INTRODUCTION — Diabetes mellitus is a common chronic disorder, affecting at least 5 percent of North Americans [1]. In general, these patients have poorer health compared to those without diabetes mellitus, and this often translates into more surgical interventions [1]. Moreover, diabetic complications and the greater frequency of macrovascular disease result in more frequent surgery to address renal failure and its treatment, cataracts and retinal disease, foot ulcers, and peripheral vascular and coronary heart disease. It is estimated that a diabetic patient has a 50 percent chance of requiring surgery in his or her lifetime [2].

Careful assessment of diabetic patients prior to surgery is required because of their complexity and high risk of coronary heart disease, which may be relatively asymptomatic compared to the nondiabetic population. Diabetes mellitus is also associated with increased risk of perioperative infection [3] and postoperative cardiovascular morbidity and mortality [4].

One key aspect of the perioperative assessment is glycemic control; complex interplay of the operative procedure, anesthesia, and additional postoperative factors such as sepsis, hyperalimentation, and emesis can lead to labile blood glucose levels. A rational approach to diabetes mellitus management allows the physician to anticipate alterations in glucose and improve glycemia perioperatively [5].

This topic review will discuss the preoperative evaluation of patients with diabetes, effect of surgery on glucose control, general goals of glycemic control, and management of diabetes mellitus in the early and late perioperative phase. The special circumstances of glucocorticoid therapy and hyperalimentation are also reviewed. More details regarding glucose control in hospitalized patients in general is found separately. (See "Management of diabetes mellitus in the acute care setting" and see "Nutritional support in the critically ill").

PREOPERATIVE EVALUATION — The preoperative evaluation of any patient, especially those with diabetes mellitus, focuses on cardiopulmonary risk assessment and modification. Coronary heart disease is much more common in individuals with diabetes than in the general population [6,7]. In addition, patients with diabetes have an increased risk of silent ischemia. (See "Prevalence of and risk factors for..."
coronary heart disease in diabetes mellitus").

Several cardiac risk stratification indices, such as the Eagle index for vascular surgery [8] and the Revised Cardiac Index of Lee and colleagues [4], cite diabetes mellitus as a major risk factor for perioperative cardiac events. (See "Estimation of cardiac risk prior to noncardiac surgery").

All patients require a careful history and physical examination, with further evaluation required in certain individuals. Key elements of the initial assessment include the following:

- Long-term complications of diabetes mellitus, including retinopathy, nephropathy, neuropathy, autonomic neuropathy, coronary heart disease, peripheral vascular disease
- Assessment of baseline glycemic control, including frequency of monitoring, average blood glucose levels, range of blood glucose levels
- Assessment of hypoglycemia, including frequency, timing, awareness, and severity
- Pharmacologic and nonpharmacologic therapy, including type of medication, dosing and specific timing, diet, and exercise
- Characteristics of surgery, including when the patient must stop eating prior to surgery, type of surgery (major or minor), timing of the operative procedure, and duration of the procedure
- Type of anesthetic, including epidural versus general anesthesia (epidural anesthesia has minimal effects on glucose metabolism [9] and insulin resistance)

**Preoperative laboratory investigations** — Basic investigations should include a baseline electrocardiogram and assessment of renal function. ECG abnormalities such as abnormal q waves suggestive of previous myocardial infarction and chronic kidney disease are each risk factors for major postoperative cardiac events in the Revised Cardiac Index.

Baseline glucose levels can also help to stratify risk for postoperative wound infections. Elevat ed preoperative glucose levels (>200 mg/dL [>11 mmol/L]) were associated with deep wound infections in a case control study (OR: 10.2, 95% CI: 2.4-43) [10].

There is some suggestion that elevated A1C levels may also predict a higher rate of postoperative infections. A retrospective cohort study of 490 diabetic men who underwent major noncardiac surgery in a VA setting found that a preoperative A1C >7 percent was associated with a small but significant increase in postoperative infections compared to those with A1C <7 percent (adjusted odds ratio [OR] 2.13, 95% CI 1.23-3.70) [11].

Further investigations including noninvasive cardiac testing should be considered on an individual basis. (See "Estimation of cardiac risk prior to noncardiac surgery").

**EFFECT OF SURGERY ON GLUCOSE CONTROL** — Surgery and general anesthesia can cause a state of relative insulin hyposecretion and insulin resistance [12-20] via release of hormones such as glucocorticoids, growth hormone, catecholamines, and glucagon [9,21-24]. The magnitude of counterregulatory hormone release varies per individual and is related to the extent of the surgery and additional postoperative factors such as sepsis. The hyperglycemic response to these factors may be attenuated by the lack of caloric intake during and immediately after surgery, making the final glycemic balance difficult to predict.

