CHAPTER 18:

DIABETES MANAGEMENT IN THE FUTURE

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A frequently asked question is, "When will there be a bionic pancreas?" A bionic pancreas would be one in which a continuous glucose monitor (CGM) controls an insulin pump to give more or less insulin depending on the person's needs. It is referred to medically as a "closed loop pancreas." The answer is both encouraging and discouraging for the near future. It is likely that a partially bionic pancreas will be available in the next decade. Unfortunately, it will not be a complete system for at least another decade. Five of the current reasons for this are shown in Table 1 and are discussed here.

TABLE 1:

LIMITATIONS PREVENTING A BIONIC PANCREAS

- **Lack of accuracy of CGM systems**
- **Lack of an optimal insulin**
- **Lack of accurate algorithms**
- **Individual variability in insulin sensitivity**
- **The Food and Drug Administration (FDA)**

LACK OF ACCURACY OF CGM SYSTEMS

As discussed in Chapters 15, 16 and 17, the three second-generation CGMs are advanced over the two first-generation CGMs. They are unfortunately still lacking in accuracy and reliability. The accuracy of the current CGMs is similar to the accuracy of blood sugar meters 10 years ago. The most critical area of accuracy is reliable detection of low glucose levels. This remains an area of varying concern for the three current CGMs. An added limitation is that sometimes the sensors do not function well. In addition to accuracy and reliability limitations, two of the three current CGMs are not associated with a company that makes an insulin pump. Fortunately, research combining CGM readings with insulin pump features is progressing. This is true for both the MiniMed Paradigm REAL-Time and the Abbott Navigator CGMs. In spite of the limitations, there is no question that most people achieve better diabetes management when they use both an insulin pump and a CGM system. People with diabetes can benefit even though the CGM cannot currently control the insulin pump. The two must now be used independently (even though the glucose results of the Paradigm REAL-Time can be transmitted to the face of the insulin pump).

LACK OF AN OPTIMAL INSULIN

The lack of an optimal rapid-acting insulin has been noted throughout this book. The three rapid-acting insulins (Humalog, NovoLog, and Apidra) can be administered by the pump subcutaneously. The insulin starts to get into the blood in 10 minutes but does not peak for 100 minutes. Blood sugar levels generally begin to decline about 30 minutes after increasing pump insulin delivery. This is in contrast to the normal

pancreas that delivers insulin directly into the blood and has the first peak in three to five minutes (the "first-phase" peak). It is also in contrast to the normal peak in blood sugar levels after eating a meal, which occurs in 60 minutes (see Figure 1, Chapter 6). To add to the problem, the CGM measures subcutaneous glucose levels. The glucose must leave the blood vessel and diffuse into the subcutaneous tissue before the CGM can measure the glucose value. It is thus an average of 10 minutes behind the blood sugar level. This delay may be even greater with rapid sugar changes such as the spike in blood sugars after beginning to eat. All in all, there is no way current CGM systems can relay information to an insulin pump rapidly enough to prevent high sugar levels after meals. This is particularly true considering the lag in the peak of insulin action. Researchers have tried having the insulin delivered directly into the abdomen, or even into the blood stream. The potential serious complications of these routes of administration are infections or blood clots. There is the possibility of a new even more rapid acting insulin, which would be of some help. In the meantime, the only way to currently control blood sugar levels with meals is to have the person/family manually administer the bolus 15 to 30 minutes prior to eating. Thus, the initial bionic pancreas will have to be a partial system. Then more parts can be added later as technology advances.

LACK OF ACCURATE ALGORITHMS

The third limitation is a current lack of accurate algorithms. These are the formulas to increase or decrease insulin output from the pump as glucose levels rise or fall. The Juvenile Diabetes Research Foundation (JDRF) is currently supporting research to develop these formulas. For example, if a glucose level is falling, at some point in time the CGM would need to tell the pump to decrease or halt the insulin infusion. When the decrease in insulin infusion occurs will depend on how rapid the glucose level is falling, what the current glucose level is, the insulin on board, any food eaten in the past few hours, the person's insulin sensitivity, and many other factors. Research at the Barbara Davis Center and at Stanford University (and other centers) is currently focusing on the development of formulas (algorithms) to safely decrease or turn off a pump to prevent hypoglycemia.

