A Short Course on Diabetes Mellitus
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2.0 Hours

Learning Objectives

1. To learn about the two principal hormones involved in the regulation of blood glucose levels
2. To review the criteria for properly diagnosing Diabetes Mellitus
3. To learn about Type 1 and Type 2 Diabetes Mellitus
4. To learn about the various management options for Diabetes Mellitus

Diabetes Mellitus is commonly defined as "a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both."1 This disease can cause significant damage to many organ systems throughout the body resulting in dramatic loss of quality of life for many patients. Chronic hyperglycemia results in fats and proteins causing widespread damage throughout the body. This elevated blood sugar eventually causes damage to the eyes, kidneys, nerves, heart and blood vessels. As optometrists, we have an ever-growing role in the management of our patients’ health. This is especially apparent in patients with diabetes mellitus where managing this disease often involves interaction with the patient’s primary care physician and/or nutritionist. Let’s discuss the role we can all play to improve the clinical outcome for this disease for our patients.

Pathophysiology

Blood glucose levels are largely regulated by two hormones – glucagon and insulin – which are respectively secreted by the alpha and beta cells of the islets of Langerhans of the pancreas. These hormones have antagonistic roles in the body. In lay man’s terms, insulin tells your body to use the food recently consumed for energy while glucagon tells your body to dip into reserves for energy. By maintaining a homeostatic mechanism involving glucagon and insulin, the body is able to keep a certain blood glucose concentration.

Insulin is secreted into the blood stream shortly after a person ingests food, particularly one rich in carbohydrates. In the first phase, a small burst of insulin is released and functions to decrease the coming postprandial elevation in glucose caused by the food intake. The second phase is a more sustained insulin secretion and directly proportional to blood glucose concentration. This biphasic release is commonly called a "bolus" secretion of insulin.2 There is also a "basal" level of secretion which occurs as a low level continuous secretion of insulin and functions to counteract ongoing daily hormonal influences. The main function of insulin is to help glucose travel from the blood and into the cells where it is converted into energy. Excess glucose is converted to either glycogen, which is stored in
the liver or muscle, or stored as fatty tissue. Thus, the net effect of insulin is to lower blood glucose concentration.

Conversely, alpha cells secrete glucagon maximally during fasting states. The overall effect of glucagon is to free up energy reserves by one of three mechanisms: glycogenolysis (breakdown of stored glycogen in the liver to make glucose); gluconeogenesis (conversion of non-glucose substrates into glucose); and glucose sparing (a process in which ketones are formed in the liver). Thus the net effect of glucagon is to elevate blood glucose concentration.

**Classifications**

DM was traditionally classified as type 1 insulin-dependent (IDDM) and type 2 non-insulin-dependent (NIDDM), which were also called juvenile-onset and adult-onset diabetes, respectively. Although we still use the terms type 1 and type 2 diabetes, we rarely use the terms IDDM and NIDDM. One of the chief reasons for this is that a relatively large percentage of patients with type 2 diabetes use insulin to maintain proper control over blood glucose levels.

**Prediabetes.** This is an intermediate category of patients with elevated blood glucose levels but who do not meet diagnostic criteria for either Type 1 or Type 2 diabetes. These intermediate categories include impaired fasting glucose (IFG) and impaired glucose tolerance (IGT). Patients with IFG or IGT are at high risk for developing Type 2 diabetes.1

**Type 1 DM.**

Type 1 DM accounts for approximately 10 percent of all diabetes. Patients with type 1 are typically young, thin and undergo a progressive loss of endogenous insulin leading to hyperglycemia. The mechanism behind this progressive loss is believed to be an autoimmune reaction involving destruction of beta cells. Recent evidence suggests that environmental factors may help trigger this autoimmunopathy. Viruses, such as rubella, Coxsackie’s B and mumps, are possible triggers for beta cell destruction. Exposure to cow’s milk (due to cross-reaction of beta cell protein and the albumin in cow’s milk) has also been implicated.3

These patients are often diagnosed after they experience an abrupt onset of symptoms. The classic triad of symptoms includes the 3 P’s: Polydipsia (increased thirst), Polyphagia (increased hunger) and Polyuria (increased urination). Since these patients eventually lose the ability to make any insulin, they are highly prone to ketoacidosis, a life-threatening complication that results from severe insulin deficiency. If left untreated, this condition can result in diabetic coma and death.

