

## In Brief

Hypoglycemia is a worrisome condition for hospitalized patients. Nurses, physicians, and other health care workers must be vigilant in detecting, treating, and most of all preventing hypoglycemia in diabetic patients. Systems and protocols for treating patients with diabetes guide the health care team in achieving glycemic goals for healing and health promotion while providing a safe environment.

# Detection, Prevention, and Treatment of Hypoglycemia in the Hospital

Donna Tomky, MSN, RN, C-ANP, CDE

There is widespread appreciation of glycemic control for outpatient management of diabetes. However evidence for tight glucose control for inpatient management is also increasing.<sup>1</sup>

Barriers to tight glucose control stem from concerns about hypoglycemia recognition in patients who are bedridden and those who have altered mental status, who are less likely to be capable of seeking assistance for this condition.<sup>2</sup> Diabetes-related cardiovascular events, including stroke and heart disease, are leading reasons for hospitalization. Many of these patients are at risk for hypoglycemia because of their critical health status and altered mental status. Furthermore, medical intervention may place them at risk for sensing signs and symptoms of hypoglycemia.<sup>1</sup> The threat of hypoglycemia requires the inpatient team to be vigilant in detecting signs and symptoms, preventing episodes without compromising glycemic control for adequate healing, and treating hypoglycemia episodes appropriately.

Hypoglycemia constitutes a medical emergency; however, most individuals recover completely. In the Diabetes Control and Complications Trial (DCCT), there were > 1,000 episodes of loss of consciousness associated with hypoglycemia. However, there were no deaths, myocardial

infarctions, or strokes definitively attributed to hypoglycemia, and to date there is no evidence of brain damage resulting from any of these episodes.<sup>3</sup>

Although no deaths occurred in the individuals participating in the DCCT, hypoglycemia that is not reversed can progress from lethargy to coma and ultimately to death. Even with treatment, there are reported cases of long-lasting severe hypoglycemia leading to transient and even permanent cerebral damage.<sup>3</sup>

## Detection

Hypoglycemia occurs from a relative excess of insulin in the blood and results in low blood glucose levels. The level of glucose that produces symptoms of hypoglycemia varies from person to person and varies for the same person under different circumstances.<sup>4</sup> Hypoglycemia is common in insulin-treated diabetic patients and may occur in patients taking an insulin secretagogue. It may range from a very mild lowering of glucose (60–70 mg/dl), with minimal or no symptoms, to severe hypoglycemia, with very low levels of glucose (< 40 mg/dl) and neurological impairment.<sup>5</sup>

## Signs and symptoms

Symptoms of hypoglycemia can be divided into adrenergic (rapidly falling and changing glucose levels) and

neuroglycopenic (low central nervous system [CNS] glucose). The adrenergic symptoms are inversely correlated to the developing rate of hypoglycemia, being most pronounced with acute onsets. Adrenergic features, when present, precede neurobehavioral features, thus functioning as an early warning system.

Inpatient team members must be alert to early adrenergic hypoglycemia signs and symptoms, including anxiety, irritability, dizziness, diaphoresis, pallor, tachycardia, headache, shakiness, and hunger.<sup>4</sup> When symptoms occur, early treatment involves having the patient eat simple carbohydrate. In an NPO (nothing by mouth) patient, viable alternatives for treating early hypoglycemia include giving an intravenous (IV) bolus of 50% dextrose, or, if absent an IV, giving intramuscular glucagon. However, when sympathetic dysfunction (e.g., diabetic autonomic neuropathy) exists or when adrenergic blockers are being used, these signs and symptoms may be unnoticeable.