**GENERAL GOALS OF GLYCEMIC CONTROL** — The goals of perioperative diabetic management include:

- Avoidance of marked hyperglycemia
- Avoidance of hypoglycemia
Uncontrolled diabetes can lead to volume depletion from osmotic diuresis, and life-threatening conditions such as diabetic ketoacidosis (DKA) or nonketotic hyperosmolar state (NKH). (See "Clinical features and diagnosis of diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults"). Patients with type 1 diabetes mellitus are insulin deficient and are prone to developing ketosis and acidosis. A common mistake is to manage these patients like type 2 diabetic patients who are not ketosis prone. As an example, one might hold insulin if the glucose level does not appear "too elevated" with the consequent risk of ketoacidosis. Type 2 diabetic patients are susceptible to developing NKH that may lead to severe volume depletion and neurologic complications, and may even develop ketoacidosis in the setting of extreme stress.

Hypoglycemia is another potentially life-threatening complication of poor perioperative metabolic control. Even a few minutes of serious hypoglycemia (ie, serum glucose concentration <40 to 50 mg/dL [2.2 to 2.8 mmol/L]) can be harmful, possibly inducing arrhythmias, other cardiac events, or transient cognitive deficits. Hypoglycemia and subsequent neuroglucopenia can be difficult to detect in sedated patients postoperatively.

Beyond avoidance of marked hyperglycemia and hypoglycemia, it is less clear as to how "tight" glucose control needs to be perioperatively. There is a paucity of controlled trials on the benefits and risks of "loose" or "tight" glycemic control in these patients (with the exception of patients in the intensive care unit or who have had an acute MI). Studies show that achieving normoglycemia (80 to 110 mg/dL [4.4 to 6.1 mmol/L]) in cardiac surgery patients or those requiring postoperative surgical or medical ICU settings may reduce mortality. These trials are discussed in detail elsewhere. (See "Nutritional support in the critically ill", section on Glucose control).

Whether these findings from ICU patients apply to diabetic inpatients undergoing other types of surgical procedures or with less severe disease is unclear [25]. There is a paucity of evidence on a broader spectrum of surgical patients undergoing non-cardiac procedures, and procedures not requiring ICU care. Furthermore, the practicalities of implementing intensive IV insulin regimens in non-ICU settings are unclear. The lack of clear evidence is reflected in the varying glucose targets recommended by national guidelines [26-28].

Despite some variability in proposed targets, these published guidelines collectively propose attempting to achieve "reasonable" normoglycemia in a majority of surgical patients with, if possible, a majority of glucose readings below 200 gm/dL (<11.0 mmol/L). This assertion is supported by an observational study of 531 patients admitted to a surgical and medical ICU, 523 of whom underwent analysis of their glycemic control [29]. Regression models from that analysis suggest that there is an association between lower glucose levels (less than 200 mg/dL [<11 mmol/L]) among critical care patients and lower mortality.

**EARLY PERIOPERATIVE PHASE** — Several strategies exist to maintain target range glucose levels perioperatively, but there is no consensus as to the optimal strategy. There are limited data on the optimal strategy has been well studied for the prevention of important outcomes such as DKA/NKH, neuroglycopenia, wound infections, or postoperative myocardial infarction. However, the strategies presented by one review, which are the focus of discussion here, reflect practical and seemingly safe protocols for perioperative glucose management [15].

Ideally, all patients with diabetes mellitus should have their surgery as early as possible in the morning to minimize the disruption of their management routine while being nil per os. In addition, patients should be cautioned about symptoms of hyper/hypoglycemia and on appropriate strategies for dealing with these problems prior to leaving the hospital.

**Type 2 diabetes treated with diet alone** — Generally, patients with type 2 diabetes managed by diet alone do not require any therapy perioperatively. Supplemental short-acting insulin (eg, regular or lispro) may be given as a subcutaneous sliding scale in patients whose glucose levels rise over the
desired target ([see "Sliding scale development" below](#)). Blood glucose should be checked preoperatively and soon after the surgery. Intravenous solutions do not require dextrose if insulin is not given.

**Type 2 diabetes treated with oral hypoglycemic agents** — Patients with type 2 diabetes who take oral hypoglycemic drugs are advised to continue their usual routine of oral antidiabetic medications until the morning of surgery. On the morning of surgery, they should hold their oral hypoglycemic drugs (including alpha glucosidase inhibitors, biguanides, sulfonylureas or thiazolidinediones). Previously, biguanides ([metformin](#)) were discontinued 48 hours prior to surgery because of concerns regarding lactic acidosis, but current practice is to discontinue on the day of surgery [5]. For patients who develop hyperglycemia, supplemental short-acting insulin (regular or lispro) may be administered subcutaneously as a sliding scale, based on frequently measured glucose levels which are often obtained on capillary "fingerstick" samples ([see "Sliding scale development" below](#)).