**Type 2 DM.**

Type 2 diabetes is the more common form, accounting for 90% of the total disease population. Hyperglycemia in these patients is caused by insulin resistance – a lack of effect on target cells. When this patient eats a meal, there is still some insulin secretion, but at reduced levels. Over time, the body cannot make enough insulin to meet the metabolic needs. As a result, plasma glucose levels rise and eventually become toxic to the pancreas (i.e. glucose toxicity) and lead to an inadequate insulin secretion response.

Type 2 DM typically occurs in people who are over 40 years old, are obese and/or have a family history of diabetes. Unlike Type 1 diabetes where the symptoms are pronounced, the onset of type 2 diabetes is gradual and is often found in asymptomatic patients during routine physical examinations when their laboratory work shows elevated blood glucose levels or when a urine test demonstrates a spill over of glucose. Other patients may experience a gradual onset of polyuria, polydipsia or polyphagia.4
**Gestational Diabetes Mellitus**

This condition, which occurs in 4% of all pregnancies, is defined by any degree of glucose intolerance with first onset in a pregnant woman. This term is not used for a woman who suffered from diabetes mellitus prior to pregnancy. Risk factors include obesity, positive family history of diabetes, and being of Hispanic, Asian, Native American or African-American descent. Screening for gestational diabetes usually occurs in the 24th to 28th week of pregnancy. If diagnosed, management can range from strict diet-control to medical therapy. In most cases, glucose levels normalize after delivery. In rare cases, it may not and the patient may develop diabetes indefinitely.

**Diagnosing DM**

We commonly think of diabetes mellitus as a disease associated with elevated blood glucose levels, but there are specific guidelines for screening patients suspected of having diabetes. For example, individuals with polyuria, polydipsia, polyphagia, blurred vision, dry itchy skin, repeated infections like yeast vaginitis, or impotence are commonly screened for diabetes. In the elderly, unusual tiredness and weight loss may be early symptoms so the risk for these patients should be evaluated as well.

To screen patients for diabetes, doctors often ask patients the following questions when taking medical histories:

1. Do you have a first-degree relative (sibling, parent, child) who has diabetes? If the patient answers "yes," this means he is genetically predisposed to developing the disease.
2. Have you recently given birth to a baby weighing more 9 lbs? If the patient answers "yes," this means she is at high risk for diabetes because women with elevated blood sugar tend to have large babies.
3. Were you diagnosed with gestational diabetes during your pregnancy? If the patient answers "yes," this is important because women who've suffered from gestational diabetes are more likely to develop diabetes later in life.
4. Do you have hypertension? If the patient answers "yes," this is important, as patients who have hypertension are at higher risk for developing diabetes.
5. Do you have high cholesterol? If the patient answers "yes," this is significant, as a high-density lipoprotein level of 35mg per (deciliter) dL (0.90mmol per L) or lower and/or a triglyceride level of 250mg per dL (2.83mmol per L) or higher puts a person at great risk for diabetes.
6. Have you been experiencing an increase in thirst (polydipsia)?
7. Have you been experiencing an increase in appetite (polyphagia)?
8. Have you been urinating more frequently (polyuria)?

Although there is some variability in screening criteria, many practitioners routinely screen any patient over the age of 45 and, if normal, repeat this screening at three-year intervals. Patients are tested at an earlier age or more frequently if one or more of the following criteria are met:

- Obesity (120% of desirable body weight or greater, or a body mass index of 27kg per m2 or more)
- A first-degree relative with diabetes mellitus
- African-American, hispanic or Native American decent
- Women who have delivered a baby weighing more than 4,032g (9lb), or who were diagnosed with gestational DM during pregnancy
- Hypertension

A high-density lipoprotein level of 35mg per dL (0.90mmol per L) or lower and/or a triglyceride level of 250mg per dL (2.83mmol per L) or higher.