Neuroglycopenic signs occur when the brain's dependence on glucose, coupled with its limited glycogen stores, results in rapid CNS dysfunction.<sup>6</sup> If warning signs are absent or ignored and the blood glucose level continues to fall, more severe hypoglycemia may lead to alteration of mental function that proceeds to headache, malaise, impaired concentration, confusion, disorientation, irritability, lethargy, slurred speech, and irrational or uncontrolled behavior, which may be confused with dementia.<sup>4</sup> Notable CNS dysfunction, including focal seizures, hemiplegia, paroxysmal choreoathetosis, and patchy brain stem and cerebellar involvement mimicking basilar artery thrombosis, has also been reported. The medullary phase of hypoglycemia, characterized by deep coma, pupillary dilatation, shallow breathing, bradycardia, and hypotonicity, occurs at a blood glucose level of ~ 10 mg/dl.<sup>6</sup> Most individuals with diabetes never suffer such severe hypoglycemia.

Individuals with type 1 diabetes are at higher risk for hypoglycemia. The risk is associated with C-peptide negativity (decreased insulin secretion).<sup>7</sup> The first line of defense against hypoglycemia is lost when an individual receives exogenous insulin and is unable to regulate insulin levels as plasma glucose declines. Islet secretion

is normally a potent stimulus to the glucagon secretory response to hypoglycemia.<sup>8</sup> The absent glucagon response may be a direct result of absent insulin secretion and accurately predicts that the second defense against hypoglycemia (increased glucagon secretion) is lost. Therefore, patients with established (i.e., C-peptide-negative) type 1 diabetes are largely dependent on the third defense against hypoglycemia: increased adrenalin or epinephrine secretion.

Patients with type 1 diabetes who have combined deficiencies of glucagon and epinephrine responses have been shown in prospective studies to suffer severe hypoglycemia at rates  $\geq 25$ -fold those of patients with absent glucagon but intact epinephrine responses during aggressive glycemic therapy.<sup>9</sup> Individuals with type 2 diabetes are at substantially lower risk for severe hypoglycemia than those with type 1 diabetes.<sup>10</sup> Those who experience recurrent episodes should be individually evaluated and, when appropriate, should have their target glucose ranges and insulin regimen modified. Many of the CNS symptoms can be mistaken for other signs of illness. Hence, bedside blood glucose monitoring is essential to making an appropriate diagnosis (Table 1).

#### Risk factors

Several factors put individuals at risk for a hypoglycemic episode. These include a mismatch in the timing, amount, or type of insulin and the carbohydrate intake; undernutrition; a history of severe hypoglycemia; renal failure; liver disorders; glucocorticoid or catecholamine deficiencies; and leukemia (caused by a possible abnormality in glucose metabolism including reduced levels of liver glucose-6-phosphatase).<sup>11</sup> Other individuals at risk are those who have ingested large amounts of alcohol or

salicylates and those who have surgery with general anesthesia, which places them in an altered consciousness and hypermetabolic state<sup>11</sup> (Table 2).

Hypoglycemia does not occur in people with diabetes who are treated with medical nutrition therapy (MNT) and exercise alone and is rare in people treated only with  $\alpha$ -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.<sup>4</sup>

Hospital personnel must consider timing of procedures for individuals with diabetes. It is best to schedule patients first thing in the morning or after a meal to avoid potential hypoglycemia. Sometimes, patients are taken off the nursing unit for procedures during scheduled meal times. Blood glucose monitoring should be performed before the patient leaves the unit, and precautions for treating the patient in the event that hypoglycemia symptoms occur must be considered. Ideally, a hospital staff member or the patient will be able to monitor capillary blood glucose while the patient is off the unit to ensure safety. If the patient is able to eat but is to be taken off the unit just before mealtime, then supplemental carbohydrate can be given to patient.

