the cells that need it, insulin levels gradually drop. But blood glucose levels drop, too, which once again stimulates hunger.

Recall from Chapter 2 that hyperinsulinemia is often associated with obesity. This occurs both as a response to high carbohydrate consumption and as a consequence of insulin resistance resulting from enlarged fat cells. When insulin resistance occurs, hyperinsulinemia worsens.

There are insulin receptors in the hypothalamus, and insulin can cross the blood–brain barrier. In the laboratory, high glucose and insulin levels in the ventromedial hypothalamic nucleus cause animals to gradually slow, and finally stop, eating. Increased food intake can occur for two insulin-related reasons: (1) high insulin levels coupled with low blood glucose, which might occur in hyperinsulinemia or type 2 diabetes, stimulates eating, and (2) low insulin levels (and low blood glucose) have been shown to increase synthesis of neuropeptide Y in the hypothalamus, resulting in increased intake.[13] Table 5-1 summarizes these effects.

Insulin may also play a role in restoring the set point after people lose weight through calorie restriction. When enlarged fat cells shrink in response to dieting, plasma insulin levels become more normal. This may lower insulin binding in the hypothalamus, which will promote the production of neuropeptide Y. The result: increased food intake, which may rapidly restore the prediet fat cell size.

Summary

The digestive system helps regulate body weight through its role as receptor of information about hunger, appetite, and satiety, and its role as effector of appropriate responses. The taste and the smell of food bring you to the table and keep you there until satiety signals from elsewhere in the digestive system slow and finally halt eating.

Physical characteristics of the stomach and the small intestine could promote weight gain or weight maintenance in susceptible people. Some obese individuals and binge-eaters may be able to ingest more food than nonobese or normal eaters. In addition, a lack of functioning CCK receptors in the brain could prevent this duodenal peptide from doing its job—inducing satiety.

Insulin has a broader and more complex role. Insulin secretion increases after a meal or in response to signals from the brain. High levels of insulin cross the blood–brain barrier and promote satiety but, under certain conditions, may induce hunger, such as when insulin levels are high and blood glucose is low (type 2 diabetes) or when both insulin and glucose levels are low (food deprivation). The resultant consumption of excess calories could promote weight gain.

Application 5.1 The Obese Family, Part 1

Mr. and Mrs. Rhys are both obese. Mrs. Rhys has a BMI of 35 and recently developed type 2 diabetes. Mr. Rhys has a BMI of 33 and takes medication for high blood lipids and hypertension. They are worried about their 7-year-old son, Joey, who is in the 97th BMI percentile.

Everyone in the family loves to eat. On a typical busy evening, one parent stops at a pizza restaurant on the way home and brings in two large pizzas for dinner. No one stops eating until both pizzas are gone. And by 8:30 P.M. at least one family member is foraging for cookies in the kitchen.

- Consider the potential roles of the brain and digestive system in this behavior.
- Are there strategies that the Rhys family could take to reduce the impact of physiological factors on eating behavior?

There may also be genetic influences on the effectiveness of various diets in promoting weight loss. Stanford University researchers analyzed DNA from 101 overweight women for genes needed to metabolize fats and carbohydrates and classified women as having a low-carbohydrate diet responsive genotype, a low-fat diet responsive genotype, or a balanced diet responsive genotype. These women were previously in a 2005 study that examined the effectiveness of several low-fat or low-carbohydrate diets in reducing weight over 1 year. In that study women were randomly assigned to the Atkins, Zone, Weight Watchers, or Ornish diets. While adherence to the diets was low, those who stuck with the program for a year lost small amounts of weight, and there were no noticeable differences between diets. After the researchers reanalyzed 2005 study findings with information about genotype, they reported at an American Heart Association conference in March 2010 that women who had been in the diet group that matched their genotype lost two to three times more weight than women who followed a diet that did not match their genotype.[39]

Genetic Influences on Food Choice

Most food choices are based on learned preferences for the flavor, texture, temperature, and appearance of various foods. If there is any hereditary influence on food choice, then it is more likely related to nutrient intake than to eating specific foods. In other words, people may inherit a preference for carbohydrate but probably do not inherit a preference for specific carbohydrate-containing foods (like spaghetti instead of potatoes).

This chapter has already discussed several neuropeptides that may regulate nutrient intake. Neuropeptide Y, for example, seems to entice people to eat more carbohydrate foods, whereas agouti gene–related protein, melanin-concentrating protein, and galanin are associated with overconsumption of high-fat foods. So any genetic factors that influence the neuropeptides might explain genetic influences on food choice.

Application 5.2 The Obese Family, Part 2

The Rhyses recently read about a family obesity study in which all family members would undergo genetic testing and counseling. The study is looking at several "obesity genes," including the MC4R receptor. The family attended an information session at the university that was conducting the research with funding from a federal agency. They learned that they would all undergo several medical tests, as well as genetic testing. After being informed in more detail about the risks and benefits of the study, Mr. and Mrs. Rhys signed informed consents. Joey also received information about the study, and both he and his parents signed his consent form. All procedures were consistent with university and federal requirements for research involving human subjects.

Do some reading about genetic testing guidelines (both the American Academy of Pediatrics and American Medical Association have guidelines) and specifically about the MC4R gene.

- How is this type of genetic testing done? Is it painful or invasive?
- Consider some of the issues that arise when parents decide for a child that he or she should undergo genetic testing.
- Do the benefits of learning about one's MC4R gene status outweigh the risks of having such information?
- Should Joey be informed about the results of his genetic testing? Should others in the Rhys family be informed?
- How do you think the outcome of genetic testing might affect Joey's psychological status, self-esteem, and future health risks?