The definitive diagnosis of DM is made on the basis of any one of the following criteria 5:
1) Elevated plasma glucose (greater than 200 mg/dL or 11.2 mmol/L) along with the classic signs and symptoms of diabetes in addition to unexplained weight loss (type 1) or obesity (type 2).

2) A fasting plasma glucose (FPG) value of 126 mg/dL (7.0 mmol/L) or greater on at least two separate tests.

3) Oral glucose tolerance test values at 2 hours and at least one other sampling during the exam greater than 200 mg/dL.

Fasting plasma glucose (FPG) is the most common test and is done after the patient fasts for at least 8 hours. This is usually done in the morning hours before a patient has breakfast. It is one of the quickest and easiest ways to measure a patient’s blood glucose levels. Plus, it doesn’t fluctuate as much as readings taken at other times during the day. Another common diagnostic test is the oral glucose tolerance test. In this test, the patient ingests a 75 g glucose load dissolved in water and has their blood glucose levels checked after 1 and 2-hour intervals.

The presence of glucose (and sometimes ketone bodies) in the urine and elevated glycosylated hemoglobin (HbA1c) are also useful diagnostic tools. Hb Alc is formed by the glycosylation of hemoglobin by blood glucose. It is believed that this link is a function of the tightness of glycemic control. Because glycated hemoglobin levels are highly correlated to adverse clinical outcomes like retinopathy, this test is commonly used to monitor glycemic control in patients with diagnosed diabetes. Hb Alc levels rise when blood glucose levels have been elevated over the previous 1-3 months. Normal Hb Alc levels are 5.05+/-.050. This value is also used in patients with diabetes as a measure of the long-term stability of the blood glucose concentration. Many practitioners prefer for this value to be 7.0 or less for their diabetic patients.

In most cases, this test is not used in the initial diagnosis because there is currently no agreement on standardization. So, a variety of measurement methods and normal ranges are utilized. The major advantage to using glycated hemoglobin is that the specimen can be collected regardless of when the patient last ate.

**Treatment of Diabetes**

**Goals of Therapy**

The obvious goal in managing patients with diabetes mellitus is to decrease blood glucose levels to normal. A secondary goal is to decrease the range of fluctuation in blood glucose levels in a 24-hour period. Although there are individual variations on what those exact values should be, glycemic control guidelines are based principally on two studies: the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS). The Diabetes Case Control Trial studied 1,441 patients with type 1 diabetes and found a decreased risk of complications in those patients who exerted tight glycemic control—frequent blood glucose monitoring, plus an external insulin pump or 3-4 daily insulin injections—compared to those patients who practiced conventional therapy (1-2 daily insulin injections). For example, the risk of developing diabetic retinopathy was lowered by 76%, diabetic nephropathy and neuropathy, 60%; microalbuminuria, 39%; and albuminuria, 54%. The UK Prospective Diabetes Study, looked at 3,867 newly diagnosed patients with type 2 diabetes, and found similar results. This study found a decrease in the risk of microvascular complications in patients who maintain their hemoglobin A1c at normal levels.

**Self-Monitoring**

As with many other diseases, the patient is an integral part of managing the disease. In the case of diabetes, many patients are educated to check their own blood glucose levels. This self-monitoring of blood glucose (SMBG) is one of the most important aspects of managing their condition. The rationale behind this concept is that blood glucose levels are constantly...
changing depending on medical treatment and other lifestyle factors. These include when, what, and how much a patient eats, when they exercise and sleep, other medications a patient may take, stress, etc. It is impractical for a patient to visit the doctor every day or multiple times a day to check the status of their blood glucose. Instead, there are many commercially available self-monitoring devices which allow patients to safely and accurately test their blood at home. What most patients do is keep a log of their blood glucose values and take that log to their doctor visits so that the physician may view the results.