Another potential risk for hypoglycemia is the use of  $\beta$ -blocker medication in cardiac and hypertensive patients. Using medications for  $\beta$ -blockade may shift the glycemic threshold for some adrenergic symptoms, but it does not reduce neuroglycopenic symptoms. Several studies evaluating patients taking  $\beta$ -blockers did show a reduction in symptoms of tremulousness and hunger, but they did not reduce the incidence of symp-

**Table 1. Signs and Symptoms of Hypoglycemia**

Early Adrenergic Symptoms	Neuroglycopenic Signs
<ul style="list-style-type: none"> <li>• Pallor</li> <li>• Diaphoresis</li> <li>• Tachycardia</li> <li>• Shakiness</li> <li>• Hunger</li> <li>• Anxiety</li> <li>• Irritability</li> <li>• Headache</li> <li>• Dizziness</li> </ul>	<ul style="list-style-type: none"> <li>• Confusion</li> <li>• Slurred speech</li> <li>• Irrational or uncontrolled behavior</li> <li>• Extreme fatigue</li> <li>• Disorientation</li> <li>• Loss of consciousness</li> <li>• Seizures</li> <li>• Pupillary sluggishness</li> <li>• Decreased response to noxious stimuli</li> </ul>

**Table 2. Risk Factors for Hypoglycemia****Common Risk Factors**

- Mismatch of insulin timing, amount, or type for carbohydrate intake
- Oral secretagogues without appropriate carbohydrate intake
- History of severe hypoglycemia
- General anesthesia or sedation that places patient in an altered consciousness
- Reduction of oral intake
- New NPO status
- Unexpected transport after injection of rapid- or fast-acting insulin
- Critical illnesses (hepatic, cardiac, and renal failure; sepsis; and severe trauma)

**Less Common Risk Factors**

- Endocrine deficiencies (cortisol, growth hormone, or both), non- $\beta$ -cell tumors
- Ingestion of large amounts of alcohol or salicylates
- Sudden reduction of corticosteroid dose
- Emesis
- Reduction of rate of intravenous dextrose
- Unexpected interruption of enteral feedings or parenteral nutrition
- Drug dispensing error

toms such as diaphoresis or impaired cognition.<sup>12</sup> At one time,  $\beta$ -blockers were contraindicated for insulin-treated patients. Evidence suggests that this hypothetical risk is not clinically significant for cardiac patients with diabetes.<sup>12</sup>

**Prevention**

Balancing glycemic control by preventing hyperglycemia and hypoglycemia is key for providing optimum care of individuals with diabetes. The inpatient team can prevent or reduce hypoglycemic events by 1) recognizing precipitating factors or triggering events; 2) ordering appropriate scheduled insulin or anti-diabetic oral agents; 3) monitoring blood glucose at the bedside; 4) educating patients, family, friends, and staff about symptom recognition and appropriate treatment; 5) providing appropriate nutritional requirements; and 6) applying systems for eliminating or reducing medication and treatment errors in hospitalized patients.

**Recognition of precipitating factors**

This includes delay in the timing of meals or dosage of oral hypoglycemic agents or insulin; errors in dosages administered; timing of the medication, particularly insulin; and the presence of a comorbidity, such as renal insufficiency, adrenal insufficiency, and pituitary insufficiency, which heightens the risk for hypoglycemia. Inpatient staff can prevent hypoglycemic episodes by conveying appropriate instructions for meal timing and medication administration, heightening awareness of medical con-

ditions that influence glucose control, and, if appropriate, encouraging patient self-care.<sup>5</sup> Self-management by patients whose diabetes is well controlled as outpatients and who possess the capability of managing their insulin regimen in the hospital, such as those who wear an insulin pump or who use multiple daily injections of glargine and aspart or lispro, can be a means to reduce hypoglycemia.<sup>1,4</sup> Often, capable patients can match their required needs in respect to timing and amount of carbohydrate better than most nurses or physicians.

**Scheduled insulin therapy**

Concerns about hypoglycemia are often exhibited in physician orders. Although endocrinologists have been warning against its use for decades, the regular or rapid-acting analog insulin sliding scale without basal insulin replacement remains a common method of attempting to control hyperglycemia in the hospital.<sup>13</sup> Usually, out of concern for hypoglycemia, no basal insulin is given, and prandial insulin is given only if the pre-meal blood glucose is elevated.

