# New Technologies for Managing Diabetes Mellitus

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## Learning Objectives

1. Evaluate and compare different types of insulin delivery devices and justify the appropriateness of each for specific patient scenarios.
2. Assess glucose monitoring systems based on patient specific needs.
3. Analyze continuous glucose monitoring systems and their usefulness in promoting optimal glycemic control.
4. Apply knowledge of software technology to the overall treatment plan of a patient with diabetes mellitus (DM).
5. Assess the risks and benefits of invasive technology interventions such as artificial pancreas or human islet cell transplantation.
6. Given a specific patient case, create a telemedicine plan to prevent, treat, and manage DM.
7. Analyze the usefulness of home monitoring devices for foot care assessment and monofilament testing.
8. Evaluate mobile phone applications for improving blood glucose control.
9. Assess the pharmacist's role in using telehealth disease management programs in the community.

## Introduction

In 2002, about 17.7 million people in the United States had received a diagnosis of diabetes mellitus (DM). It is estimated that DM will affect 30.3 million people by 2030. In 2002, the estimated total cost of DM in the United States was $132 billion, including $92 billion in direct costs and $40 billion in indirect costs. Costs will continue to rise as the number of patients with a diagnosis of DM increases. By 2020, an estimated 44% more patients will be given a diagnosis of DM compared with 2002, and diabetes technology and supplies will constitute more than 13% of the direct cost of diabetes care.

The discovery of insulin in the 1920s revolutionized the treatment of DM. In addition, tremendous advances in diabetes technology have occurred in the past 30 years. New technologies include a variety of alternatives to needle injection for insulin delivery, advances in blood glucose (BG) monitoring devices, and novel treatment technologies. The overall goal of DM technology is to improve BG control, prevent long-term complications, and improve patient quality of life. Although these new technologies may be interesting to use, they must improve outcomes such as BG and prevent long-term complications to be effective and receive widespread acceptance. This chapter provides a basic understanding of these new technologies and how patients can use them to improve outcomes.

## Insulin Delivery Devices

During the past few years, many new insulin delivery devices have been developed and promoted; some

### Baseline Review Resources

The goal of PSAP is to provide only the most recent (past 3–5 years) information or topics. Chapters do not provide an overall review. Suggested resources for background information on this topic include:

- American Diabetes Association. Clinical practice recommendations 2010. Diabetes Care 2010;33(suppl 1):S1–S99.
- Triplitt CL, Reasner CA II, Isley WL. Diabetes mellitus. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM, eds. Pharmacotherapy: A Pathophysiologic Approach, 7th ed. Boston: McGraw-Hill, 2008:1205–42.
- Wolfsdorf JI. Intensive Diabetes Management, 4th ed. Alexandria, VA: American Diabetes Association, 2009.

**Abbreviations in This Chapter**

| | |
|---|---|
| A1C | Hemoglobin A1C |
| BG | Blood glucose |
| CGMS | Continuous glucose monitoring system |
| CSII | Continuous subcutaneous insulin infusion |
| DM | Diabetes mellitus |
| MEMS | Microelectromechanical system |

of these, such as the inhaled insulin Exubera, have since been removed from the market. Health care providers are able to offer patients a wide range of new technologic devices for insulin delivery, including insulin pumps, subcutaneous injection ports, and insulin delivery systems that use air pressure.

**Subcutaneous Injection Ports**

Subcutaneous injection ports are similar to the insulin infusion sets typically used with insulin pumps. Traditionally, subcutaneous injection ports are used in the inpatient setting; however, outpatient use of these devices is also feasible. Potential candidates for the use of injection ports are patients who have a fear of many daily injections or who become combative at the site of needles, such as children or patients with dementia.

A few kinds of ports are available. The Insuflon is placed with an angled subcutaneous injection, whereas the i-port is placed in the skin at a 90° angle into the abdomen or buttocks. The needle and port are inserted into the skin, and then the needle is removed. Application of a local anesthetic or numbing cream 30–60 minutes before injection may provide pain-free administration. The port remains in place, and insulin is delivered intermittently into the port for up to 72 hours. Patients and/or caregivers need only place a new subcutaneous injection port every 72 hours, thereby reducing the number of daily injections. The port will accept both syringe and insulin pen needles. Children who use subcutaneous injection ports achieve lower hemoglobin A1C (A1C) values, with a baseline average of 9.4% at screening reduced to 8.5% at 6 months, than children using traditional insulin delivery. Children who use subcutaneous injection ports also experience less anxiety with each insulin injection.

**Insulin Pumps**

Developed in the late 1970s, insulin pumps have been used in patients of all ages to deliver a continuous subcutaneous infusion of rapid-acting insulin. All rapid-acting insulins (insulin lispro, insulin glulisine, and insulin aspart) are labeled for use in insulin pumps. Advantages over injections with a syringe and needle include fewer daily injections, improvement in A1C values, more accuracy in delivery of insulin doses, greater flexibility in the timing of meals and exercise, and fewer fluctuations in BG concentrations.

Before continuous subcutaneous insulin infusion (CSII) is prescribed, the clinician should ensure that patients have advanced knowledge of their DM and are motivated to use the equipment correctly. Most diabetes education practice sites ensure that patients complete diabetes self-management training. All insulin pump manufacturers provide training to patients referred for use of an insulin pump, and pharmacists can be certified to train patients on the use of individual pumps. Before initiating pump training, patients need to have an advanced understanding of carbohydrate counting, insulin-to-carbohydrate ratio, and insulin sensitivity. A component of the training is to ensure patients understand insulin action curves (i.e., duration of action of the insulin that the patient has delivered as a correction bolus, meal bolus, or basal rate) and its relationship to their BG concentrations.

Patients may become anxious and recheck their BG concentration within an hour of administration of an insulin bolus; they then want to administer a correction bolus to "fix" their readings. However, the insulin correction bolus may be active for several hours after delivery of the dose. For example: a patient administers insulin aspart by bolus, checks his/her BG concentration 3 hours later, and finds an elevated reading. The patient may want to add a correction bolus to achieve the target BG concentration. However, about 40% of the full effect of the insulin aspart will be remaining and must be adjusted for before administering an additional insulin bolus. Administering boluses too often may cause hypoglycemia and frustration with the insulin pump. Several insulin pumps adjust for active insulin and lower subsequent bolus doses if there still is active insulin remaining.

Several new insulin pumps are available in the United States, as well as older models that patients are still using. All insulin pumps marketed today have standard features such as low battery warning, vibration option, small size, ability to download results to a personal computer, multiple basal program capability, and 24-hour toll-free telephone assistance (Table 1-1).

Some insulin pumps have an audio bolus feature that provides a "beep" for each unit of insulin bolus delivered. The patient can deliver a set-increment bolus dose by pressing a single button versus navigating through a menu to deliver the bolus. For example, if a patient has his/her audio bolus set for 1.0 unit, he/she can discreetly deliver a bolus of insulin to cover a meal in a social setting. Although this feature is desirable, the bolus may not be accurate if the patient needs only a fraction of a unit.

Initial costs of these devices range from $3000 to $6000, with an additional cost of about $1500 a year in monthly supplies. In general, third-party payers will

**Table 1-1.** Comparison of Commercially Available Insulin Pumps

| Insulin Pump Name | Unique Feature(s) | Advantages |
|---|---|---|
| Roche Accu-Chek Spirit | Screen that can rotate 180°<br>Personal digital assistant with software<br>Backup insulin pump | Allows wearing the pump on different parts of the body<br>Facilitates calculation of boluses and carbohydrate content of foods |
| DANA Diabecare IIS | Icon-based screen | Somewhat less expensive |
| MiniMed Paradigm | Interfaces with both the OneTouch UltraLink BG meter and its Guardian REAL-Time Continuous Glucose Monitoring System<br>Determines insulin boluses<br>Provides real-time trends of BG concentrations without several fingersticks | Permits fewer calculations by the patient before delivering insulin boluses |
| OneTouch Ping | Food database that stores up to 500 foods<br>BG monitor that sends results wirelessly to the insulin pump | |
| OmniPod | Built-in infusion set and cannula<br>"Pod" can be used for 72 hours and is disposable | Has no wires |
| Personal Diabetes Manager | Has remote control device for insulin delivery<br>Has glucose monitor (the FreeStyle BG monitor)<br>Controls insulin delivery through the pod<br>Recommends an insulin correction dose | Can be used to check the patient's BG |

BG = blood glucose.

cover around 80% to 90% of the cost. In addition, some state Medicaid agencies will pay up to 100% for insulin pumps. One product, the OmniPod (which has an infusion set but no tubing), has a lower initial cost of $800 for the controller but costs $30 per pod. Patients will need about 10 OmniPods a month compared with 10 infusion sets a month for traditional insulin pumps. Patients should determine whether this is an appropriate and worthwhile investment.

***Infusion Sets***

There are two main types of infusion sets: those with a stainless steel cannula, and those with a soft Teflon cannula. Stainless steel cannulas are only used if patients are allergic to the soft cannula or have large muscle mass and a low percentage of body fat. The stainless steel cannulas are durable and will not kink, but they cause more discomfort than the soft cannula and require site changes every 24–48 hours. Although more comfortable to wear, the flexibility of the soft Teflon cannula may lead to kinking and interruption of insulin delivery.

Patients can manually insert the infusion sets or can use a spring-loaded insertion device that pushes the infusion set rapidly into the skin. Patients who do not like needles or who have arthritis may prefer this method. Most spring-loaded devices do not allow the patient to control the angle or depth of insertion. Manually placing the infusion set will allow the patient to control the insertion speed and direction of the needle. This process may feel less painful; however, some patients may prefer the spring-loaded insertion devices.

Patients can select straight infusion sets that are set at 90° or other infusion sets placed at an angle of 20°–45°. It is beneficial to allow patients to try different infusion sets and let them select the most comfortable one. Although most infusion sets will not come loose with normal tugging on the tubing, some patients find an infusion set with an angled, longer cannula will hold in place better during extreme activity. There are few data to support one approach over another. Patients also need to select tubing length; some patients prefer short tubing that does not get in the way, whereas others prefer longer tubing so they can place their pump on a bathroom counter while getting ready.

Site choices for CSII insertion include the buttocks, abdomen, outer thighs, back of the arms, and hips. Sites on the thigh and the arm have lower insulin absorption rates than the abdomen but can be used as long as patients do not exercise excessively. In children, the buttocks are often the preferred insertion site to prevent the child from pulling out the infusion set. When changing infusion sites, the previous area of administration should be avoided by about 2 inches, and patients should

wait 7–10 days before using that site again. If BG concentrations are trending upward and insulin boluses are not correcting the BG concentration, the patient should remove the infusion set and place a new one in a different area of the body.

***Disadvantages of CSII***

Before using a CSII pump, the patient or caregiver must be proficient at math calculations, have a good knowledge of DM, and be able to calculate the carbohydrate content of food accurately; this makes the CSII device a poor fit for some patients. In addition, patients are required to know their insulin sensitivity and insulin-to-carbohydrate ratios before initiating CSII therapy. These education requirements are time-consuming but vital to the correct use of CSII devices. In addition to the intense education and learning curve, it may take several months for the patient to become proficient in using the device.

Patients may also require more frequent BG concentration monitoring, usually three times/day or more. When patients start on an insulin pump, it is recommended they test the BG concentration up to 8–10 times/day, and that they continue to monitor it rigorously to sustain good control. Patients using an insulin pump should not be separated from the pump for more than 1 hour; should they require a separation, they should supplement with syringe injections of basal insulin until they can be reconnected.

