Learning Objectives

At the conclusion of the activity, the learner will be able to:

- Describe the pathophysiology of diabetes.
- Describe the use of both fasting and post-prandial glucose levels to assess glucose control.
- Explain the risks of uncontrolled post-prandial hyperglycemia.
- Identify medications that can be used to decrease post-prandial glucose levels per the ADA guidelines.
- Discuss basic characteristics of currently available post-prandial medications including mechanism of action, administration, common adverse effects, advantages, and disadvantages.
- Design an evidence-based medication regimen for a patient with post-prandial hyperglycemia.

Post-test Rationale

1. The initial core pathophysiologic defect of type 2 diabetes is:
   a. Beta-cell destruction
   b. Decreased glucagon secretion from the pancreas
   c. Increased insulin resistance***
   d. Increased urinary glucose excretion

Correct Answer: C
The initial, core pathophysiologic defect in T2D is insulin resistance in the muscle, liver, and adipocytes, leading to impaired glucose uptake into cells after meals and increased hepatic glucose output. This is followed initially by increases in pancreatic insulin secretion and later by beta-cell destruction, increases in glucagon secretion, and increased renal glucose reabsorption threshold.

2. Which of the following statements accurately describes the contribution of fasting plasma glucose (FPG) and postprandial glucose (PPG) on A1C?
   a. FPG and PPG contribute equally at all A1C levels
   b. FPG contributes more as the A1C increases***
   c. PPG contributes more as the A1C increases
   d. PPG contributes more at all A1C levels

Correct Answer: B
The A1C level reflects an average glucose over a 3 month period with contribution of both FPG and PPG levels. The relative contribution of these components varies depending on the degree of hyperglycemia. As A1C levels increase, there is more contribution by FPG; as A1C levels approach normal levels, there is more contribution by PPG.
3. Which of the following treatment goals is recommended by the American Diabetes Association?
   a. 1-hour PPG < 140 mg/dL
   b. 2-hour PPG < 140 mg/dL
   c. 2-hour PPG < 180 mg/dL
   d. 2-hour PPG < 130 mg/dL

   Correct Answer: C
   The American Diabetes Association recommends a goal PPG of < 180 mg/dL 1-2 hours after meals.

4. Which of the following statements is correct regarding the risks of postprandial hyperglycemia?
   a. Postprandial hyperglycemia has been associated with increased cardiovascular mortality
   b. FPG is a better predictor of cardiovascular mortality compared to PPG
   c. Long term studies have consistently shown that lowering PPG reduces the risk of cardiovascular mortality
   d. Postprandial hyperglycemia does not appear to increase the risk of long term diabetes complications

   Correct Answer: A
   Increasing evidence confirms an independent association between PPG and overall mortality, cardiovascular mortality, heart disease, and microvascular complications. Some data indicate that elevations in PPG may be a better predictor of cardiovascular mortality than FPG elevations. There remains, however, a need for consistent evidence that lowering PPG levels reduces the risk of long term complications.

5. Which of the following medications primarily targets PPG?
   a. Glyburide
   b. Metformin
   c. Pioglitazone
   d. Nateglinide

   Correct Answer: D
   Metformin and pioglitazone primarily target FPG and have little direct impact on PPG levels. Sulfonylureas increase insulin secretion and thus lower both FPG and PPG indiscriminately, but because of their slow onset of action, they do not impact first phase insulin secretion. The meglitinides have a faster onset and shorter duration of action compared to sulfonylureas and target PPG.

6. Which of the following medications lowers A1C by slowing the rate of carbohydrate absorption in the small intestine?
   a. Repaglinide
   b. Acarbose
   c. Linagliptin
   d. Canagliflozin
Correct Answer: B
Acarbose is an alpha-glucosidase inhibitor that lowers PPG by slowing the rate of carbohydrate absorption in the small intestine. Repaglinide increases insulin secretion from the pancreas. Linaglaptin is a DPP-4 inhibitor which increases physiologic levels of GLP-1 and GIP, thus increasing insulin secretion and decreasing glucagon secretion. Canagliflozin is an SGLT-2 inhibitor and increases urinary glucose excretion.

7. Which of the following medications that targets PPG has the lowest risk of hypoglycemia?
   a. Regular human insulin
   b. Insulin aspart
   c. Repaglinide
   d. Exenatide***

Correct Answer: D
Exenatide, a GLP-1 receptor agonist, has a low risk of hypoglycemia because it increases insulin secretion from the pancreas in a glucose-dependent manner. Repaglinide increases insulin secretion from the pancreas in a glucose-independent manner and thus has a higher risk of hypoglycemia. Prandial insulins such as regular human insulin and rapid-acting insulin analogs have the highest risk of hypoglycemia.

8. Mr. Parker is a 59-year-old obese man with type 2 diabetes for 12 years. He takes metformin 1000mg twice daily and insulin glargine 36 units subcutaneously once daily. His A1C today is 7.9%. He self-monitors his blood glucose levels in the morning before breakfast. His average FPG is 118 mg/dL. Which of the following plans is most reasonable?
   a. Increase insulin glargine to 40 units subcutaneously once daily
   b. Start an alpha-glucosidase inhibitor
   c. Start a sulfonylurea
   d. Start a GLP-1 RA***

Correct Answer: D
The patient case illustrates a scenario where the patient has achieved the FPG target of 80-130 mg/dL but still has an elevated A1C. The glucose profile abnormality is likely increased PPG levels and a medication that targets PPG, with low risk of hypoglycemia and beneficial effects on weight should be considered. A GLP-1 RA is recommended by the ADA and AACE in this situation. Alpha-glucosidase inhibitors lower PPG but have modest impacts on A1C and have high rates of GI AEs. Sulfonylureas do not specifically target PPG and also cause weight gain and hypoglycemia. The FPG target has been reached, so increasing insulin glargine will not achieve A1C goals and may increase the risk of hypoglycemia.