Predictably, this approach does not work. If no insulin is given before a meal, the blood glucose level rises substantially and remains elevated at the time of the next meal. Then, a large dose of regular, lispro, or aspart insulin is given, which could cause hypoglycemia, particularly if administered at bedtime without a meal. Standard insulin sliding scales are ineffective, carry the risk of hyperglycemia and hypoglycemia, and generally should be avoided.<sup>14</sup>

On the other hand, basal and bolus insulin provides a more physiological replacement of insulin. The recent ADA technical review on inpatient diabetes used the term “programmed” or “scheduled insulin requirement” to refer to the dose requirement during hospitalization that is necessary to cover both basal and nutritional needs.<sup>1,15</sup> When patients are eating scheduled meals, basal and separate prandial insulin requirements provide good options.

**Inpatient use of oral agents**

Oral agents should not be used by inpatients who are too ill to maintain adequate caloric intake or who are on NPO status because of illness or planned procedures. Secretagogues can cause hypoglycemia,  $\alpha$ -glucosidase inhibitors are ineffective without carbohydrate intake, and metformin puts patients at risk who are renal-compromised or in heart failure. Thiazolidinediones (TZDs) should be discontinued in patients with Class III or Class IV heart disease, although the lingering effects of TZDs last several weeks.<sup>14</sup>

A common error in this population of patients is the discontinuation of oral agents in the absence of an alternate method for diabetes control. These patients should instead be converted to a subcutaneous or IV insulin regimen during hospitalization. Management with insulin in these circumstances is safer and has the added benefit of increased dosing flexibility when caloric intake is erratic.<sup>2</sup>

**Glucose monitoring**

Bedside monitoring of capillary blood glucose should be performed at least four times daily (i.e., before meals and at bedtime for patients who are eating). A glucose check at 3:00 a.m. can also be useful in patients with fasting hyperglycemia. An elevated glucose level at that time could indicate insufficient nighttime insulin dosing, whereas a low glucose level at that time may indicate an early peak in evening insulin or insufficient caloric intake at bedtime.

Patients with persistent hypoglycemia may require an overall reduction in insulin dose. Patients who are NPO or require continuous tube feedings should have glucose levels checked at least every 6 hours. In special circumstances, such as an unusual bolus tube-feeding schedule,

the timing of the bedside glucose checks should be carefully coordinated with the timing of the feedings.<sup>2</sup>

### Medical nutrition therapy

Appropriate nutrition in the hospital is paramount, not only for patients who rely solely on dietary control of their diabetes, but also for any inpatient with diabetes. A consistent carbohydrate diet is important to appropriately match the insulin regimen or secretagogue activity to food for optimum

**Table 3. Carbohydrate Sources for Oral Treatment of Mild Hypoglycemic Episodes**

The following are examples of readily available sources offering 15 g of carbohydrate:

- 4 oz apple juice or orange juice (Do not give orange juice to renal patients.)
- 4 oz regular sugar-sweetened cola
- 6 oz sugar-sweetened ginger ale
- 3 BD glucose tablets
- 4 Dex4 glucose tablets