When a pump fails to deliver insulin, it creates an increased risk of diabetic ketoacidosis in the unsuspecting. A disruption of insulin delivery may be caused by a blocked or kinked cannula, lack of insulin in the pump, or pump failure. Diabetic ketoacidosis can occur within 4–10 hours if an insulin pump fails. It is imperative for patients using an insulin pump to carry an emergency kit with syringes and traditional insulin such as neutral protamine Hagedorn insulin or regular insulin.

Other disadvantages of CSII include increased cost and weight gain. Often, more weight gain occurs with insulin pumps than with delivery through syringes because of enhanced insulin activity, improved glycemic control, and increased carbohydrate consumption. In addition, although patients who are slightly visually impaired may be able to use the CSII, patients with full vision loss are unable to use the equipment. As with all new technology, patients may become bored with the device and not use it to its full capacity.

***Inpatient Use of CSII***

Several studies have shown that CSII can be safely continued in patients admitted to the hospital if a protocol exists to determine whether the patient is a good candidate for self-management during the hospitalization. Patients who are under suicide precautions or otherwise incompetent at the time of admission should not be considered candidates for continuation of CSII. A trial assessing hospitalized patients who were allowed to continue CSII showed similar glycemic control and less risk of hypoglycemia compared with hospitalized patients receiving standard treatment. Most hospital staff are relatively unfamiliar with insulin pumps; however, education of hospital personnel can help patients safely continue their CSII during admission. For patients admitted in critical condition, fewer data are available to show the benefit of CSII in the inpatient setting.

During critical hospital admissions, rapid reductions in hyperglycemia are similar between continuous intravenous regular insulin infusion and CSII in hospitalized patients with both type 1 and type 2 DM. Recent controversy exists regarding how to manage tightly controlled BG concentration in the inpatient setting. Current recommendations are as follows. (1) Critically ill patients should be initiated on insulin treatment when BG values are 180 mg/dL or greater with a target of 140–180 mg/dL. (2) Non-critically ill patients treated with insulin should have a premeal BG target of less than 140 mg/dL and a random target of less than 180 mg/dL. Several studies have shown improved outcomes with decreases in hyperglycemia; however, recent trials examining the achievement of normal BG concentrations have not shown improvements in mortality and may show an increase in mortality because of severe hypoglycemia. However, it appears that CSII use by protocol in an inpatient setting is safe and favorable. Nevertheless, more research is needed to assess whether CSII is superior to continuous intravenous regular insulin infusion.

***Delivering Boluses/Bolus Calculator***

Bolus calculators help patients determine their insulin bolus dose when using a CSII. Patients are also required to know their insulin sensitivity and insulin-to-carbohydrate ratios before initiating CSII therapy. Bolus calculator Web sites such as *www.diabetesforums.com/forum/converters/bolus/setup.php* and *www.perinatology.com/calculators/insulinpump.htm* enable patients to enter their insulin sensitivity, insulin-to-carbohydrate ratios, BG concentration, and the number of carbohydrates consumed; the site then calculates their bolus insulin dose. Bolus calculators are available in all the insulin pump devices listed in Table 1-1. These calculators allow patients to check their BG, calculate the quantity of carbohydrates consumed, and manually enter these values in the remote or the insulin pump directly. Some BG monitors will send the results to the insulin pump by infrared transmission. This process minimizes the number of buttons the patient must push. The insulin pumps prompt the patient for confirmation before delivering the new bolus dose of insulin.

Several different types of boluses (e.g., standard, dual wave, square wave) can be delivered by CSII pumps. A standard bolus of insulin by CSII delivers the desired

dose within several seconds of activation. If a standard bolus of insulin is delivered when the patient consumes a low-glycemic-index food, hypoglycemia may ensue before the glucose from the food is systemically available. The patient who plans to consume a certain amount of carbohydrates can deliver an insulin bolus using the individualized insulin-to-carbohydrate ratio. For example, the patient with a BG reading of 180 mg/dL and a correction goal of 100 mg/dL with a insulin sensitivity factor of 1:40 would need 2 additional units to "correct" BG concentration.

Dual- and square-wave delivery of insulin boluses from the insulin pump mimics first- and second-phase insulin secretion. In dual-wave delivery, the insulin pump releases a self-determined percentage of the insulin bolus immediately (i.e., in seconds) and then releases the remainder of the bolus dose over a specific period. In square-wave delivery, the bolus dose is released consistently over 30 minutes–3 hours compared with the standard bolus via insulin pump is released over seconds. Some CSII pumps combine dual-wave boluses with square-wave delivery. The square- and dual-wave boluses assist patients in eating high glycemic index foods such as pizza, where high-fat and high-carbohydrate content may delay systemic absorption of the glucose for several hours. For low-glycemic-index food, a dual-wave bolus would deliver 20% of the insulin dose immediately and the remainder over a 2-hour period, resulting in less hypoglycemia and lower postprandial BG concentration. These types of insulin boluses deliveries are also useful when patients are eating for a longer period (e.g., having appetizers for several hours) or for patients with gastroparesis.

### *Future Insulin Pumps*

There are some new devices and patents using microelectromechanical system (MEMS) technology. The insulin pump uses a MEMS to deliver insulin and is wirelessly controlled by an external remote. One of the pumps under investigation, the Insulin Nanopump is manufactured in Switzerland. Other insulin pumps under evaluation would act similarly to the pancreas and automatically deliver insulin in response to elevations in BG concentration; they would stop insulin infusion if the BG concentration fell below a certain value (e.g., less than 80 mg/dL). The MEMS technology appears to have features similar to other insulin pumps, such as low battery, system errors, and air detection. There are currently no human trials using this technology with insulin.

## Insulin Pen Devices

Insulin pen devices have several advantages (Table 1-2). Compared with traditional syringes and vials, insulin pen devices are more accurate. Using a vial of insulin and a syringe requires the patient to have good visual acuity, the ability to read measurements on the syringe, and the dexterity to withdraw the insulin from the vial. Insulin pen devices alleviate some patient error in insulin measurement and reduce the need for dexterity and visual acuity. One insulin pen device even has a built-in magnifying lens to aid patients with poor vision. Pen devices are more portable than syringes and vials and are favored by patients who would like to be more discreet with their injections. In addition, insulin pens allow accurate dosing from 1 unit and higher without the problems encountered with a traditional syringe (e.g., human error from poor visual acuity, air bubbles, less markings on larger syringes).

Insulin pen devices have some disadvantages as well. Some are extremely intuitive, requiring only a small amount of patient education; others are more complex and require intensive training. Their cost is higher than that of vials and syringes. In addition, most pen devices recommend that the pen be primed with 2 units of insulin before each use, which wastes insulin from the device. Insulin pen devices also take longer to deliver insulin than the plunger of a regular syringe. This delay requires patients to keep the insulin pen needle under their skin for 5–10 seconds after depressing the plunger. Many patients are uncomfortable maintaining the pen needle subcutaneously for this amount of time; they may remove the pen device too soon and fail to administer the full dose of insulin. In addition, insulin pens may only deliver a maximum of 36–80 units at a time; this is not beneficial for patients using more than 80 units per dose, who would need two or more injections to receive the entire dosage.

## Novel Insulin Delivery Technologies

### *Inhaled Insulin*

Advances in insulin delivery systems led to the availability of orally inhaled insulin, marketed in January 2006. The product was a dry powder form of insulin, which was pulverized to 1–3 microns in diameter to allow absorption in the alveoli of the lungs after inhalation. The product was withdrawn from the market in October 2007 because of poor sales, lack of managed care formulary acceptance, and interference with pulmonary function in some patients.

Another inhaled insulin delivery system currently being investigated is Afrezza, an ultra–rapid-acting mealtime insulin that uses Technosphere technology. This technology employs organic, pH-sensitive molecules that organize into small particles in acidic environments. Insulin is combined with Technosphere material, which is then dried to form a powder. An oral inhaler slightly larger than the palm of the hand delivers the insulin. This product is currently under evaluation in phase III trials. The trials have shown non-inferiority compared with the other rapid-acting insulins. However, patients with type 1 DM and some patients with type 2 DM will still need to use injectable basal insulin.

**Table 1-2.** Comparison of Commercially Available Insulin Pen Devices

| Insulin Pen by Maker | Insulin Compatibility | Pen Needle Compatibility | Dose Range (Units) | Measuring Increment (Units) | Notes |
|---|---|---|---|---|---|
| Lilly | | | | | |
| Humalog Pen | Prefilled[a]<br>Contains 3 mL (300 units) of insulin lispro | BD pen needles | 1–60 | 1 | Magnified dosing window<br>Audible dosing clicks<br>Dose can be adjusted backward and forward without wasting insulin |
| Humalog Mix 50/50 Pen | Prefilled[a]<br>Contains 3 mL (300 units) of 50% insulin lispro protamine suspension and 50% insulin lispro | BD pen needles | 1–60 | 1 | Magnified dosing window<br>Audible dosing clicks<br>Dose can be adjusted backward and forward without wasting insulin |
| Humalog Mix 75/25 Pen | Prefilled[a]<br>Contains 3 mL (300 units) of 75% insulin lispro protamine suspension and 25% insulin lispro | BD pen needles | 1–60 | 1 | Magnified dosing window<br>Audible dosing clicks<br>Dose can be adjusted backward and forward without wasting insulin |
| Humalog KwikPen | Prefilled[a]<br>Contains 3 mL (300 units) of insulin lispro | BD pen needles | 1–60 | 1 | Magnified dosing window<br>Audible dosing clicks<br>Dose can be adjusted backward and forward without wasting insulin |
| Humalog Mix 50/50 KwikPen | Prefilled[a]<br>Contains 3 mL (300 units) of 50% insulin lispro protamine suspension and 50% insulin lispro | BD pen needles | 1–60 | 1 | Magnified dosing window<br>Audible dosing clicks<br>Dose can be adjusted backward and forward without wasting insulin |
| Humalog Mix 75/25 KwikPen | Prefilled[a]<br>Contains 3 mL (300 units) of 75% insulin lispro protamine suspension and 25% insulin lispro | BD pen needles | 1–60 | 1 | Magnified dosing window<br>Audible dosing clicks<br>Dose can be adjusted backward and forward without wasting insulin |
| HumaPen Luxura HD | Reusable[b]<br>3 mL-Humalog insulin cartridges by Lilly | BD pen needles | 1–30 | 0.5 (starting at a minimum of 1) | Dose can be adjusted backward and forward without wasting insulin |
| HumaPen Memoir | Reusable[b]<br>3-mL Humalog insulin cartridges by Lilly | BD pen needles | 1–60 | 1 | Records the date, time, and amount of previous 16 insulin doses<br>Dose can be adjusted backward and forward without wasting insulin |
| Humulin N Pen | Prefilled[a]<br>Contains 3 mL (300 units) of NPH human insulin isophane suspension | BD pen needles | 1–60 | 1 | Magnified dosing window<br>Audible dosing clicks<br>Dose can be adjusted backward and forward without wasting insulin |
| Humulin 70/30 Pen | Prefilled[a]<br>Contains 3 mL (300 units) of 70% human insulin isophane suspension and 50% human insulin | BD pen needles | 1–60 | 1 | Magnified dosing window<br>Audible dosing clicks<br>Dose can be adjusted backward and forward without wasting insulin |
| Novo Nordisk | | | | | |
| Levemir FlexPen | Prefilled[a]<br>Contains 3 mL (300 units) of insulin detemir | NovoFine 30 or 32G Tip pen needles | 1–60 | 1 | Large dialing window<br>Audible dosing clicks<br>Dose can be adjusted backward and forward without wasting insulin |
| NovoLog FlexPen | Prefilled[a]<br>Contains 3 mL (300 units) of insulin aspart | NovoFine 30 or 32G Tip pen needles | 1–60 | 1 | Large dialing window<br>Audible dosing clicks<br>Dose can be adjusted backward and forward without wasting insulin |