When and how often should a patient test their blood glucose? Unfortunately, there is no one right answer to this question. Much of the answer depends on the severity of disease, the patient’s lifestyle and ability for compliance, the type of diabetes a patient has, and the philosophy of the practitioner. For example, patients with diet-controlled diabetes may check their blood glucose levels every month or so. Patients on oral medications often check their blood sugar once or twice a day. Patients taking insulin often check their blood glucose multiple times a day.

**Treatment of Type 1 DM**

Since patients with Type 1 DM suffer from relative or absolute loss of insulin, these patients have no choice but to utilize insulin injections. Insulin therapy regimens vary greatly among patients based on their clinical condition, their meal times, exercise schedule, and waking/sleeping patterns. In most cases, patients self-adjust their insulin dosage based on their blood glucose level and daily schedule.

Clinicians generally use these three therapeutic approaches to insulin therapy: 1. Conventional therapy. This involves one or two daily injections of intermediate acting insulin either alone or in conjunction with rapid acting insulin. 2. Multiple subcutaneous injections. This technique requires a rapid-acting insulin prior to each meal and either intermediate or long-acting insulin at bedtime. The advantage, of course, is tighter glycemic control than conventional therapy. Continuous subcutaneous insulin infusion. This involves a battery-powered insulin pump to inject insulin into the abdominal wall. A basal rate of insulin infusion occurs throughout the day with additional amounts delivered before each meal. The patient usually checks his or her glucose level before eating, and programs the insulin pump accordingly. Many patients will also check their glucose level 2 hours after the meal to make sure that the levels are consistent. This method provides the tightest glucose control, but also the greatest risk of inducing hypoglycemia (when the blood glucose drops below 70 mg/dL). Common symptoms of hypoglycemia include shakiness, sweating, tingling lips, irritability, hunger and fatigue. Common causes of hypoglycemia include taking too much medication, eating less food than normal, or getting more exercise than usual. If the blood glucose continues to drop without treatment, loss of consciousness, coma, and even death can occur.

Human insulins are produced by recombinant DNA technology and are the most widely used insulins today. Insulins available from animal sources generally induce more allergic reactions, have a less predictable activity profile, and may induce antibody formation. The most common concentration of insulin used is U-100 (100 units of insulin per mL). If needed, there is also a rarely used variation -U-500 (500 units of insulin per mL).

**Description of insulins**

Insulin is broken down into three basic categories – short acting, intermediate, and long acting. Short-acting insulin, such as insulin lispro, insulin aspart begin to work about five minutes after injection, peaks in one hour, and works for two hours to four hours.

Meanwhile, regular insulin (also called a short-acting insulin) reaches the bloodstream in thirty minutes after injection, peaks in two to three hours and lasts from three to six hours. Due to the long peak time, the glucose levels will
typically rise after a meal before the regular insulin can be fully absorbed. Furthermore, the body is exposed to high levels of insulin due to the longer duration of action of regular insulin. This often results in between-meal hypoglycemia, necessitating the need for snacks. This can be a problem for the overweight diabetic patient trying to lose weight.

The intermediate-acting insulins, NPH and Lente, reach the bloodstream two to four hours after injection, peak four to twelve hours later, and last for approximately 12 to 18 hours. These insulins are commonly used in combination with a short-acting insulin. Generally, two or more injections of NPH or Lente are required to cover basal insulin needs in patients with Type 1 diabetes.

The long-acting insulin, Ultralente, reaches the bloodstream six to ten hours after injection and is effective for 18 to 24 hours. It is often used in combination with a rapid or short-acting insulin as the basal insulin.

Insulin mixtures (Short or rapid insulin mixed with intermediate acting insulin) include 70% NPH and 30% regular mixture and a mixture of 50% NPH and 50% regular insulin. Also available is a mixture consisting of 75% insulin lispro protamine suspension and 25% insulin lispro (known as Humalog® Mix 75/25®). This mixture combines the rapid onset of lispro with the prolonged action of an intermediate-acting insulin.

