokines)
  - NF kappa B
  - Superoxide generation
  -

Understanding these mechanisms may help develop additional targets for therapy.

3. What research is needed to improve practical aspects of delivery of inpatient glycemic control?

- Refinement of insulin protocols
- Glucose sampling sites and rates
- Closed loop systems
- Continuous glucose monitoring
- The role of feeding – enteral and parenteral
- Improve protocols to SC insulin on step down from ICUs
- Role of oral agents – alone and combined with insulin
- Strategies to minimize hypoglycemia
- Transition from in-hospital “basal-bolus” to a discharge regimen

4. What further randomized controlled trials are needed to document the benefits of glycemic control?

- Optimal glycemic targets on medical/surgical floors – desirable end points would include hypoglycemia rates, in-hospital complications, readmission rates, long-term glycemic control, etc.
- Additional MICU studies
- Use of insulin sensitizers in the inpatient setting
- Use of intensive insulin therapy in special populations of patients with hyperglycemia (e.g., cancer patients, age extremes, diverse ethnic backgrounds, socioeconomic status)

5. What are strategies of discharge planning that support maintaining glycemic control?

- Insulin versus oral agents for longterm management
- Lifestyle modification (nutrition and exercise)
- Self-care behaviors
- Continuity of care

## **Improving Inpatient Diabetes Care: A Call to Action Conference Consensus Development Conference**

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American Association of Clinical Endocrinologists  
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American Heart Association  
American Society of Anesthesiologists  
Joint Commission on Accreditation of Healthcare Organizations  
Society of Critical Care Medicine  
Society of Hospital Medicine  
Veterans Health Administration

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