*(continued)*

**Table 1-2.** Comparison of Commercially Available Insulin Pen Devices

| Insulin Pen by Maker | Insulin Compatibility | Pen Needle Compatibility | Dose Range (Units) | Measuring Increment (Units) | Notes |
|---|---|---|---|---|---|
| NovoLog Mix 70/30 FlexPen | Prefilled[a]<br>Contains 3 mL (300 units) of 70% insulin aspart protamine suspension and 30% insulin aspart | NovoFine 30 or 32G Tip pen needles | 1–60 | 1 | Large dialing window<br>Audible dosing clicks<br>Dose can be adjusted backward and forward without wasting insulin |
| NovoPen 3 | Reusable[b]<br>3-mL PenFill insulin cartridges by Novo Nordisk | NovoFine pen needles | 2–70 | 1 | Simple dial dose selector<br>Correctable dose feature<br>Compatible with the PenMate automatic needle-insertion device |
| NovoPen Junior | Reusable[b]<br>3-mL PenFill insulin cartridges by Novo Nordisk | NovoFine pen needles | 1–35 | 0.5 | Compatible with the PenMate automatic needle-insertion device |
| Owen Mumford | | | | | |
| Autopen Classic | Reusable[b]<br>For use with 3-mL insulin cartridges by Lilly and Wockhardt UK | Compatible with most pen needles | Model AN3810: 1–21<br>Model AN3800: 2–42 | Model AN3810: 1<br>Model AN3800: 2 | Side release button for insulin delivery |
| Autopen 24 | Reusable[b]<br>For use with 3-mL insulin cartridges by sanofi-aventis | Compatible with most pen needles | Model AN3810: 1–21<br>Model AN3800: 2–42 | Model AN3810: 1<br>Model AN3800: 2 | Side release button for insulin delivery |
| sanofi-aventis | | | | | |
| Apidra SoloSTAR | Prefilled[a]<br>Contains 3 mL (300 units) of insulin glulisine | BD Ultra-Fine pen needles | 1–80 | 1 | Dose cannot be dialed past the number of units remaining in the pen |
| Lantus SoloSTAR | Prefilled[a]<br>Contains 3 mL (300 units) of insulin glargine | BD Ultra-Fine pen needles | 1–80 | 1 | Dose cannot be dialed past the number of units remaining in the pen |
| OptiClik | Reusable[b]<br>Lantus 3 mL insulin cartridges<br>OR<br>Apidra 3 mL insulin cartridges | BD or Ypsomed pen needles | 1–80 | 1 | Digital dose displays the number of units of insulin to be used<br>Dosage knob locks into place when the entire insulin dose has been delivered<br>Compatible with screw-on and push-on (click) pen needles |

[a]Disposable single use.
[b]Replaceable cartridge.
NPH = neutral protamine Hagedorn.
Modified with permission from Monthly Prescribing Reference, May 19, 2010. Available at *www.empr.com/insulin-pen-devices/article/170526/*. Accessed December 1, 2010.

Another inhaled insulin product, AIR inhaled insulin, saw development halted in 2008 because of uncertainties in the regulatory market and other products that were already available. The product was not abandoned because of safety concerns.

***Buccal Insulin***

A buccal insulin product called Oral-Lyn has been approved for use in several countries and is in phase III trials in the United States. This product uses a RapidMist inhaler device to deliver small particles of a recombinant oral insulin spray into the buccal cavity. The insulin is similar to the rapid-acting insulin analogs (insulin lispro, insulin glulisine, and insulin aspart). Like injectable insulin, buccal insulin spray is dissolved in a buffer with a neutral pH. The non-chlorofluorocarbon spray delivers about 10 units of insulin but is equivalent to only 1 unit of actual insulin secondary to the absorption rate of 10%. Therefore, if a patient needed 10 units of insulin, he/she would have to administer 10 sprays of buccal insulin.

The spray includes inactive ingredients that enhance absorption by stabilizers. Absorption enhancers form microfine micelles that surround and protect the insulin during administration. Buccal insulin spray is absorbed in the oropharyngeal cavity within 5–10 minutes after administration, and the product is not delivered to the lung tissue. Oral insulin has been compared with regular insulin, not the rapid-acting insulin analogs in the currently available literature. Comparing oral insulin with subcutaneous regular insulin shows that oral insulin is absorbed more rapidly (32 minutes vs. 78 minutes) and has a shorter peak (44 minutes vs. 159 minutes) and shorter duration of action (85 minutes vs. 319 minutes). The shorter onset and peak may be beneficial in treating postprandial BG concentration elevations; however, it could cause hypoglycemia in patients with gastroparesis or after the consumption of a high-fat meal (which could cause delayed absorption of carbohydrate). In addition, if patients need 20 units of insulin, they will have to use 20 sprays of the inhaler, which may be time-consuming. Some potential benefits to using oral insulin spray include improved adherence compared with subcutaneous administration, lack of pain of during administration, and use in patients who fear injections.

***Air Pressure/Jet-Injected Insulin Delivery***

Needle-free delivery of insulin across the skin was invented more than 50 years ago. However, because of pain and bruising at the air injection site, these devices have not been used globally. Recently, nanoliter-volume pulsed microjets have allowed insulin to be delivered at a more shallow depth and possibly with less discomfort.

Current devices on the market facilitate the deep penetration of insulin by air injection. The Medi-Jector VISION Needle-Free Syringe has three different syringe sizes for penetration depending on the thinness or toughness of the skin. Patients purchase the needle-free syringe and the spike adapters to attach to the insulin vial to withdraw the insulin. Some patients feel that needle-free injections hurt less than traditional syringes; others feel that needle-free injections are more painful. Some patients may have bruising at the injection site.

Benefits of needle-free injections include eliminating sharps disposal, increasing the convenience of injection, and avoiding the use of needles in patients who are fearful. Jet-injected insulin delivery is only recommended in patients using between 2 units and 50 units of insulin; the patient requiring more insulin will have to administer additional needle-free injections or use traditional syringes.

## Blood Glucose Concentration Monitoring

**BG Monitors**

Available BG monitoring devices include traditional systems that use whole BG, ultrasonic BG monitoring, and continuous glucose monitoring systems (CGMSs). Traditional whole BG monitoring systems are the most common machines available for checking BG concentrations at home and in the inpatient setting. These devices are constantly undergoing change and improvement.

Several factors determine which BG monitor a patient should use. Diabetes educators, pharmacists, and physicians often prefer certain devices and may choose the monitor for the patient. However, providers should explain the features of each monitor and involve patients in the process of choosing the monitor that best fits their needs. Features that vary among monitors include alternative-site testing, increased memory storage of BG readings, accompanying BG software evaluation tools (either for free or for purchase), intuitiveness of use, the way BG readings are downloaded from the monitor and evaluated, and the cost of the monitor and test strips. Monitors with coding requirements are more difficult to use than those that do not require coding. Usually, the cost and third-party coverage of BG monitoring supplies ultimately drive the choice of meter.

Using BG monitors in patients with type 2 DM has shown only small improvements in BG concentrations; therefore, patients should be in the preparation or action stage of behavior change before using a monitor. For example, if a patient determines that his/her BG concentration rises when a certain food or amount of food is eaten, the optimal situation is for the patient to make adjustments to the meal by reducing the meal portion or substituting other, lower-carbohydrate choices the next time that situation presents itself. If patients are not

willing to make lifestyle adjustments, BG concentration monitoring becomes costly and ineffective.

**Accuracy**

The accuracy of BG measurements fluctuate among monitors. International Organization for Standardization requirements are to be within 20% of laboratory standards 95% of the time; however, these standards are for BG concentrations of 70–80 mg/dL, and as BG values rise, the accuracy of the measurement diminishes. Many factors affect the accuracy of monitors, such as storage of test strips, size of the blood sample, where the blood sample was obtained, calibration errors, outside temperature, cleanliness of the monitor, high concentrations of ascorbic acid in the bloodstream, and quality of the blood sample. Patients and providers must be aware of the discrepancy of actual plasma BG concentrations and whole blood home BG meters.

Pharmacists often recommend changes to insulin or drugs on the basis of BG readings recorded by patients. It is important to make sure that patients are using the same BG meter or are at least consistent in reporting BG measurements if the measurements are from a different BG monitor. Providers should think of these readings as ranges rather than as precise BG concentrations. It is much safer to make adjustments to insulin or other diabetes drugs with several BG data points than with only a few glimpses of BG readings.

One issue with inpatient use of BG monitors pertains to their accuracy and to the making of therapeutic changes from these values. Hypoglycemic readings of 70 mg/dL or less can be accurate with most BG monitors, whether capillary whole blood or venous whole blood samples are used, but at the higher BG concentration, the variability increases. The median relative absolute difference in meter accuracy in the inpatient setting is about 5% and is close to 100% accuracy in detecting hypoglycemia.

**Novel Whole BG Monitors**

Every year, manufacturers release new BG monitors with new features. Manufacturers usually expand on the previous year's model and try to make improvements. The Bayer Contour meter was the basis for the new Contour USB (Universal Serial Bus) meter. It uses the Contour BG meter test strips and has a USB port that can be connected to a personal computer to download BG readings. The Contour USB is compatible with standard operating systems such as Windows 7, Windows XP, Vista, and Mac OS. There are also glucometer and cell phone combinations, such as the GlucoPhone. Currently, GlucoPhone is only available with one phone model from LG. The battery cover on the back of the phone is replaced by a glucometer. Patients can check BG concentration, transmit the results to a Web site database, and send them to a caregiver by text message. The patient may also keep track of and retrieve the BG results at the MyGlucoSite Web site and send the results to his/her health care provider.

In addition, there is an attachment (dongle) for the iPhone application for BG monitors to connect by a wireless or wired connection. The iPhone application allows certain BG monitors to be compatible with the phone and download BG readings to the application or software. Patients can also record food intake and other vital information in the application. The DIDGET monitor from Bayer uses Contour monitor technology and directly connects to the Nintendo DS or Nintendo DS lite gaming systems. The BG testing is performed while connected to the gaming system. Points awarded for good testing habits allow participants to attain new levels on the game or power up alternative games.

Noninvasive BG monitors that use ultrasound technology are currently being investigated in clinical trials. These include the GlucoTrack and Glucoband. The GlucoTrack, which clips onto the ear lobe for measurement, is currently in phase I and II trials. The Glucoband is an ultrasonic wristwatch that may be available in the United States in 2011. Another noninvasive method of BG testing is near-infrared optical spectroscopy. This technology uses multivariate analysis and software algorithms to measure BG when the monitor is near the conjunctiva of the eye. It is unknown when this type of technology will be available in the United States.