**Treatment of Type 2 DM**

Although many patients in this category use oral medications and even insulin, the cornerstone of therapy for type 2 DM is proper nutrition, weight loss and exercise. Patients must attain and maintain ideal body weight, reduce intake of fats, increase intake of high fiber carbohydrates (e.g., bran, beans, fruits and vegetables), reduce intake of refined sugars and salt and restrict alcohol consumption. Meals should be spaced evenly and incorporated into a regular daily routine. According to the American Diabetic Association Clinical Practice Guidelines, 60 to 70 percent of caloric intake should come from monounsaturated fats and carbohydrates, 10 to 20 percent from protein, and less than 10 percent from saturated and polyunsaturated fats. In addition, the daily intake of cholesterol should be less than 300 mg.10,11 This change in lifestyle is what makes management of diabetes so complicated. Proper management is not as easy as swallowing a pill or taking an injection.

**Oral Antihyperglycemic Therapy**

Five different oral drug classes are available for the management of Type 2 diabetes. In many cases, patients with Type 2 patients cannot adequately maintain long-term glycemic control with a single agent. For that reason, it is not unusual to have patients on multiple medications or a combination of oral medications and insulin therapy.

**Sulfonylureas**

Sulfonylureas (SU) glibenclamide (Daonil, Euglucon), gliclazide (Diamicron), glimepiride (Amaryl), glipizide (Glibenese, Monodiab), gliquidone (Glurenorm) and tolbutamide. Sulfonylureas work by binding to receptors on the pancreatic b-cell, causing a cascade of reactions leading to insulin secretion. The two most common side effects of sulfonylurea therapy are weight gain and hypoglycemia.12 These drugs are metabolized by the liver and eliminated renally so they should be used cautiously in patients with liver and/or kidney disease.

**Meglinitides**

The mechanism of action of the two metiglinides, repaglinide (Novonorm, Prandin®) and nateglinide (Starlix®), is very similar to the SUs: stimulation of pancreatic insulin release. The difference is that Meglinitides have a shorter half-life, which results in brief stimulation of insulin release. These medications are taken at each meal to decrease postprandial blood glucose. This is
beneficial to patients with erratic meal schedules but this may also limit compliance. These medications act as bolus agents, similar to the use of lispro or aspart insulins in Type 1 diabetic patients. The drawback to their use is that there is limited data on their long-term effectiveness in decreasing microvascular or macrovascular risk in diabetic patients. The side effects of the meglinitides are similar to the sulfonylureas, but less pronounced. Meglinitides also are hepatically metabolized and renally cleared, so caution is needed in patients with hepatic or renal impairment.

**Biguanides**

Metformin is the only biguanide clinically available in its original form as Glucophage and with two alternative formulations - Glucovance®, a combination product containing metformin and glyburide (a sulfonylurea), and an extended release formulation, Glucophage XR®. It lowers blood glucose primarily by inhibiting hepatic glucose production and secondarily by enhancing peripheral muscle glucose uptake. Metformin also helps to combat insulin resistance, which may help decrease the risk of cardiovascular disease. Metformin provides other benefits, such as decreasing lipid levels (low density lipoprotein cholesterol and triglycerides). An overweight subgroup of the UKPDS experienced a 39 percent reduced risk of myocardial infarction and a 30 percent reduction of all macrovascular complications with metformin therapy.13.

Metformin therapy is associated with weight loss, but the most common adverse effects are abdominal pain, nausea and diarrhea. Pharmacists can educate patients to take this medication with food to decrease these adverse reactions. Relative contraindications for metformin therapy are hepatic and/or renal impairment, congestive heart failure requiring pharmacologic therapy, metabolic acidosis, dehydration and alcoholism.

**α-Glucosidase Inhibitors**

α-Glucosidase enzymes, which are found in the small intestinal epithelium, break down complex starches into oligo- and monosaccharides and glucose, which are more easily absorbed. The medications, acarbose (Precose®) and miglitol (Glycet®), inhibit these enzymes which delay carbohydrate absorption. By doing so, they function to decrease the postprandial glucose elevation. They have little or no effect, however, on fasting glucose levels.

Side effects of therapy include gastrointestinal side effects such as flatulence and bloating due to undigested carbohydrate in the intestines. Titrating the dose slowly and avoiding large amounts of starchy foods can help alleviate these symptoms. This class of medications should not be used in patients with inflammatory bowel disease, colonic ulceration, any degree of intestinal obstruction or in patients with malabsorption disorders. 14.

