

DIABETES MELLITUS FUNDAMENTALS: A REVIEW AND CURRENT UPDATE[©]

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Contact Hours: 4.0 (ANCC) and 4.8 (ABN) contact hours valid Nov. 8, 2019 – Nov. 8, 2021

Target Audience: Registered Nurses and Licensed Practical Nurses

Purpose/Goal: The purpose of this activity is to provide a basic comprehensive review of Diabetes Mellitus

Objectives: At the conclusion of this activity the learner should be able to:

1. Explain normal physiology and pathophysiology of Diabetes Mellitus.
2. List 4 cornerstones of Diabetes Mellitus and its effect on blood glucose.

Fees: ASNA Member - \$28.00 Non-Member - \$40.00

Instructions for Credit: Participants should read the purpose/goal and objectives and then study the activity on-line or printed out. Read, complete, and submit answers to the post-test at the end of the activity. Participants must complete the evaluation on line and submit the appropriate fee to receive continuing nursing education credit. **The certificate of completion** will be generated after the evaluation has been completed. ASNA will report continuing nursing education hours to the ABN within 2 weeks of completion.

Accreditation: *The Alabama State Nurses approved as a provider of **nursing continuing professional development** by The Mississippi Nurses Foundation, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation.*

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Virginia G. Miller, PHD, RN, FNP-BC

INTRODUCTION

This home study program provides information about diabetes mellitus. An explanation of normal and abnormal physiology is provided to enhance understanding of the condition. Learner activities are included where appropriate to provide experiential learning. A current and comprehensive reference list is also provided, as is an up-to-date list of useful resources for the health care provider and/or the person with diabetes. A glossary of terms is offered as are two appendices to help explain the pathophysiology of diabetes and the various activity profiles of different kinds of insulin.

PROCESS OF THE COURSE

It is recommended that the learner review the post-test first to determine what is already understood about diabetes and what needs to be learned. Afterward, the learner should read the content and participate in the learner activities included in the program. Then, the post-test should be completed. Last, the learner is asked to complete the evaluation form. In the past, improvements in the course have been made, in part, on the basis of this feedback, so the author is asking each learner to provide constructive feedback – both positive and negative.

COURSE OUTLINE

Introduction

- I. Unit I – Diabetes Mellitus – An Overview
- II. Unit II: Normal Physiology And Pathophysiology
 - A. Normal Physiology
 - B. Pathophysiology
 - C. Uncontrolled/Undiagnosed Diabetes
 - D. Types Of Diabetes – Detailed Descriptions
 - E. How To Diagnose Diabetes
 - F. Risk Factors For Diabetes
 - G. Waist Circumference, The Metabolic Syndrome, And Diabetes
 - H. History Of Diabetes And The Discovery Of Insulin
 - I. History Of The Development Of Insulin
- III. Unit III: Overview Of The Cornerstones Of Control Of Diabetes
 - A. Introduction
 - B. Four Cornerstones Of Control Of Diabetes
- IV. References
- V. Resources
- VI. Glossary
- VII. Appendix A – Pathophysiology Of Diabetic Ketoacidosis

INTRODUCTION

Diabetes is a chronic disorder predominantly of carbohydrate metabolism. Disorders of carbohydrate metabolism, however, ultimately influence protein and fat metabolism. Data collected in 2015 documented that there were an estimated 30.3 million people of all ages in the United States (9.4% of the population of the United States) who had all types of diabetes. Approximately 7.2 million of these (28.3%) were unaware of their condition and therefore, undiagnosed (National Center for Chronic Disease Prevention and Health Promotion-Division of Diabetes Translation, 2017).

The Centers for Disease Control and Prevention (CDC) indicated that in 2015 approximately 84 million Americans had pre-diabetes (FBG 100-125 mg/dL or A1c of 5.7% - 6.4% on two separate days), a condition which, if left untreated is likely to lead to diabetes. Like the above, a large percentage of these are unaware of their condition (National Center for Chronic Disease Prevention and Health Promotion-Division of Diabetes Translation, 2017). "Total diabetes prevalence (diagnosed and undiagnosed cases) is projected to increase...to 21% of the US adult population by 2050" (Boyle, Thompson, Gregg, Barker, & Williamson, 2010, pg. 1).