A few BG monitors allow visually impaired patients to become more independent in DM self-care behaviors. However, only one monitor, the Prodigy meter, is available in the United States at the time of this writing. The Prodigy monitor requires no coding, has a human-recorded voice that states the current BG reading as well as 14-day and 30-day averages, uses notched test strips, and discards the test strip after use. A talking meter called the SensoCard Plus is marketed in the UK but is currently unavailable in the United States. It is similar to the Prodigy BG monitor but requires coding by a code card strip inserted in the meter.

Alternative BG site testing in the forearms and thighs is an option for patients who are weary of lancing their fingertips. However, there may be large discrepancies when BG concentrations are changing rapidly, such as after meals or during hypoglycemic episodes. For either situation, patients should use a fingertip to check BG. Alternative-site testing has not shown improvements in A1C values or accuracy compared with fingertip testing but may improve adherence in patients with an aversion to fingertip testing.

**Continuous Glucose Monitoring Systems**

Continuous glucose monitoring systems are used mainly in patients with type 1 DM; however, CGMSs have been used in patients with type 2 DM treated with diet and exercise. Continuous glucose monitoring systems are

well tolerated and acceptable to most patients. Patients with type 1 and type 2 DM can visually see how food and activity affects their BG concentrations. Patients calibrate their CGMS unit by testing their BG concentrations. Once the CGMS unit is calibrated and working, the patient can enter "events" such as the amount of insulin used, the amount of carbohydrates consumed, exercise or other activity, and other BG measurements.

Continuous glucose monitoring sensors are inserted into the subcutaneous tissue, usually on the abdomen or upper buttocks, where they measure BG concentrations in the interstitial fluid and/or send the value to the insulin pump. Most CGMS devices used today are patient owned and used daily or several times a week. Before CGMS devices were home monitoring devices, they were office-based devices that providers would lend to patients. Patients would calibrate the device each day and record events (e.g., food consumed, exercise, other daily occurrences) and then bring the monitor back to have the data uploaded at the office. The provider would see graphic glycemic changes in their BG concentrations and make changes to their insulin therapy or daily routine accordingly.

Currently, three home CGMS devices are available in the United States: the Guardian REAL-Time Continuous Monitor, the Dexcom SEVEN PLUS, and the FreeStyle Navigator. These sensors can be worn for 3, 7, and 5 days, respectively. To function, they all require calibration readings from whole BG monitors. All CGMS devices report specific BG values and provide graphic trends of exercise, food, insulin, and drugs; they also alert the patient during episodes of hypoglycemia or hyperglycemia. The Guardian REAL-Time CGMS device measures BG concentrations every 5 minutes. Patients need to remember, however, that there is a small delay in measuring BG response of about 10–24 minutes (average = 15 minutes) compared with serum plasma BG concentrations. This is secondary to taking the measurement within the interstitial tissue.

The largest impact of CGMSs in overall DM management is in reducing severe or problematic hypoglycemia. In addition, CGMSs estimate insulin requirements for patients taking drugs that may affect BG concentrations, such as prednisone. Patients are often fearful of hypoglycemia and sometimes maintain BG concentrations higher than glycemic targets to avoid the risk of hypoglycemia. Continuous glucose monitoring systems will alert the patient if the BG concentration is rising or falling by a certain amount, allowing patients to prevent hypoglycemic and hyperglycemic excursions.

The literature contains some controversy regarding whether CGMS devices reduce A1C values compared with intermittent whole blood fingerstick testing. A meta-analysis of five CGMS studies showed no real benefit on A1C reduction compared with intermittent whole blood fingerstick testing; however, there was an important reduction in nocturnal hypoglycemia. The use of CGMS devices in children with type 1 DM was found to reduce the baseline A1C average in 13 weeks.

An office-based CGMS device, such as the CGMS *i*Pro recorder, can be used by patients for a few days and then returned to the health care provider for review. The health care provider can then identify potential problems, such as inadequate basal or bolus insulin doses or foods that cause high BG excursions, which are not identified by standard BG monitors. Providers can be reimbursed by Medicare, and many private insurance companies cover this service in the United States using Current Procedural Terminology (i.e., CPT) codes 95250 and 95251.

Continuous glucose monitoring systems have been used successfully in hospitalized patients to prevent hypoglycemia. In critically ill patients, the patient care staff can use CGMSs to maintain and improve glycemic control and prevent hypoglycemia. In addition, CGMSs may be useful in maintaining glycemic control in patients admitted to intensive care units who are at risk of hyperglycemia. Continuous glucose monitoring systems also estimate BG excursions in very low-birthweight infants. Finally, CGMSs may reduce the nursing workload by minimizing illness-related severe hypoglycemia or hyperglycemia.

***Glucometer and Web Site Interfaces***

Each of the BG monitor manufacturers markets software that can accompany the monitors (Table 1-3). Patients can upload BG readings from their glucometer and make decisions about their management of DM or share the information with their health care provider. The MyGlucoHealth monitor and wireless device sends BG information wirelessly by Bluetooth to personal computers, mobile phones, or health care providers. This is advantageous when patients try to self-manage their BG readings without their providers and delay health care. Possible disadvantages include improper access to medical data; for example, the Glucofacts Deluxe program receives BG readings from a USB device, and personal BG readings could become intercepted.

Several of the CSII pumps interface with BG monitors. The monitors send the information wirelessly to the CSII pump to make it easier for the patient to choose a bolus dose of insulin. The MiniMed Paradigm and Real-Time CGMS device are currently the only compatible CSII pump and CGMS device. In young children, the use of real-time CGMS devices in conjunction with CSII has allowed caregivers to have fewer episodes and less anxiety regarding hypoglycemia.

**Lancet Devices**

One of the largest barriers to testing BG concentration is the pain incurred from during fingerstick measurements. Alternative-site testing is an option for

patients seeking less painful testing methods. Another option is to change to a different device because some (e.g., OneTouch) are considered less painful than others (e.g., Accu-Chek Compact Softclix lancet system). Third-party payers do not cover most lancet devices.

Another barrier to using lancet devices may be patient dexterity. Most lancets and lancet devices are small and have intricate pieces, and patients with arthritis or dexterity issues may have difficulty using them. One lancing device, MultiClix, has a drum with six preloaded lancets; this may benefit patients with dexterity problems, who find it difficult to pick up the small lancets. The Lasette device (not currently available) uses laser technology to obtain a whole blood sample. Patients 5 years and older insert a finger in the device, and the laser vaporizes a tiny area of skin, allowing release of the blood sample. The Lasette monitor was priced at $495 and still required test strips; therefore, the total cost was considerably higher than the traditional lancet device and disposable lancets.

**Future Technologies**

The search continues for innovative technologies that address the limitations of current BG monitoring. Several companies are investigating contact lenses that monitor BG concentrations. Another company has created a sensor that can be placed in the interstitial fluid under the conjunctiva of the eye by an ophthalmologist and remain in place for 1 year. The patient holds a small photometer in front of the eye to measure the florescence signal and obtain BG readings several times a day. Many companies are developing devices similar to binoculars that determine BG by shining infrared beams into the eyes. Yet another device in development would check BG from measurements in the ear canal, similar to an ear thermometer.

Most of these technologies are still under development with no scheduled release date. One of the optical sensors has six patents being researched, with the manufacturer planning to send the U.S. Food and Drug Administration application in 2010.

**Hemoglobin A1C Testing**

Several A1C testing kits are available for home use. Patients may consider using a self-care A1C kit if they pay cash for their blood work or if they are eager to see the outcomes of recent drug or lifestyle changes. Some kits require the patient to prick their finger to obtain a blood sample, which is applied to a specified spot on the testing card. The card is then sent to a laboratory, and the results are mailed back to the patient. Another A1C testing monitor is available over the counter for home monitoring. Called the A1CNow (home use) and A1CNow+ (provider use), it delivers the A1C information to the patient within 5 minutes. Although the instructions are slightly more complex than those with BG home monitoring, most patients will find the device easy to use, convenient, and more economical than a laboratory measurement. The cost is about $25–$30 for two test kit cartridges.

**Fructosamine Testing**

Fructosamine is an indicator of BG control for about 10–14 days. The normal range for fructosamine is 174–286 micromoles/L, which corresponds to an A1C of 4% to 6%. A fructosamine concentration of 213 micromoles/L is equivalent to an A1C of 5%, and a fructosamine of 363 micromoles/L is about equal to an A1C of 9%. A formula to estimate this difference is fructosamine = $(A1C - 1.61) \times 58.82$.

Patients with anemia, a hemoglobinopathy, iron deficiency, hemolytic anemia, sickle cell anemia, lack of a spleen, recent blood loss, or pregnancy will have inaccurate A1C readings. In general, anemias that cause a reduction in red blood cells will cause a falsely low A1C, whereas patients with a higher number of red blood cells than normal (as in patients who lack a spleen) may have a falsely elevated A1C. Patients with iron-deficiency anemia will have higher A1C readings until their anemia has been treated. In these patients, fructosamine testing may be beneficial, however, the cost-benefit should be evaluated.

**Table 1-3.** Available Glucometer and Insulin Pump Web Site Interfaces

| Glucometer or Insulin Pump | Interfaces |
|---|---|
| Bayer Glucose Monitors | Glucofacts Deluxe |
| OneTouch Lifescan Glucose Monitors | OneTouch Diabetes Software |
| FreeStyle Glucose Monitors | CoPilot |
| Accu-Chek Glucose Monitors | Accu-Chek SmartPix |
| | Accu-Chek Diabetes 360 degree software |
| MyGlucoHealth Glucose Monitors | MyGlucoHealth.net |
| MiniMed Insulin Pump | REAL-Time CGMS, OneTouch UltraLink BG meter |

When home fructosamine testing was compared with usual care of daily intermittent BG testing, the A1C results did not vary significantly at 1 year; however, target A1C values were achieved sooner in the group using home fructosamine testing at 3 months compared with patients using traditional BG monitors. Some providers encourage fructosamine testing to reduce the time to reach target BG concentrations. When elevated fructosamine concentrations require patients to contact their health care provider to make drug changes, the laboratory test becomes quite useful.

Fructosamine home testing kits were marketed several years ago until the company that manufactured them was sold. At that time, concerns regarding falsely elevated test results surfaced, and the product was discontinued. The In Charge meter cost about $80 and used 15 microliters of blood. The cost of the test strips was $37 for a pack of BG test strips and four fructosamine strips. It is unclear whether fructosamine home monitoring will become available again.

## Technology Treatments

### Insulin-like Growth Factor 1

Insulin-like growth factor 1 is a polypeptide hormone structurally related to insulin that has several positive effects in adult patients with DM. Insulin-like growth factor has a synergistic effect on BG concentrations with endogenously and exogenously administered insulin. However, it may cause less hypoglycemia, improve insulin sensitivity, and have a neutral effect on body weight.

Several clinical trials have studied recombinant insulin-like growth factor 1 for a variety of conditions, including type 1 and type 2 DM. Insulin-like growth factor 1 lowered A1C and reduced insulin requirements. However, research with this hormone in relatively healthy patients with DM was discontinued because it was found to increase the risk of developing diabetic retinopathy.

### Invasive Technology

Allogenic human islet cell transplantation is at the phase I/phase II developmental stage in the United States. Only nine sites are approved to perform these procedures in patients with DM. The inclusion criteria for transplantation are stringent, such as hypoglycemia unawareness with documented episode of cognitive dysfunction, type 1 DM for more than 5 years, long-term DM complications, and unstable diabetes control with BG greater than 200 mg/dL and less than 80 mg/dL.