Because severe hypoglycemia is dangerous, this ability to stop insulin infusion may be the first part of the partial bionic pancreas that is approved. In children, 75% of severe lows occur during sleep (18). Warning alarms during sleep are not heard 71% of the time (19). Thus, decreasing basal insulin or turning a pump off with pending hypoglycemia during the night could be extremely valuable. It is known that the pump can be turned off for two hours without danger of ketone formation. Better warning alarms will also be valuable and are being developed.

INDIVIDUAL VARIABILITY IN INSULIN SENSITIVITY

Individual variability in insulin sensitivity is a fourth limitation in developing a bionic pancreas. It may be that each person will need to have checks to determine their overall insulin sensitivity. Early in the course of diabetes, people are often extremely sensitive to insulin. This is likely in part due to their own continued insulin production. It is known that teenagers are more insulin resistant, as are some overweight individuals. Insulin resistance may also vary from time to time in the same person. Women are more insulin resistant during their menses. People are frequently more resistant during infections. It may be that insulin pumps will have settings for insulin resistance. The trick will be to find the correct setting to use at the right time and for the right person.

THE FDA

Finally, the Food and Drug Administration (FDA) has the responsibility to protect us through regulation of new medicines and new devices.

The FDA is well aware of the current level of accuracy in glucose determinations by CGM. It may thus be several years before the FDA will allow a CGM to control insulin administration from a pump. However, there will likely be partial approvals along the way. For example, the FDA might approve reduced or discontinued pump insulin delivery with pending hypoglycemia. This could add to the safety of people with diabetes with very little risk. It would be the start of the partial bionic pancreas. It is likely that the second area approved would be in the control of basal insulin rates. This might initially be during the nighttime hours when food, exercise and other factors are not affecting glucose levels. This could be particularly helpful in preventing extended periods of high blood sugars.

THE FUTURE IS NOW: USE OF AN INSULIN PUMP AND A CGM

Good glucose control NOW is important in the prevention of later diabetes complications. It is essential to do all that a person/family is able to do to reach or maintain good diabetes control. Taking the approach that a bionic pancreas or a transplant or other help is just around the corner and so one can put off doing all that is possible NOW is an error.

People will ask, "Why include insulin pump therapy and use of a continuous glucose monitor (CGM) in the same book?" The answer is easy. They complement each other tremendously and together provide the optimal diabetes care that is currently available. The problems with insulin pumps used alone (although generally better than multiple daily injections) have been presented in earlier chapters. They include suboptimal glycemic control, cannulas dislodging, missed food boluses and continued episodes of hypoglycemia. The latter remains the number one fear of people/families with diabetes. The use of a CGM along with an insulin pump can be helpful with all of these issues. One should not wait for future developments. The future is NOW and it includes use of both insulin pumps and continuous glucose monitors.

SUMMARY

The total bionic pancreas will not be available in the near future. However, it is likely that individual components will be added gradually. In the meantime, the independent use of an insulin pump and a continuous glucose monitor can do much to improve diabetes management.

DEFINITIONS

Algorithm: A formula to increase, decrease, or discontinue insulin delivery based on glucose levels done by the continuous glucose monitor (CGM).

Bionic pancreas/closed loop pancreas: A system in which a continuous glucose monitor (CGM) communicates with an insulin pump to regulate all insulin delivery.

Insulin sensitivity: How sensitive a person is to insulin. Some people reduce their blood sugar level with a low dose of insulin (more insulin sensitive) while others require a higher dose (less insulin sensitive).

REFERENCES

18. Davis, EA, et al, Diabetes Care 20; 22, 1997.

19. Buckingham, B, Chase, HP, et al, Diabetes Tech. and Ther. 7; 440, 2005.

YES! SOMEDAY A BIONIC PANCREAS!