**Type 1 or type 2 diabetes treated with insulin** — Generally patients who use insulin can continue with subcutaneous insulin perioperatively (rather than an insulin infusion) for procedures that are not long and complex [9,22,24,30-37].

Some clinicians switch their patients taking long-acting insulin (eg, glargine) to an intermediate-acting insulin one to two days prior to surgery because of a potential increased risk for hypoglycemia with the former. However, if the basal insulin is correctly calibrated in a patient with type 1 diabetes, it is reasonable to continue their long-acting insulin while the patient is NPO and on intravenous dextrose. There are no available data to support one approach over the other.

It may be prudent to reduce the night time (supper or HS) intermediate-acting insulin on the night prior to surgery to prevent hypoglycemia if the patient has borderline hypoglycemia or "tight" control of the fasting blood glucose.

**Timing of procedure** — For short, early morning procedures where breakfast is likely only delayed, patients may delay taking their usual morning insulin until after the surgery and before eating.

For patients undergoing morning procedures where breakfast is likely to be missed but lunch will be eaten:

- If the patient normally takes once-daily, intermediate-acting insulin in the morning, then the patient should receive two-thirds of his/her usual dose of intermediate-acting insulin.
  
- If the patient normally takes twice-daily insulin, then the patient should receive one-half of his/her total morning insulin dose (including any usual short acting) as intermediate acting insulin in the morning.

Morning procedures where both breakfast and lunch are likely to be missed will require less morning insulin:

- Patients normally taking once daily insulin (intermediate +/- short acting) should receive one-half of their total morning insulin dose as intermediate-acting insulin in the morning.

- Patients normally taking insulin twice daily should take one-third of the total morning dose as intermediate-acting insulin.

- Patients on a morning intermediate-acting insulin, supper short-acting, and bedtime intermediate-acting insulin should take one-third of the total morning dose as intermediate-acting insulin.

- Patients on multiple short-acting doses of insulin should take one-third of the premeal dose of short-acting insulin at the appropriate time.

- Patients on continuous insulin infusion pumps may continue their usual basal infusion rate.
For surgery scheduled later in the day, the patient will require less insulin but should also receive dextrose-containing intravenous solution (5 gm glucose/hour = 100 cc/hr of D5W solution) to avoid the metabolic changes of starvation [9,24,30-37]. Basal metabolic needs use up approximately one-half of an individual's insulin even in the absence of oral intake; thus, patients may continue with some insulin even when not eating [38].

- Patients usually taking once-daily insulin dosage should take one-half of their total morning dose of insulin as intermediate-acting insulin.

- Patients treated with two or three daily dosages of insulin should receive one-third of the total morning dose of insulin as intermediate-acting insulin.

- Patients taking multiple doses of short-acting insulin should receive one-third of their morning dose as short-acting insulin and one-third of their lunch dose at the appropriate time.

- Patients using insulin pumps should maintain their basal rate without boluses, and hyperglycemia may be treated with short-acting insulin sliding scale.

**Long and complex procedures for type 1 or type 2 diabetes requiring insulin** — Intravenous insulin is usually required for long and complex procedures (eg, coronary artery bypass graft, renal transplant, or prolonged neurosurgical operations). Studies comparing subcutaneous insulin administration versus intravenous infusion have found a marked increase in variability of the glucose concentration when using the subcutaneous route [39,40]. This variability in plasma insulin has been attributed to the varying degrees of tissue perfusion associated with long and complex procedures.

The safety of intravenous insulin infusion has been demonstrated by many studies [39-49]. In addition, insulin infusions are more readily titrated because the half-life of intravenous insulin is short (ie, 5 to 10 minutes), allowing for more precise glucose control.

Intravenous insulin regimens require close monitoring of blood glucose and electrolytes as well as appropriate interpretation by well-trained staff. Generally insulin infusions should be started early in the morning prior to surgery to allow time to achieve glycemic control. There are multiple types of intravenous solutions such as intermittent bolus, fixed rate insulin infusion, variable glucose-insulin-potassium infusion, and variable separate glucose and insulin infusion. No optimal protocol has been devised. The most commonly used infusions are described below.