Human islet cell transplantation is delivered by three separate infusions into a branch of the portal vein. Most patients receive a local anesthetic and remain awake while the radiologist guides the catheter into the portal vein; however, some patients may require general anesthesia. After the transplant, euglycemia without the use of exogenous insulin may not be achieved long term. Most patients will require exogenous insulin within 4 years of islet cell transplantation. In addition, patients require pretreatment with immunosuppressants such as antithymocyte globulin, sirolimus, and tacrolimus, and must remain on sirolimus and tacrolimus after the transplant. Adverse effects of these drugs are of concern, especially the nephrotoxic effects. Patients with preexisting nephropathy are at higher risk of nephrotoxicity.

A closed-loop artificial pancreas may be the next advance in insulin delivery systems. This system uses three different components: a source of insulin delivery, a CGMS, and a computer algorithm that adjusts insulin delivery (i.e., the closed loop). Ideally, the algorithm would anticipate changes in BG concentrations and food intake and adjust insulin release to compensate for these variables. A barrier to the effective medical management of patients with type 1 DM is the risk of nocturnal hypoglycemia. Closed-loop systems decrease both nocturnal hypoglycemia and hyperglycemia. Expected values of BG are tested with various feedback control algorithms and estimates of meal-sized simulators to reproduce natural insulin consumption for the closed-loop system. As technology with prediction modeling and CGMSs advances, development of the closed-loop artificial pancreas will continue to evolve.

### Predictive Modeling

Predictive modeling of BG concentrations would assist in reducing the incidence of hypoglycemia and hyperglycemia. There is a delay in detecting hypoglycemic and hyperglycemic excursions with the current technology. Some computer programs have begun to examine patient-specific recursive linear models that use the patient's own CGMS information to predict hypoglycemia and hyperglycemia. These models could be installed in closed-loop systems (the computer makes the decision) or open-looped systems (a human is in the loop and makes the decision) and be set as alarms that would warn patients of impending changes earlier than standard CGMS devices.

### Software Technology

Web-based tools can educate providers and patients on how to manage and improve DM care. When compared with self-management educational group programs, outcomes such as behavior change, A1C improvement, and diabetes education improved overall with the Web-based educational programs. Important clinical markers in DM such as systolic and diastolic blood pressure and A1C lowering were better in patients enrolled in an individualized electronic decision-support and reminder Web-based program than in those receiving usual care.

Patients were reminded to obtain laboratory tests such as A1C, take or refill medications, and schedule upcoming physician visits.

Some Web-based technology programs assess patients for the presence of risk factors and place them in categories on this basis. Studies are ongoing to investigate the effectiveness of Web-based insulin titration and address issues such as reducing hypoglycemia, improving A1C values, and increasing diabetes self-efficacy. One Web site, *www.dlife.com*, incorporates videos, the American Association of Diabetes Educators 7 Self-Care Behaviors, diabetes recipes, a link to the dLife television program and videos on CNBC, and other resources into an inclusive diabetes community of patients and caregivers. There are also insulin management software programs that help patients lower A1C and increase motivation to perform more BG testing if they have type 1 DM.

Companies are beginning to incorporate diabetes management software into mobile technology. Several mobile phone applications use diabetes software or equipment to transfer diabetes and patient information to parents, caregivers, and health care providers. For parents of children with type 1 and type 2 DM, mobile devices facilitate communication with their child's health care provider. Children can send their parents BG readings, and the parents can forward this information to the provider.

Although mobile phone technologies that deliver tailored diabetes messages to patients may not improve A1C values, they may improve DM self-efficacy. Self-efficacy is based on social cognitive theory, which proposes that a patient's confidence in his/her ability to perform certain health behaviors will help determine which behaviors he/she will perform. An application for the iPhone called Diabetes Pilot has a food database, software to enter BG readings, insulin delivery assistance with insulin-to-carbohydrate ratios, and guidelines for insulin adjustments. Another application for the iPhone or iTouch is the WaveSense Diabetes Manager, which has features such as BG data graphing, statistical analysis of BG readings, integrated food and BG logs, and medication data management. To gain widespread acceptance, mobile phone technologies must be easy to use, have reasonable fees for patients, and provide easy ways for patients to keep track of their drugs and insulin.

## Long-term Complications of DM and Treatment Technologies

### Gastroparesis Treatment

Gastroparesis, a condition of delayed gastric emptying, is commonly caused by DM. The vagus nerve controls the muscular movements of food through the digestive tract. As the vagus nerve is damaged, food transit through the digestive tract slows and patients may experience severe nausea and vomiting, epigastric pain, abdominal bloating, early satiety, weight loss, and loss of appetite. Prokinetic agents and antiemetics are often used to treat gastroparesis. Metoclopramide, a prokinetic agent, should not be used in the long term (greater than 12 weeks) because of an increased risk of tardive dyskinesia, depressive symptoms, and suicidal ideation. Several alternatives to these agents are now under investigation and may be helpful for patients who are unable to tolerate or who do not respond to prokinetic agents and antiemetics.

One investigational intervention is gastric electrical stimulation, which consists of an endoscopic procedure to implant two intramuscular leads and a neurostimulator into the lower gastric region (antrum). Gastric electrical stimulation is somewhat effective in reducing intractable nausea and vomiting in patients who are refractory to drug therapy, and may relieve other symptoms of gastroparesis as well. Botulinum toxin may reduce the symptoms of gastroparesis and decrease solid-phase gastric emptying time from an average of 339 minutes to 227 minutes after 1 week of treatment; however, its benefit has been less clear in randomized clinical trials, with some showing no difference in gastric emptying time after 1 month of treatment compared with placebo. However, the benefits of botulinum toxin may vary with the amount and number of doses. Combination therapy that includes botulinum toxin injections and gastric electrical stimulation is also under investigation.

### Telemedicine for DM Retinopathy Screening

Retinopathy screenings are recommended for all patients with DM. Patients with type 1 DM should be assessed within 3–5 years after diagnosis, and patients with type 2 DM should be assessed shortly after receiving the diagnosis and screened yearly thereafter. However, the average retinal screening rate in U.S. patients with type 1 and type 2 DM is around 51% to 78% depending on the geographic area. Patients living in rural areas, indigent patients, and uninsured populations often do not receive important preventive tests such as retinal screenings.

Telemedicine retinopathy screening programs use technicians, nurses, or other trained staff to take digital images of the patient's retina and send them to an ophthalmologist for evaluation. When the cost of telemedicine imaging is compared with a direct fundus examination, telemedicine appears to be more expensive. However, when patient costs for missed work hours and travel to appointments are added in, digital imaging becomes more convenient and cost-effective in certain settings (e.g., Veterans Administration, Indian Health Service).

### Monofilament/Sensory Testing

Patients with DM should receive annual screenings for peripheral neuropathy. Neuropathy evaluation may occur by monofilament testing (10 g), pinprick sensation, or vibration sensation (128-Hz tuning fork).

Traditionally, patients only undergo monofilament testing; however, the American Diabetes Association's Standards of Care for Diabetes now recommends that more than one method be used to detect peripheral neuropathy. Patients with decreased vibratory sensation and a normal monofilament test have an increased risk of developing foot ulcers. Monofilament testing may be replaced with the tuning fork to help determine the risk of diabetic foot ulcers. In addition, using more than one test for peripheral neuropathy increases the sensitivity for detecting peripheral neuropathy to more than 87%.

At-home foot screening tools and kits are sold to patients in a variety of forms. For example, one available kit includes a foot mirror, brush with handle, monofilament, snap-on brushes for bathing, and snap-on sponges for applying medications to the feet and toes. The home foot screening tool kits are a good recommendation for patients to encourage them to monitor their feet and perform self-care; however, most individual items can be purchased separately. Some patients benefit from the home screening kits because all the items are in one container, which may encourage them to follow the recommendations to provide self-care for their feet; however, it is not necessary for all patients to purchase these items.

### Maggot Therapy for Wound Healing

Maggot therapy has been used in patients with diabetic foot ulcers for surgical debridement since the 1930s and has improved wound healing of diabetic foot ulcers in patients who are not good surgical candidates or who refuse surgery. Patients with diabetic foot ulcers infected with *Pseudomonas aeruginosa* may require antipseudomonal treatment in addition to maggot therapy. The application of the maggots takes about 15–20 minutes, is inexpensive compared with surgery, and can be performed by non-surgeons.

A company that specializes in distributing maggots (e.g., Monarch Labs) ships the maggots in a vial. The maggots may be at various points in their life cycle when they arrive. If the maggots are in the egg stage, the vial can be warmed to speed up the development process. However, if the maggots appear to be overly active, refrigerating the vial for 30 minutes can slow them down. The maggot application should be loosely covered with gauze to allow air to reach the maggots. The gauze-covering top should be changed every 6–8 hours, and the entire dressing kept in place for 48 hours.

## Telemedicine

### Decision-Support Software

Several decision-support software programs for chronic illnesses are incorporated in electronic medical records systems. Information is entered in the software program, and tailored recommendations are made. However, health care providers tend to underuse decision-support software within the electronic medical record. This may be a result of the time constraints placed on the provider and the complexity of the software.

One example of decision-support software for patients with DM is determining cardiovascular risk, often a difficult task in clinical practice. An Internet-based comprehensive risk program, the JADE risk engine (*www.jade.adf.org*), has been validated for this purpose. The JADE system categorizes patients into one of four risk levels: (1) very high risk (i.e., overt renal-cardiovascular complications); (2) high risk (i.e., three or more positive clinical measures); (3) medium risk (i.e., two or more positive clinical measures and/or estimated glomerular filtration rate of 60–90 mL/minute/1.73m$^2$); and (4) low risk (i.e., one or fewer positive clinical measures and normal estimated glomerular filtration rate). The JADE program bases the risk assessment on four different clinical measures: cardiovascular-renal complications (e.g., heart failure, cardiovascular disease, stroke, coronary vascular disease); conventional risk factors (e.g., smoking status, blood pressure, body mass index, foot care changes); Hong Kong Diabetes Registry risk scores based on cardiorenal complications; and category of kidney function based on estimated glomerular filtration rate. After the patient is placed into the appropriate JADE risk category, there is a corresponding care protocol based on international guidelines. Certain clinical interventions are suggested, such as recommended frequency of follow-up visits and monitoring plans (e.g., checking feet, making therapeutic recommendations, checking on patient's adherence to a recommended plan for diabetes-specific education).

Managing DM in primary care is burdensome, complex, and time-consuming. Decision-support software programs can delegate or assist non-physician providers in achieving benchmark targets such as A1C, blood pressure, cholesterol, and necessary preventive screening examinations. Traditionally, advanced practice nurses performed these tasks; however, pharmacists could also help providers and patients achieve these targets. Pharmacists have proved themselves helpful to patients in improving and halting progressive diabetes nephropathy with stepwise medication protocols, diet adherence intervention, and group medical visits.

### Home Telehealth

The U.S. Department of Health and Human Services promotes the use of telehealth programs in underserved population of rural areas, for patients with low incomes, and for the uninsured. Home telehealth devices are meant for use in patients with an average education of fifth grade. Congressionally mandated health information technology grants have been approved in most states to help promote the use of telehealth.

Many chronic illnesses, including DM, can be managed with home telehealth-based electronic devices. The response to telehealth may be age-dependent. For example, adolescent patients with type 1 DM experienced an improvement in their A1C values of 0.74%, although this was not a statistically significant difference from a control group of adolescents on a wait list to receive telehealth. However, unsupportive family behaviors and decreased parental caring were present in the adolescents who participated in the telehealth device households. These factors may explain the lack of a statistically significant effect of telehealth devices in this study.