**Thiazolidinediones**

There are two chief drugs in this class, pioglitazone and rosiglitazone (Actos® and Avandia®). They both work by increasing insulin sensitivity and increasing glucose utilization in peripheral tissues, mainly in muscle and fat. Their novel mechanism of action is not completely understood, but they may also help suppress glucose synthesis in the liver. The package literature indicates that this drug may help decrease plasma insulin and triglyceride levels, cause an increase in HDL cholesterol, and decrease lipid oxidation. It may also lead to a favorable redistribution of body fat, and decrease in vascular resistance, thereby improving endothelial cell function of blood vessel walls.

Thiazolidinediones can promote weight gain and fluid retention, particularly in combination with insulin therapy. There have also been some reported cases of anemia. Until the risk of liver injury from this drug class is fully realized, it should be avoided in susceptible patients. These drugs are approved as monotherapy and for combination therapy with sulfonylureas and metformin.
Clinical Pearls for Optometrists

- When discussing medications to diabetic patients, try to take the extra time to educate them on what to expect with the medication in terms of side effects, etc. In addition tell them when is the best time to take the medication and whether it should be taken with food or on an empty stomach, etc. By teaching patients how to evaluate their own situations, we empower them to part of managing their condition. Doing so will allow them to better take care of themselves which will ultimately enhance their clinical outcome and improve the quality of their life.

- Educate your patients on the signs and symptoms of both hypoglycemia or hyperglycemia. A blood sugar that is too high or too could place the patient at greater risk of complications and ultimately negatively effect their health. In some cases, this education may involve telling patients to carry a piece of candy and/or emergency dose of insulin to account for a rapid fluctuation in glucose levels.

- Tell your patients about new computer software which helps identify patterns in blood glucose levels. In some cases, it will help the patient or their doctor identify trends such as gradual drift in blood glucose levels over time, or glucose levels are they consistently high after eating a certain food or beverage, or are they too high or too low at certain times of the day. The more a patient knows about why changes occur in glucose levels, the more control they will have.

- Being a good primary care provider sometimes involves doing the little things.
  - Always keep up to date on new medications and new medical technology. In the field of diabetes, in particular, there are new concepts or products released frequently.
  - Ask patients about their fingertips. If there is a problem, suggest using the sides of the fingers or changing the settings on the lancet device.
  - Constantly remind patients that properly managing diabetes involves compliance with medication and proper diet and exercise.

Don't Forget These

In recent years, we have learned of new diagnostic and management technologies for our patients with diabetes.

GlucoWatch

This device is an automatic blood sugar monitoring device which is worn much like a wristwatch. It is about the size of a pager. This monitoring device actually analyzes your perspiration to indirectly calculate the blood sugar. The chief advantage is the dramatically reduced need for finger sticks and providing an almost constant blood sugar reading. Newer models can also sound an alarm when your blood sugar drops to a certain level. One of the disadvantages is that the device has a 3-hour warm up time and a 20-minute lag between readings. It must be changed and calibrated every 12 to 15 hours.

Implantable insulin pumps

These are surgically implanted disks that weigh 6 oz to 8 oz. Typically, a pump is implanted on the right side of a patient’s abdomen so that it delivers insulin directly to the liver. It delivers a constant, or basal, dose of insulin, which can be manually adjusted with the use of a remote control.

Insulin patch.

These are experimental but the concept is that a patch is placed on your skin, usually on your arm, where it delivers a constant low dose of insulin. If additional insulin is needed, the
patient can remove a tab on the patch to expose the skin to more insulin or use other forms of therapy to supplement. While the patch provides a very convenient, painless method of insulin delivery, insulin does not travel through the skin easily.

As primary care optometrists we have the opportunity to dramatically improve the quality of life for our patients. By performing our roles as optometrists we can make our patients feel better, improve their diabetes control, and help prevent complications and allow them to live a more normal life. This is a chronic disease that the patient will have to deal with for the rest of his or her life. In addition to taking prescribed medications, the patient must constantly monitor diet and exercise in order to maintain proper glycemic control.