**Fixed rate insulin glucose infusion** — This method uses separate continuous insulin and glucose infusions (dextrose 5 percent as part of a maintenance solution). The insulin infusion rate is selected according to an intravenous sliding scale, which may be adjusted based on empiric results. As examples:

- Blood glucose 201 to 250 mg/dL (11.1 to 14.0 mmol/L) — insulin infusion 1 unit per hour
- Blood glucose 251 to 300 g/dL (14.1 and 17.0 mmol/L) — insulin infusion 2 units per hour

With this approach, a continuous source of dextrose and fluid is supplied and insulin rates can be adjusted independent of dextrose rates and based upon ambient glucose levels.

**Glucose insulin potassium infusion** — The glucose insulin potassium (GIK) drip is a single solution infusion that includes 500 mL of D5W, 10 mmol of potassium chloride, and 15 units of short-acting insulin. The solution is infused at an initial rate of 100 mL/hr. The solution can be altered depending on the blood glucose measured every two hours by adding or subtracting 5 units of insulin.

This regimen is safe because the insulin and glucose are given together, but may require frequent changes of intravenous solution. The blood glucose should be monitored frequently, at least every two hours. The problem with this approach is that if glucose levels run "low", based upon the target levels...
above, and the infusion is stopped, patients with type 1 diabetes can quickly become ketotic.

**Variable separate insulin and glucose intravenous solutions** — With this regimen, dextrose is administered at approximately 5 to 10 gm of glucose/hour, and a separate insulin infusion is given using short-acting insulin (initially started at 1 unit/hr). The rate of insulin infusion may be titrated depending on the procedure and the degree of insulin resistance. For coronary artery bypass procedures, the insulin requirements may increase by 10-fold, especially after recovery from the hypothermic period, necessitating an increase in the initial insulin rate by three to five times [38].

The amount of insulin needed to account for insulin resistance and hyposecretion can be calculated by adding up the total daily intake (TDI) of insulin and then dividing by 30 (TDI/30). This factor is in turn multiplied by the initial starting rate.

Blood glucose should be measured every hour and electrolytes should be measured every four to six hours. The insulin drip can be altered by 0.5 units per hour for every 3 mmol (50 mg/dL) that the glucose is out of the target range (ie, >11.0 mmol/L or 200 mg/dL).

This regimen is flexible and does not require changes of entire solution bags like the GIK infusion. However, there is a concern that hypoglycemia will develop if the glucose infusion is inadvertently obstructed or held.

**LATE POSTOPERATIVE PHASE** — Generally the preoperative diabetes treatment regimen (oral or oral plus insulin) may be reinstated once the patient is eating well. However, there are a few caveats for certain oral hypoglycemic agents.

- **Metformin** should not be restarted in patients with renal insufficiency, significant hepatic impairment, or congestive heart failure.
- Sulfonylureas stimulate insulin secretion and may cause hypoglycemia; they should be started only after eating has been well established. A step-up approach can be used for patients on high dose sulfonylureas, starting at low doses and adjusting them until the usual dose is reached.
- Thiazolidinediones should not be used if patients develop congestive heart failure or problematic fluid retention, or if there are any liver function abnormalities.

Insulin infusions should continue in patients who do not resume eating postoperatively. Intensive insulin therapy to keep the blood glucose at or below 110 mg/dL has been found to improve outcomes in critically ill postsurgical patients requiring prolonged mechanical ventilation [50]. Once it seems likely that solid food will be tolerated, the insulin infusion can be discontinued 15 to 30 minutes prior to eating, and the patient switched to subcutaneous insulin at that time.

Patients who were taking subcutaneous insulin in the early postoperative phase, before alimentation is restarted, should continue this treatment along with intravenous dextrose (5 to 10 gm of glucose/hr = 100 to 200 mL/hr of D5W solution) to prevent hypoglycemia.

**SLIDING SCALE DEVELOPMENT** — Insulin sliding scales are often used to bridge the gap from the time of surgery to resumption of regular meals. Sliding scales can be problematic, however, causing wide fluctuations in the serum glucose as they "react" to past glucose concentrations.

The sliding scale formula proposed by Jacober and Sowers attempts to reduce problems by incorporating the patient's level of insulin resistance to guide insulin dosing [5]. The first step in this approach is to determine the total daily insulin (TDI) for the patient and then divide this value by 30. This factor (ie, TDI/30) is then used to calculate the increment needed in the sliding scale.