In the adult veteran population, contact by a nurse practitioner in addition to home-based electronic telehealth devices improved A1C values at 3 months and 6 months. In the treatment group, electronic home telehealth devices offered education, daily reminders, and questionnaires to assess health status. Patients in the control group received monthly telephone calls from a nurse practitioner. Both groups showed improvements in A1C at 3 months and 6 months, although patients who received the electronic home telehealth device and the nurse practitioner contact improved considerably more. Compared with patients not enrolled in one of these programs, patients with DM enrolled with home telehealth devices had a decrease in hospitalizations, days spent in the hospital, total hospitalizations, and 4-year all-cause mortality.

Home telehealth devices may reduce care coordinator–initiated visits to primary care providers. Because of the reduced number of primary care providers, this may continue to be an important benefit of home telehealth devices. Of note, there are very few pharmacist-led telehealth disease management programs using home telehealth devices, yet many aspects of telehealth involve medication adherence issues and dose adjustments, which is part of the pharmacist's expertise. This is a potential role for more pharmacist involvement.

Nurses and dietitians responsible for home telehealth devices were surveyed to determine the satisfaction of health care providers giving these services. Primary care providers, nurses, and dietitians were very satisfied with their experience in providing care for the underserved population and in managing patients' needs in a more timely way. Disadvantages were frustration with some technology issues and the lack of face-to-face patient contact. Few pharmacists are directly involved in providing home telehealth services. Pharmacists with collaborative practice agreements and/or prescribing privileges would be good candidates to use home telehealth for both drug and disease management. Medicare reimbursements are evolving slowly, and in some cases, reimbursement is only available if patients live in very remote areas. However, several state Medicaid organizations and managed care plans are reimbursing for nurse and provider time, although such reimbursement is inconsistent.

## Conclusion

Many new aspects of diabetes technology are available to both consumers and health care providers. Pharmacists need to maintain current knowledge of diabetes technologies and the ways in which they may assist patients in achieving treatment goals. To maximize the benefit offered by these innovative technologies, pharmacists must be able to educate patients about their appropriate use and their own role in improving glycemic control and preventing the long-term complications associated with their disease.

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   This study was a retrospective review of medical records that determined the safety of continuing CSII treatment in patients admitted to one hospital. In many inpatient settings, insulin pumps are temporarily discontinued, and patients are converted to inpatient BG and insulin management. This hospital created an initiative to allow inpatient diabetes self-management. The authors assessed 50 consecutive inpatients admitted to the hospital with CSII. The patients were divided into three groups. Group 1 used an inpatient insulin pump protocol and had inpatient diabetes services. Group 2 used an inpatient insulin pump protocol alone. Group 3 was treated with usual care. Groups 1 and 2 had better bedside BG concentrations (70 mg/dL up to 300 mg/dL) than group 3, but there were no differences in incidence or severity of hypoglycemia among the three groups. The mean BG concentrations were as follows: group 1 = 173 ± 43 mg/dL; group 2 = 187 ± 62 mg/dL; and group 3 = 218 ± 46 mg/dL. The authors concluded that patients who use CSII as outpatients can safely continue to use these devices as inpatients, even if hospital personnel are unfamiliar with the devices. In addition, 86% of patients reported satisfaction with continued use of the insulin pump during hospital admission. This study shows that patients who successfully manage their BG concentrations using CSII as outpatients can continue to use CSII as inpatients. This may reduce the BG excursions that cause patients to remain hospitalized and increase patient recovery time in many areas of inpatient care. This study is limited by its inability to differentiate the status of patients; this would determine the patients with the best outcomes (i.e., critically ill patients vs. stable), those who could manage their own BG, those who should be removed from their insulin pump, and those whose treatment could be managed with continued use of their CSII with diabetes service consultation.

2. Tamborlane WV, Beck RW, Bode BW, Buckingham B, Chase HP, Clemons R, et al. Continuous glucose monitoring and intensive treatment of type 1 diabetes. N Engl J Med 2008;359:1464–76.

This study evaluated the change in A1C in patients who used a CGMS. The authors assessed 322 adults and children (older than 8 years) who had been given a diagnosis of type 1 DM more than 1 year earlier, who were already receiving intensive therapy by insulin pump, or who were receiving three or more daily injections. Adults and children were randomly assigned to home BG monitoring with a traditional monitor (n=157; control group) or with continuous monitoring (n=165). All patients wore a continuous BG monitor for 6 of 7 days before randomization and were required to check BG concentrations with a home BG monitor three times/day. Patients were divided into three age groups (25 years and older, 15–24 years old, and 8–14 years old). Patients randomized to the CGMS arm were given the choice of one of three devices (MiniMed Paradigm REAL-Time insulin pump and CGMS device, Dexcom SEVEN, or FreeStyle Navigator). Patients underwent follow-up at 1, 4, 8, 13, 19, and 26 weeks. In study participants 25 years or older, a significant difference in A1C was observed between the patients in the CGMS group and the control group (–0.53%; 95% confidence interval, 0.71% to 0.35%; $p<0.001$). There was no significant difference in A1C between control and CGMS for either of the other two age groups. Secondary analysis showed a 10% or more decrease in the mean A1C value in patients in the CGMS group compared with baseline ($p=0.003$). In addition, more patients in the CGMS group achieved an A1C of less than 7% in the CGMS group ($p=0.0005$). Again, there was no difference in the secondary variables between control and CGMS for the other two age groups. This study is important because it showed that CGMS use improves A1C in adults. However, adolescents and young adults have more obstacles to care than younger children and older adults; therefore, the potential benefits of CGMSs are less clear in this age group. In addition, studies typically enroll highly motivated patients, and the benefit of CGMS general use in less well-controlled or less well-motivated individuals is unknown.

3. Phillip M, Battelino T, Rodriguez H, Danne T, Kaufman F; for the Consensus Forum participants. Use of insulin pump therapy in the pediatric age-group. Consensus statement from the European Society of Paediatric Endocrinology, the Lawson Wilkins Pediatric Endocrine Society for Pediatric and Adolescent Diabetes, endorsed by the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2007;30:1653–62.

   This consensus statement reviews the literature regarding the use of insulin pump therapy in pediatric and adolescent patients. The article discusses a variety of considerations, such as the risks and benefits of pump use, development of severe hypoglycemia, impact on A1C and weight gain, incidence of infusion-site reactions, possible psychosocial issues related to pump use, and need for dosage calculations. Detailed information on each of these categories and recommendations for each situation are included. The consensus group recommends using insulin pump therapy as long as all parties (children, parents, and providers) are interested. The long-term benefit of A1C lowering in these age groups is not conclusive. Observational studies have shown a decrease in the development of severe hypoglycemia; however, randomized, controlled trials have not shown a significant decrease. A reduction in the risk of microvascular complications has been shown with tight control using CSII; therefore, it is strongly recommended in pregnant adolescents. Selecting an insulin pump is a team decision, and the features of individual insulin pumps should be evaluated to help patients choose the most appropriate device. This statement provides a good resource for health care providers deciding whether their pediatric or adolescent patient should use insulin pump therapy.

4. Soffer E, Abell T, Lin Z, Lorincz A, McCallum R, Parkman H, et al. Review article: gastric electrical stimulation for gastroparesis – physiological foundations, technical aspects and clinical implications. Aliment Pharmacol Ther 2009;30:681–94.

   This review examines various aspects of the physiology of the electrical stimulation of gastric activity. In addition, the article discusses specific aspects of gut tissue and how electrodes deliver the electrical stimulation. Most clinical trials reviewed were single-center, open-label studies. This methodologic flaw is probably because of the end-stage nature of intractable nausea and vomiting secondary to gastroparesis and the approach to initially use oral or systemic drugs to relieve the symptoms of gastroparesis. After drugs are found to be ineffective, gastric electrical stimulation may be offered. Patients with diabetic gastroparesis had better outcomes from gastric electrical stimulation than did patients with idiopathic gastroparesis, but for reasons unknown. The clinical results summarized in this review showed improvements in symptoms, quality of life, and nutritional status of the patient and a reduction in health care interventions. This review also found that although patients' nausea and vomiting were improved, symptoms of pain and bloating were much less likely to improve.

5. Holbrook A, Thabane L, Keshavjee K, Dolovich L, Bernstein B, Chan D, et al. Individualized electronic decision support and reminders to improve diabetes care in the community: COMPETE II randomized trial. CMAJ 2009;181:37–44.

   This is one of the few published studies to review an electronic decision-support system to manage DM. The authors recruited 46 community-based primary care providers in Canada, together with 511 of their patients, to participate in the study. Only patients older than 18 years with type 2 DM were included. The intervention included a Web-based diabetes tracker that interfaced with the provider's electronic medical record and an automated telephone reminder system. The intervention also included a color-coded diabetes tracker that the patient received quarterly by mail. Patients were encouraged to bring this tracker to their provider visits. Automated telephone calls reminded patients to obtain laboratory tests and make provider appointments. The control group consisted of usual care appointments. Patients underwent monitoring for about 6 months.

The primary outcome was improvement in the process of DM care among these patients. These outcomes were scored, and a composite score was calculated. The composite score included health care provider monitoring of A1C, blood pressure, low-density lipoprotein cholesterol, body mass index, albuminuria, foot check, smoking, and physical activity. Secondary outcomes were actual improvement in clinical markers such as A1C, low-density lipoprotein cholesterol, blood pressure, and quality-of-life measures. On the basis of the primary outcome of improvement in the process composite score, benefit from the intervention was evident, with 61.7% of the intervention group showing benefit compared with 42.6% of the control group ($p<0.001$). Potential study limitations include the short duration (6 months), the inability to distinguish which intervention in the Web-based interface was most effective, and the use of mostly surrogate markers for diabetes as outcomes. The study shows that individual Web-based interventions are likely to be helpful to patients with DM; however, the specific aspects of the intervention that work best are still unknown.

6. Holzinger U, Warszawska J, Kitzberger R, Wewalka M, Miehsler W, Herkner H, et al. Real-time continuous glucose monitoring in critically ill patients: a prospective randomized trial. Diabetes Care 2010;33:467–72.

There has been controversy regarding the benefit and monitoring of tight glycemic control in patients receiving treatment in an intensive care unit. This recent study evaluated continuous BG monitoring in critically ill patients. Patients undergoing mechanical ventilation were randomly assigned in a 1:1 ratio to CGMS device monitoring or monitoring using a standard glucose insulin treatment algorithm. The resultant insulin infusion was based on an algorithm that was the same for patients in the control group and CGMS device group. Patients in the CGMS intervention group had real-time BG measurements displayed every 5 minutes, and nurses guided the insulin therapy according to protocol. Maintenance of BG concentrations less than 110 mg/dL was the primary outcome. Secondary outcomes included severe hypoglycemia, percentage of time the BG concentration was less than 150 mg/dL, mean BG concentration, and median time the BG concentration of less than 110 mg/dL was similar in the two groups (59% intervention vs. 55%; $p=0.25$). However, the secondary outcome of severe hypoglycemia was significantly lower in the real-time CGMS group than in the control group (1.6% vs. 11.5%; $p<0.031$). Other secondary outcomes were not significantly different. Recent controversial trials have not conclusively shown that tight glycemic control in critically ill patients reduces morbidity and mortality. This trial shows that BG concentrations in patients using CGMSs did not achieve the 23% improvement as compared with non-CGMS users; however, severe hypoglycemia was greatly reduced in the CGMS group. The traditional BG control algorithm in this hospital may have been more effective at reducing BG concentrations than algorithms at other hospitals. Patients had CGMS readings drawn every 5 minutes, although many times the nurses had insufficient time to look at these BG concentrations before the 2-hour required check. Other study limitations include the small number of patients enrolled. Even though the number of patients enrolled provided sufficient power to assess the primary outcome, showing significant differences in a larger number of patients would be required to evaluate effects on morbidity and mortality.