REFERENCES:

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QUESTIONS:

1. Which hormone or hormones are involved in the regulation of blood glucose levels?
   A. Aqueous humor
   B. Glucagon
   C. Vitreous humor
   D. Testosterone

2. Insulin is secreted by ________
   A. Alpha cells of the pancreas
   B. Beta cells of the pancreas
   C. Delta cells of the pancreas
   D. Gamma cells of the pancreas

3. Which hormone works to lower blood glucose levels?
   A. Glucagon
   B. Estrogen
   C. Testosterone
   D. Insulin

4. Which is an intermediate category of patients with elevated blood glucose levels?
   A. Type 1 DM
   B. Type 2 DM
   C. Gestational DM
   D. Pre-diabetes

5. Type I DM accounts for ________ % of the total diabetic population
   A. 5
   B. 10
   C. 15
   D. 20

6. Which of the following is NOT a classic symptom of diabetes?
   A. Polydipsia
   B. Polyphagia
C. Polyuria
D. Low blood glucose values

7. Screening for gestational diabetes usually takes place during what phase of pregnancy?
   A. 16th to 20th week
   B. 20th to 24th week
   C. 24th to 28th week
   D. 28th to 32th week

8. Normal glycoslated hemoglobin levels are
   A. 3.05
   B. 4.05
   C. 5.05
   D. 6.05

9. Glycoslated hemoglobin levels rise when the blood glucose levels have been elevated for
   A. 1 to 3 hours
   B. 1 to 3 days
   C. 1 to 3 weeks
   D. 1 to 3 months

10. Which of the following studies found that tight glycemic control of blood glucose levels decreased risk of complications?
    A. DCCT – the Diabetes Control and Complications Trial
    B. OHTS – the Ocular Hypertension Study
    C. The Finnish Diabetes Prevention Study
    D. The Diabetes Prevention Program

11. The principal source for insulin used in treatment is ________________.
    A. Pork
    B. Humans (recombinant DNA technology)
    C. Birds
    D. Insects

12. Which of the following is a long-acting insulin?
    A. Insulin lispro
    B. Insulin aspart
    C. Ultralente
    D. NPH

13. Which of the following is NOT a mixture of insulin on the market?
    A. 99% NPH and 1% regular
    B. 70% NPH and 30% regular
    C. 50% NPH and 50% regular
    D. 75% insulin lispro protamine suspension and 25% insulin lispro

14. Which of the therapeutic approaches offers the tightest glycemic control, but also the greatest risk for hypoglycemia?
    A. Oral Therapy
B. Conventional Insulin therapy  
C. Continuous subcutaneous insulin infusion  
D. Multiple subcutaneous insulin injections

15. What is the cornerstone of therapy for Type 2 DM? 
   A. Proper Nutrition, weight loss, and exercise  
   B. Oral Medications  
   C. Insulin Therapy  
   D. Surgical intervention

16. According to the ADA Clinical Guidelines, how much of the caloric intake for diabetic patients should be from protein? 
   A. 0 %  
   B. 5 to 10%  
   C. 10 to 20 %  
   D. 20 to 30%

17. Hypoglycemia occurs when blood glucose levels drop below ___________. 
   A. 140 mg / dL  
   B. 100 mg / dL  
   C. 90 mg / dL  
   D. 70 mg / dL

18. Repaglinide and nateglinide are both examples of what class of oral diabetic medications? 
   A. Sulfonylureas  
   B. Meglinitides  
   C. Biguanides  
   D. Thiazolidinediones

19. Metformin works primarily by ___________. 
   A. Inhibiting glucagon production  
   B. Inhibiting hepatic glucose production  
   C. Binding to insulin to decrease its concentration in the blood  
   D. Decreasing the half-life of insulin

20. Which drug class works by inhibiting the enzyme which breaks down complex starches? 
   A. a-Glucosidase Inhibitors  
   B. Biguanides  
   C. Meglinitides  
   D. Thiazolidinediones