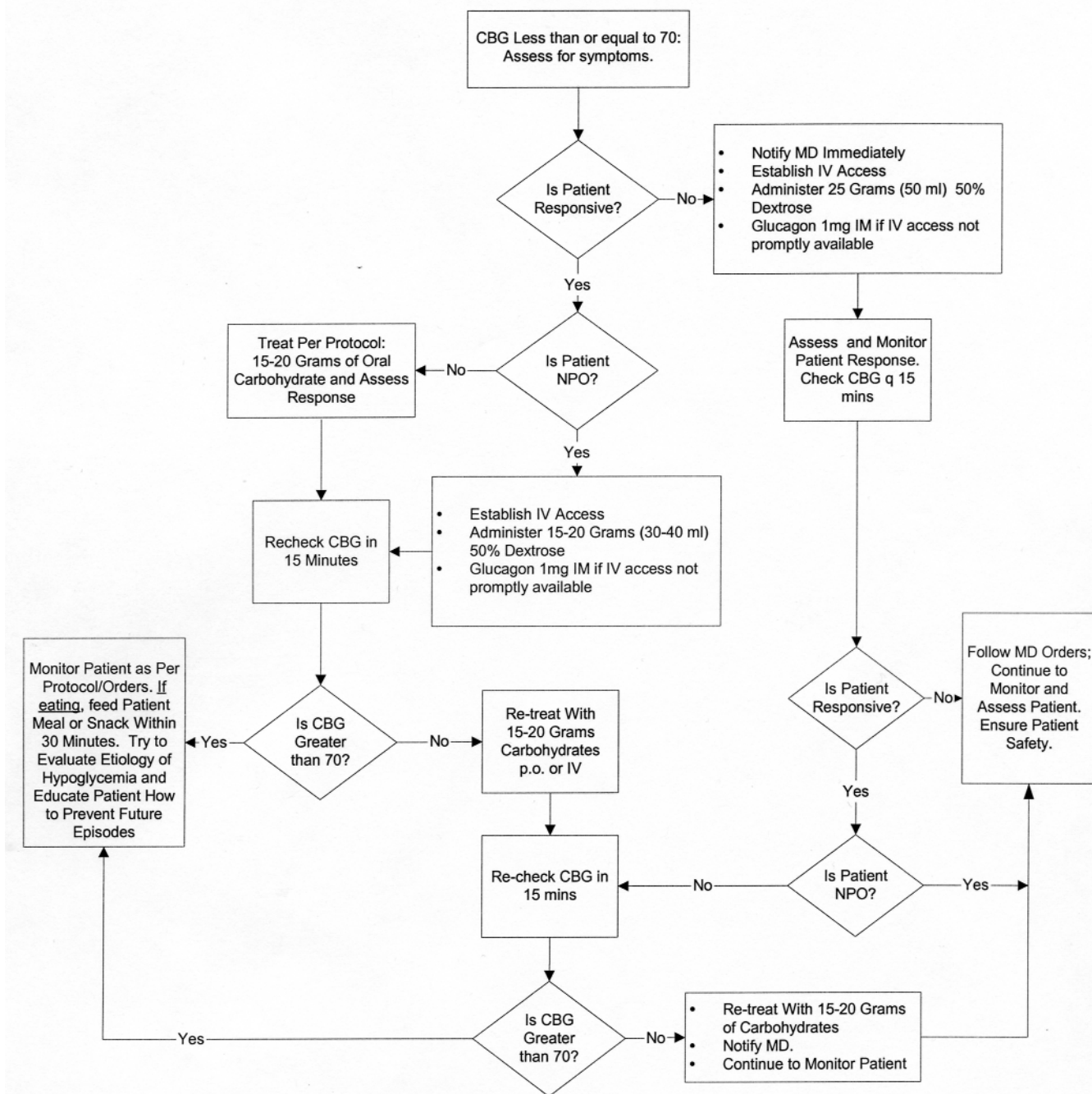


Figure 1. Adult hypoglycemia treatment protocol developed by the Lovelace Medical Center Diabetes Episodes of Care (EOC) Inpatient Team including, in alphabetical order, Marjorie Cypress, Edward Ripley, Tanya Krafft, Jeremy Gleeson, Linda Skogmo, Jackie Rolfson, and Donna Tomky. A decision tree format provides a quick glance of treatment strategies for nursing staff to follow. CBG, capillary blood glucose; IM, intramuscular. Reprinted with permission.



glucose control and prevention of hypoglycemia. All three meals should follow a consistent carbohydrate approach that emphasizes the importance of a mixed meal. Carbohydrate should be consumed in a balanced meal with protein, fat, and fiber.<sup>3</sup>