7. Insulin Pumpers: Support and Information for Adults and Children with Diabetes. Available at *www.insulinpumpers.org*. Accessed December 7, 2010.

This Web site is a good resource that includes general insulin pump information for patients considering an insulin pump, for novice insulin pump users, and for veteran pump users needing an answer to a pump question. It is maintained by a not-for-profit organization, initiated in 1997, that currently has a membership of more than 5000 individuals with DM and their families. Patients can enter chat rooms on a variety of insulin pump topics. The site also has links to other diabetes support venues, places to purchase textbooks and supplies, and a physician referral system. Under the How-to tab, patients can research how to calculate insulin-to-carbohydrate ratios, how to graphically estimate their basal insulin rates online, how to perform a square-wave bolus, and how to calculate carbohydrates from recipes. The FAQs tab has basic and advanced questions regarding insulin pumps, good pictures of where to insert infusion sets, videos on using insertion sets, and general diabetes information. The Web site is good for insulin pump users seeking specific and general questions. The site is not designed to provide clinical care, and patients should be cautioned to contact their health care providers if they are having specific problems managing their BG concentrations.

8. Garg SK, Bookout TR, McFann KK, Kelly WC, Beatson C, Ellis SL, et al. Improved glycemic control in intensively treated adult subjects with type 1 diabetes using insulin guidance software. Diabetes Technol Ther 2008;10:369–75.

This open-label, randomized, controlled trial evaluated the change in A1C values in patients using the Accu-Chek Advisor Insulin Guidance Software compared with standard care. The trial also evaluated sustained A1C values for 12 months. Secondary measures included BG concentration monitoring frequency, likelihood of accepting recommendations of the software, adverse events such as hypoglycemia or hyperglycemia, unscheduled clinic visits, emergency department visits, and hospitalizations. The Accu-Chek Advisor system uses personal data assistants as the platform for maintaining the information. The study enrolled 123 patients with type 1 DM for at least 6 months. The primary outcome was a reduction in A1C greater than 0.4%. Patients in the experimental group had a significant reduction in A1C of greater than 0.6% ($p<0.02$) from 3 months to 12 months compared with the usual care group. A further benefit was the lack of insulin dose change or weight change, which

may have been caused by the lifestyle modifications that patients were making because of the intervention. Nocturnal hypoglycemia was not different between the two groups; however, patients in the experimental group had more severe hypoglycemic reactions that required assisted interventions. The importance of this study was the introduction of insulin guidance software to help improve patient BG control without necessarily increasing the patient's dose of insulin.

9. Dros J, Wewerinke A, Bindels PJ, van Weert HC. Accuracy of monofilament testing to diagnose peripheral neuropathy: a systematic review. Ann Fam Med 2009;7:555–8.

These authors reviewed the process of diagnosing diabetic peripheral neuropathy in the feet. The Semmes-Weinstein monofilaments are routinely used to assess the presence of diabetic peripheral neuropathy. Monofilament testing is easy and portable, and it is recommended by several practice guidelines to detect diabetic peripheral neuropathy. The authors reviewed MEDLINE and EMBASE databases and identified 173 primary literature articles. After excluding 119 references, 54 primary articles were retrieved and reviewed. An additional number of articles were excluded for various reasons. Three studies (n=589) were included for systematic review. None of the studies was performed in the United States. A meta-analysis could not be performed because of the heterogeneity of each trial. On the basis of their review, the authors concluded that even though monofilament testing is recommended in many practice guidelines, it is not accurate as the sole method for detecting peripheral neuropathy in patients without foot ulcers. The authors' recommendations were similar to those made in the Standards of Care for Diabetes from the American Diabetes Association, which include inspection, assessment of the foot pulses, testing loss of sensation by the 10-g monofilament, assessing vibratory sensation using the 128-Hz tuning fork, pinprick sensation, ankle reflexes, or vibration perception threshold. The authors recommend using monofilament testing in addition to clinical examination with vibration perception, pinprick testing, assessment of ankle reflexes, and nerve conduction tests, if necessary. Overall, the authors appear to question the standards of practice because of the lack of conclusive data on a method of testing routinely performed in all patients with DM.

10. Stone RA, Rao RH, Sevick MA, Cheng C, Hough LJ, Macpherson DS, et al. Active care management supported by home telemonitoring in veterans with type 2 diabetes: the DiaTel randomized controlled trial. Diabetes Care 2010;33:478–84.

The Veterans Administration uses many aspects of telemedicine, including home telehealth monitors. This study evaluated monthly telephone calls made by a nurse educator care coordinator compared with home telehealth monitoring with a nurse practitioner actively managing care. Active care management in this study included nurse practitioner adjustment of insulin doses, education information sent to the patient by the telehealth machine, telephone call reminders, and follow-up calls. More than 1050 veterans were screened for this study, and 150 consented to treatment. Baseline A1C was 9.4% in the care coordinator group and 9.6% in the active care management with home telehealth group. Patients were assessed at baseline and 3 months and 6 months after the initial visit. Patients enrolled in the active care management group had A1C reductions of 0.7% or lower at both the 3-month and 6-month follow-up visits ($p<0.001$ for each). Other secondary end points were total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and systolic and diastolic blood pressure, which improved in both groups. Study limitations were the short follow-up of 6 months, as well as a failure to determine which interventions were most affected. A longer study duration would help determine the recommended time for use of home telehealth. The benefit of this study is the conclusion that patients can improve various clinical measures if they use this type of technology.

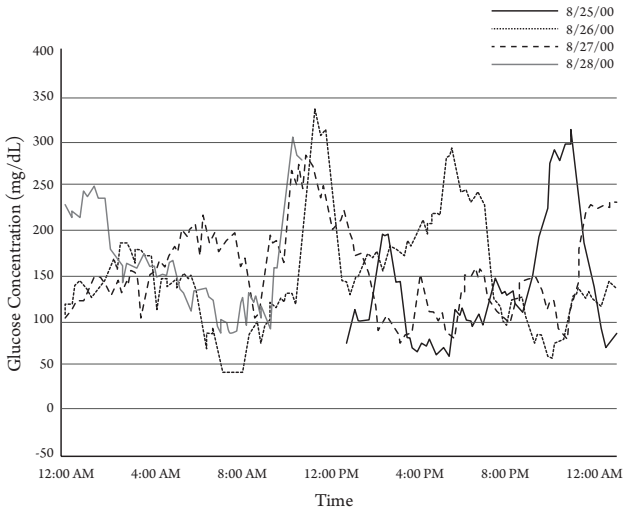
# Self-Assessment Questions

**Questions 1 and 2 pertain to the following case.**
G.G., a 2-year-old girl with type 1 diabetes mellitus (DM), comes with her family to the clinic for an urgently scheduled appointment after an issue last night with her insulin pump. The pump was placed 3 months ago; G.G. has since had only one hypoglycemic reaction after lunch, and her most recent hemoglobin A1C (A1C) is 7.3%. At this visit, G.G.'s stay-at-home mother and stepfather are present and are doing most of the talking. G.G.'s biologic father, in the corner of the room, is saying very little. The mother and stepfather have asked what to do if they need to stop the insulin pump. G.G. slept at her father's house last night and woke up at 4:30 AM because of the insulin pump alarm. Her blood glucose (BG) reading was 43 mg/dL. G.G.'s father called her mother's house, and the stepfather told the father to stop the pump immediately. G.G.'s father removed the infusion set from G.G.'s skin and gave her some peanut butter and crackers. When G.G. felt sleepy, her father placed her back in bed. He returned G.G. to her mother's house at 8:15 AM. At that time, she ate one-half cup of Cheerios and three-fourths cup of milk for breakfast. It is now 9:45 AM.

1. **Which one of the following is the most likely result for G.G. related to this series of events?**
   A. Her BG concentration will be elevated because of discontinuing the insulin pump for several hours.
   B. Her evening basal insulin rate will need to be decreased to avoid nocturnal hypoglycemia.
   C. Her BG concentration is still low because of the 3-hour to 5-hour insulin-on-board effect of the rapid-acting insulin in the insulin pump.
   D. The diabetes case manager will suggest that she not sleep at her father's house because he seems disinterested in her care and does not know how to manage her insulin pump.

2. **Which one of the following approaches would have been the most appropriate way for G.G.'s family to manage her insulin pump at 4:30 AM?**
   A. Clamp the insulin pump infusion tubing to discontinue insulin delivery.
   B. Remove the insulin pump infusion tubing from the infusion connection on the skin.
   C. Set the insulin pump basal insulin rate to 0 for 1 hour or until the BG is above 90 mg/dL.
   D. Change to insulin by syringes until the provider can be contacted.

3. A 34-year-old woman with type 1 DM who receives insulin through an insulin pump is admitted to the hospital for acute pancreatitis. Her physician states that she will likely be hospitalized for a few days with dietary restrictions of nothing by mouth. The patient is concerned about hypoglycemia and her insulin pump. **Which one of the following is the best approach to treating this patient's diabetes during her hospital admission?**
   A. Administer insulin doses intermittently using needles and syringes.
   B. Continue the insulin pump at her normal basal insulin rate.
   C. Continue the insulin pump with 30% less basal insulin.
   D. Discontinue the insulin pump, check BG every 15 minutes, and initiate intravenous insulin if BG is greater than 180 mg/dL.




**Glucose sensor profile.** (Reproduced with permission from Kaufman FR, Halvorson M, Carpenter S, Devoe D, and Pitukcheewanont P. Pump Therapy for children: weighing the risks and benefits: view 2: insulin pump therapy in young children with diabetes. Diabetes Spectrum 2001;14:87.)

4. The continuous glucose monitoring system (CGMS) tracing above is from a 4-year-old boy who is currently using 7 units of insulin glargine at 8:00 PM, insulin lispro 2 units at breakfast at 7:30 AM, 3.5 units at lunch at noon, and 4.5 units at supper at 5:30 PM. The boy eats mini-pancakes for breakfast every morning. His lunch includes peanut butter and jelly on whole wheat bread or a small can of SpaghettiOs. His dinner consistently includes meat, a vegetable, and a starch, although he does

not always eat everything. He usually eats a small snack around 7:30 PM or 8:00 PM when he takes his insulin glargine. **Which one of the following is the best recommendation based on this patient's BG profile?**

A. Include an afternoon snack.
B. Maintain the current food intake and insulin doses.
C. Increase the dose of insulin glargine to 9 units.
D. Increase the breakfast dose of insulin to 3 units.