An example of a subcutaneous sliding scale using short-acting insulin is as follows:
Blood glucose mg/dL (mmol/L) 0 to 70 (0.0 to 3.9) -- Call physician
0 to 200 (4.0 to 11.0) -- give no insulin
201 to 250 (11.1 to 14.0) -- 1 X (TDI/30) units of short acting insulin
251 to 300 (14.1 to 17.0) -- 2 X (TDI/30) units of insulin
301 to 350 (17.1 to 20.0) -- 3 X (TDI/30) units of insulin
351 to 400 (20.1 to 23.0) -- 4 X (TDI/30) units of insulin
401 to 450 (23.1 to 26.0) -- 5 X (TDI/30) units of insulin
>450 (>26) -- Call physician

For patients who were taking oral hypoglycemic agents preoperatively, the insulin sliding scale can be created using a conservative estimate of the total daily intake such as 30 units of insulin. Insulin administration for glucose less than 200 mg/dL (11 mmol/L) is generally unnecessary for nonketosis-prone diabetic patients.

Subcutaneous sliding scales may also be superimposed on regular dosing of intermediate acting insulin. Once the patient is eating however, the patient should be switched back to their preoperative medication regimen.

SPECIAL CONSIDERATIONS

Glucocorticoid therapy — Glucocorticoids are used for the treatment of many disorders and are often given in "stress" doses perioperatively. (See "The surgical patient taking glucocorticoids"). The use of glucocorticoids can worsen preexisting diabetes mellitus and may precipitate steroid-induced hyperglycemia in others. The mechanism by which glucocorticoids cause hyperglycemia is multifactorial including augmentation of hepatic gluconeogenesis, inhibition of glucose uptake in adipose tissue, and alteration of receptor and post receptor functions [51-53]. (See "Major side effects of systemic glucocorticoids").

Treatment with glucocorticoids rarely leads to ketoacidosis. A variable rate insulin and glucose infusion may be appropriate in patients receiving high dose steroids, especially with variable dosing. Oral hypoglycemic medications should be used in patients with constant dose of steroids and minimal elevation in blood glucose; insulin is often necessary for those whose glucose levels are elevated (>200 gm/dL or 11 mmol/L) [54]. Twice daily intermediate-acting insulin with short-acting insulin given in a subcutaneous sliding scale may be needed to achieve glucose control.

Hyperalimentation — Total parenteral nutrition (TPN) and nasogastric enteral feeds are commonly used in patients who are malnourished or severely ill. TPN, especially in those with type 2 diabetes mellitus, will often increase the serum blood glucose and necessitate large doses of insulin to maintain glycemic control.

Some investigators recommend using a variable rate insulin infusion when the patient is first started on TPN [54]. Once the patient is on a stable infusion rate of TPN, he/she may have the daily requirement of insulin directly added to the TPN solution bag. As an example, if the patient requires 20 units of insulin per 24 hours, add 20 units of short-acting insulin in the TPN solution that is administered continuously over 24 hours. A subcutaneous insulin sliding scale using short-acting insulin may be used if insulin infusion is not feasible.

For nasogastric feeds administered continuously over 24 hours, either a variable IV insulin infusion or subcutaneous sliding scale every four to six hours may be administered. Changes in insulin regimen must precede any changes in nasogastric feeding regimens (ie, changes from 24 hour-infusion to TID bolus feeds). Thus, good communication between the surgeon, dietitian, and the person managing diabetes care is important.
SUMMARY — Clinicians are frequently asked to manage the patient with diabetes mellitus perioperatively when there is only sparse data in the literature to guide decision-making. Many specific issues require further investigation including: optimal target range, regimen of insulin administration and the special circumstances of glucocorticoid use and hyperalimentation. Most protocols for insulin administration are formulated by expert opinion and personal experience.

The strategies described in this topic review, while sensible, have not been proven to affect outcomes of morbidity, mortality, and hospital length of stay. Other protocols call for aggressive and widespread usage of insulin infusions, but these strategies are often expensive, labor intensive, and even impossible at some hospitals. Ultimately, even well-coordinated plans for diabetic management are dynamic, being influenced by predictable and sometimes unpredictable events. Decisions of which regimens to utilize and when will depend upon individual patients and the clinician’s own judgment.

The American Diabetes Association has endorsed preprandial glucose goals of 90 to 130 mg/dL (5.0 to 7.2 mmol/L) for general hospitalized patients, with peak postprandial glucose <180 mg/dL (10 mmol/L). In addition, several organizations have suggested that in the critically ill, stricter targets (<110 mg/dL [6.1 mmol/L]) are both evidence-based and achievable, and will frequently require insulin infusion. (See “ADA position statement: Standards of medical care in diabetes”, section on Diabetes care in the hospital, and see “Nutritional support in the critically ill”, section on Glucose control).

Additional details regarding glucose control in hospitalized patients in general is found separately. (See "Management of diabetes mellitus in the acute care setting").

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