### Applying systems

The recent ADA technical review<sup>1</sup> discussed the use of protocols or standardized order sets for scheduled and correction-dose insulin, which reduces reliance on sliding scale management for maintaining glucose control in the hospital. For many reasons, outcomes using standardized pathways or dose titration protocols are superior to those achieved by individualization of care.<sup>16</sup> Despite repeated warning from the Institute for Safe Medication Practices and other organizations,<sup>17</sup> old and unsafe prescribing habits still in use continue to result in frank prescribing errors. These practices include the use of trailing zeros after decimal points (2.0 misinterpreted for 20 instead of 2) or misinterpreted abbreviations (i.e., “U” instead of “units” for insulin) and may compromise patient safety and cause hypoglycemia.<sup>18–21</sup> A team or multidisciplinary approach is needed to establish hospital pathways and implement intravenous infusion of insulin for the majority of patients having prolonged NPO status outside of critical care units.

### Treatment Strategies

A team approach is also needed in recognizing and treating patients with hypoglycemia. Reviewing the signs and symptoms of hypoglycemia with nursing staff and patients may prevent severe hypoglycemic episodes. Making bedside glucose monitoring readily available and having an easily interpretable hypoglycemia treatment protocol can ensure efficient and effective care for hypoglycemic patients.

When a patient experiences a hypoglycemic episode, assessment at the bedside must include the patient's level of consciousness, respiratory and circulatory status, capillary blood glucose test results, existence of IV access, time and amount of insulin doses, and NPO status or last food and amount of intake. If the patient can safely be treated with oral carbohydrate, use an appropriate choice of liquid or easily dissolved glucose tablets (Table 3). If the patient is unresponsive or NPO, then IV access for quick administration of dextrose or intramuscular injection of glucagon are the preferred treatment methods (Figure 1). Attempting to treat by increasing the IV rate to infuse glucose quickly places patients at risk for fluid overload because 100 cc of 5% dextrose solution offers only 5 g of carbohydrate.

A common error is to overtreat hypoglycemia with an excess of carbohydrate. This, in combination with the counterregulatory hormone response to hypoglycemia, facilitates subsequent hyperglycemia. After treatment of any hypoglycemic episode, frequent bedside glucose monitoring should be continued until a stable glucose level is achieved. Depending on the time of day and insulin peak times, a balanced snack with carbohydrate, protein, and fat (i.e., peanut butter and crackers, or milk) can prolong treatment effectiveness.

After treating a hypoglycemic event, search for the cause, correct the problem, and, if indicated, alter insulin or medication dose. This includes giving consideration to age-specific hypoglycemia concerns for pediatric and geriatric patients (Table 4).

Before discharge, patients should receive education in the form of verbal instructions, written materials, and referral for outpatient follow-up to avoid further events.

### Summary

The threat of hypoglycemia is one barrier to providing optimal glycemic control in the inpatient setting. Prevention is key in ensuring patient safety. Identifying risk factors, implementing protocols, avoiding traditional sliding scale insulin regimens, and changing unsafe prescribing behaviors are ways to avoid severe hypoglycemic events. Reviewing hypoglycemia signs and symptoms with the entire inpatient team, including patients and their significant others, allows for early detection and treatment. Establishing and publishing a simple treatment protocol affords prompt action to appropriately treat various stages of hypoglycemia.

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**Table 4. Age-Specific Considerations Regarding Hypoglycemia**

#### Pediatric

Many young people with diabetes are at risk for hypoglycemia because of the erratic eating and exercise habits typical in this age group.

#### Geriatric

Elderly individuals may have hypoglycemia unawareness (i.e., they do not experience the early symptoms of hypoglycemia). This is particularly concerning because the blood glucose level continues to drop and may reach very serious levels (< 40 mg/dl) before hypoglycemia is recognized and treated.

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*Donna M. Tomky, MSN, RN, C-ANP, CDE, is a nurse practitioner and diabetes educator in the Department of Endocrinology/Diabetes at Lovelace Medical Center in Albuquerque, N.M.*