5. A 17-year-old boy with type 1 DM is currently taking neutral protamine Hagedorn (NPH) insulin 8 units in the morning with insulin aspart 5 units, and insulin NPH 9 units in the evening with insulin aspart 6 units. He takes both doses before meals. Previously, he used an insulin pump; however, he experienced several hypoglycemic and hyperglycemic excursions requiring hospital admissions. Subsequently, he and his family decided to forego use of the insulin pump. This patient is on the basketball team and is very frustrated with his insulin schedule when he has evening games. On game nights, he eats dinner with the team and skips his evening insulin dose because of the inconvenience of injecting his doses before dinner. He is also embarrassed about all aspects of administering insulin in front of his teammates. Instead, he takes his insulin when he gets home after the game. **Which one of the following is the best recommendation for this patient?**

A. Premix insulin NPH and insulin aspart in the morning and keep it in locker or gym bag until dosing it before eating dinner.
B. Take NPH in the early afternoon with a snack and insulin aspart at home at night.
C. Offer an insulin pen device that can deliver both insulin NPH and insulin aspart.
D. Despite the family decision, the patient should be placed on an insulin pump within 24 hours with an all-basal insulin regimen.

**Questions 6–10 pertain to the following case.**
P.G. is a 34-year-old woman (height 5′5″, weight 56 kg [123 lb]) who has been using an insulin pump for 3 years. She comes to you for laboratory testing and insulin management four times/year. Today, she brings 5 days of BG readings for your review, and her recent A1C value is 8.3%. She just started a new job and wakes up earlier than she used to. Her insulin sensitivity is 1:28, and her insulin-to-carbohydrate ratio is 1:15. She eats breakfast at 7:30 AM, lunch at 12:15 PM, and dinner at 5 PM.

| Time | Basal Insulin Rate (unit/hour) |
|---|---|
| Midnight to 8:00 AM | 0.4 |
| 8:00 AM to noon | 0.7 |
| Noon to midnight | 0.5 |

| | Blood Glucose (mg/dL) | | | |
|---|---|---|---|---|
| Time | Day 1 | Day 2 | Day 3 | Day 4 |
| 7:00 AM | 189 | 156 | 178 | 212 |
| Noon | 120 | 112 | 87 | 145 |
| 2:00 PM | 245 | 303 | 211 | 189 |
| 5:00 PM | 165 | 123 | 178 | 154 |
| 6:30 PM | 112 | 98 | 112 | 111 |
| 9:30 PM | 145 | 167 | 176 | 134 |
| Midnight | 102 | 111 | 123 | 114 |

6. **Which one of the following is the best recommendation for P.G.?**

A. Increase insulin bolus and insulin-to-carbohydrate ratio at the evening meal.
B. Decrease insulin bolus and insulin-to-carbohydrate ratio at the evening meal.
C. Reduce morning basal insulin rate.
D. Test BG concentrations at 2:00 AM and 4:00 AM.

7. P.G. has become frustrated with her BG readings. She is adherent to her health care provider's recommendations to test but feels she should have better control of her diabetes. **Which one of the following is the best recommendation for P.G.?**

A. Reduce the frequency of her BG testing to two times/day rather than four times/day.
B. Consider islet cell transplantation and provide her with information about the surgical centers in the area.
C. Reset all of her basal insulin rates and her insulin-to-carbohydrate and insulin sensitivity ratios.
D. Use a Web-based tool to help manage her BG and ensure frequent contact with her health care provider.

8. P.G. likes electronic gadgets and wants to purchase a new device to help her manage her diabetes. P.G. wants a device that is easy to use, that fits into her busy schedule, and that can be carried in a small pocketbook. **Which one of the following is the best recommendation for P.G.?**

A. Purchase a smart phone with data package.
B. Get the DIDGET monitor compatible with the Nintendo DS gaming with BG attachment.
C. Wait before purchasing any product because better ones may come out in a few years.

D. Purchase the ultrasound wristwatch, Glucoband.

9. **Which one of the following diabetes technology products would be most beneficial for P.G.?**
   A. A software program for entering her exercise and food logs.
   B. A CGMS.
   C. Home telehealth device to communicate with her health care providers.
   D. Human islet cell transplantation.

10. Last Friday night, P.G. ate pizza for dinner and within 20–25 minutes experienced a hypoglycemic reaction that required her family to administer glucagon and call the ambulance. Despite the medics' recommendations, P.G. refused to go the hospital. Later that night, her BG concentration was greater than 400 mg/dL. P.G. recalls having a similar situation a few months ago after she ate a similar meal. **Which one of the following would best avoid future situations like this for P.G.?**
    A. Administer less insulin the next time she has pizza.
    B. Provide pharmacotherapy for gastroparesis to help her gastrointestinal motility.
    C. Increase her nighttime basal rate to 0.7 unit/hour.
    D. Use the dual-wave or square-wave bolus features of her pump.

**Questions 11 and 12 pertain to the following case.**
E.L. is a technology-savvy 24-year-old man with type 1 DM. He currently uses an insulin pump and CGMS interface. He has noticed that his CGMS readings often vary widely from his fingerstick BG monitor, which he checks at least twice daily to calibrate his CGMS. He loves using these devices and does not want to give them up. His current A1C is 6.3%, and he feels better than ever. He is aggressive with his insulin dosing and does not want to have complications of diabetes like those experienced by his uncle.

11. **Which one of the following is the most appropriate recommendation for E.L.?**
    A. Use both CGMS daily and BG fingerstick testing four times/day.
    B. Use CGMS.
    C. Use fingerstick monitors.
    D Use CGMS BG fingersticks.

12. **Which one of the following counseling points about variations in BG concentration is best to provide E.L.?**
    A. Before acting on a BG reading, know the duration of action of insulin; before giving a bolus of insulin, consider whether the insulin is still active.
    B. Change insulin infusion set and sensor when BG readings from both devices vary by more than 10 mg/dL.
    C. Stop using the CGMS device and continue using the fingerstick BG monitor to check BG concentration.
    D. Use a new sensor and infusion set every day to improve the accuracy of the CGMS device and insulin pump.

**Questions 13 and 14 pertain to the following case.**
M.L. is an 82-year-old man with type 2 DM. His current A1C is 8.9%, and he checks his BG three times/week. His health care provider wants him to improve his BG concentrations and lower his A1C. M.L. is leery of using complicated devices, even though he able to use a laptop, a cell phone (although he has poor cell phone coverage at his house), and a personal digital assistant device to maintain appointments and contacts. He lives alone in a remote area, and he likes to chop wood and work in the yard. His daughter lives nearby and brings him meals during the week.

13. **Which one of the following recommendations would have the greatest impact on M.L.'s BG control?**
    A. Have his daughter use a software program for diabetes data or a Web site to help monitor his BG.
    B. Use a mobile phone glucose monitor.
    C. Increase home BG fingerstick monitoring.
    D. Use a home telehealth device.

14. **If M.L. developed retinopathy and became legally blind, which one of the following BG monitoring options would be best for him?**
    A. The FreeStyle meter.
    B. Any meter used by his daughter.
    C. The Prodigy meter.
    D. A CGMS device.

15. A 39-year-old man with type 1 DM comes to your diabetes education program with tingling in his feet. He has had diabetes for 13 years, with several years of excellent BG control and A1C readings of 5.8% to 6.7%. He drives a cement mixer and works as carpenter when he is not delivering cement. He wears steel-toed boots, and until recently, his feet have been fine. **Which one of the following is most likely to help you diagnose this patient's foot problem?**

A. Semmes-Weinstein 10-g monofilament test.
B. 128-Hz tuning fork.
C. Balance test using a balance disk.
D. Combination of monofilament testing and vibratory sensation.

16. A 73-year-old woman with type 2 DM is admitted to the hospital with worsening heart failure symptoms. She currently takes insulin NPH/aspart 70/30, 36 units in the morning and 48 units in the evening. She is admitted to the intensive care unit for monitoring, diuresis, and treatment of her heart failure. Her target BG range is 70–110 mg/dL. She is placed on a continuous intravenous insulin infusion and a new hospital protocol that uses a CGMS device. Her recent BG concentration readings, every 10 minutes for a 2-hour block by CGMS, have been 78 mg/dL, 56 mg/dL, and 35 mg/dL (treated with dextrose), followed by 79 mg/dL, 89 mg/dL, 133 mg/dL, 143 mg/dL, 138 mg/dL, 165 mg/dL, 175 mg/dL, 168 mg/dL, and 172 mg/dL. **Which one of the following treatment options is best for this patient?**

A. Maintain current use of the intravenous insulin infusion and CGMS device.
B. Resume insulin NPH/aspart 70/30 36 units in the morning and 48 units in the evening.
C. Change to fingerstick BG monitoring every 15 minutes.
D. Continue the insulin infusion but decrease the dosage by 20% to prevent hypoglycemia.

17. A 60-year-old woman is considering the use of an insulin pen device. She has been using a traditional insulin syringe and vial (mixing NPH 92 units twice daily and regular insulin 34 units in the morning and 67 units in the evening). However, she has a very active social life and often misses some of her doses of insulin because she does not want to draw up insulin around her friends. She is interested in learning about the insulin pen but is not sure whether she would be a good candidate. The patient is on a fixed income and has difficulty affording some of her drugs. **Which one of the following will have the greatest impact on the patient's decision to use a pen device?**

A. Accuracy of dose administration.
B. Number of missed doses.
C. Cost of supplies.
D. Number of daily injections.

18. A 29-year-old man was given a diagnosis of type 1 DM 5 months ago. Today he comes to the diabetes clinic with an advertisement for CGMS devices and is interested in using one. He is quite motivated, but he questions whether CGMS would be a good option for him because he has vision difficulties and needs to wear glasses for reading. In addition, he has seasonal allergies and is allergic to bee stings. He loves exercising and rides his bicycle more than 100 miles per week. Three months ago, his physician told him that he was not ready to use an insulin pump because he had not yet gone through the diabetes education program. **Which one of the following is most important to consider regarding this patient's use of a CGMS?**

A. His visual acuity.
B. His allergy history.
C. The amount of his weekly exercise.
D. Accuracy of CGMA to detect changes in BG during activity.

**Questions 19 and 20 pertain to the following case.**
M.R. is a 31-year-old man with type 1 DM diagnosed 23 years ago. He is frustrated because he has developed proliferative retinopathy and microalbuminuria. He received a reassignment at work because of his poor vision. He can read documents and computer screens but requires magnification to do so, and his employer is unable to provide these accommodations. M.R. admits to nonadherence in the past but has maintained his A1C values at 6.8% for the past 2 years. He used to live in the city but now lives in a rural area close to his elderly parents and his younger brother, who is ill. He sees you once a year, but he has not seen his primary care provider or his ophthalmologist in 2½ years because they are now located 3 hours away. He wants his diabetes to "go away, even if it is for a day or a month or two," and he does not want to deal with giving himself insulin shots. He states that would do just about anything to stop taking insulin for a little while. His current insulin regimen is detemir 13 units in the morning with 5 units of insulin glulisine and insulin detemir 15 units in the evening with 6 units of insulin glulisine. His insulin-to-carbohydrate ratio is 1:12, and his insulin sensitivity is 1:45.

19. **Which one of the following is the best recommendation to prevent further decline in M.R.'s vision?**

A. Retinal telehealth screening and follow-up at a convenient local clinic.
B. Schedule his retinal examination appointment with an ophthalmologist in the city.
C. Use a Web-based diabetes tool with a large-screen computer monitor.
D. Initiate a home telehealth program with his diabetes education team and primary care provider.

20. **Which one of the following is the best DM treatment option for M.R. to investigate regarding his DM treatment?**

    A. Web sites such as *www.dlife.com,* to get back on track with his monitoring and insulin administration.
    B. A closed-loop artificial pancreas.
    C. Human islet cell transplantation.
    D. Moving to be closer to his primary care providers.