From the National Center for Chronic Disease Prevention and Health Promotion-Division of Diabetes Translation (2017):

- Diabetes is the leading cause of kidney failure, non-traumatic lower-limb amputations, and new cases of blindness among adults in the United States.
- Diabetes is a major cause of heart disease and stroke.
- Diabetes was the seventh leading cause of death in the United States in 2015.

Note the statistics published below in 2017 for the number of people diagnosed with diabetes. This reflects an "epidemic" of diabetes in this country! Can you think of explanations for it?

Prevalence of Diagnosed and Undiagnosed Diabetes in the United States, All Ages, 2015

- *Total: 30.3 million people—9.4 percent of the population — have diabetes.*
- *Diagnosed: 23.1 million people*
- *Undiagnosed: 7.2 million people*

(National Institute of Diabetes and Digestive and Kidney Diseases, 2017)

"Recently, type 2 diabetes has increasingly been reported in children and adolescents, so much so that in some parts of the world type 2 diabetes has become the main type of diabetes in children [as opposed to type 1 diabetes]. The global rise of childhood obesity and physical inactivity is widely believed to play a crucial role. Healthy eating and lifestyle habits are a strong defense against the disease" (WHO, 2017, What are the risks of diabetes in children?)

In a study published in the December, 2009 issue of *Diabetes Care*, the researchers reported the following dire predictions: "Between 2009 and 2034, the number of people with diagnosed and undiagnosed diabetes will increase from 23.7 million to 44.1 million" (Huang, Basu, O'Grady, & Capretta, 2009, p. 2225). Likewise, they forecasted expected effects on the nation's economy related to these anticipated changes: "The diabetes population and the related costs are expected to at least double in the

next 25 years. Without significant changes in public or private strategies, this population and cost growth are expected to add a significant strain to an overburdened health care system" (pg. 2225).

Any way the numbers are addressed, the world at large, and the United States specifically, faces significant increases in the numbers of people with diabetes. Along with these increases can be expected increased numbers of people suffering the complications of diabetes, not to mention the influence the disease and its complications will have on the economy. Another factor is the increase in type 2 diabetes among the children of the world which will no doubt ultimately be associated with an increase in complications of diabetes due to the longer period of time of having a major metabolic disorder.

UNIT I: DIABETES MELLITUS – AN OVERVIEW

Among those who have diabetes, approximately 90-95% have DMT2 and approximately 5-10% have Type 1 diabetes mellitus (DMT1). Gestational diabetes (GDM) – diabetes that occurs during pregnancy (ie in the 2nd or 3rd trimester), i.e. not overt diabetes -- is the third type of diabetes (American Diabetes Association (ADA), 2018, pg. S13). In light of the epidemic of obesity and, consequently, of type 2 diabetes in this country, it is reasonable to assume that the incidence of GDM will increase (ADA, 2018, pg. S20). While some aspects of treatment of individuals with diabetes are similar regardless of the type of diabetes, the causes of DMT2 and DMT1 differ significantly from one another. As a result, some aspects of treatment are quite different.

The basic problem in diabetes is the absence or reduced function of the hormone, insulin, in the body. This can be due to 1) the absence of insulin production, 2) inadequate insulin production, or 3) impaired utilization of insulin (insulin resistance). Insulin is important because without it the body cannot use glucose for energy. Glucose is the body's primary source of the energy needed for all bodily functions. Insulin moves glucose from the blood stream across the cell membrane and into the cell where glucose is made available for energy. In the absence of insulin (such as that which occurs in DMT1), the body cannot use glucose, so it resorts to less effective ways to obtain energy (e.g. the breakdown of fat), which results in toxic byproducts called ketones. Ketones appear in the blood (ketonemia) and are excreted in the urine (ketonuria) in the person who has no insulin (i.e. in DMT1).

With insulin resistance (DMT2), cells in the body resist the entrance of insulin across their cell membranes. Consequently, the blood glucose rises and stimulates the insulin-producing cells to produce more insulin (hyperinsulinemia). For a time, this satisfies the need, but the insulin resistance persists. The body tries (for as long as it can) to produce more insulin to meet the perceived deficit, but eventually, in spite of the resultant hyperinsulinemia, the blood glucose increases uncontrollably. Since the fundamental problem is insulin resistance and not an absence of insulin, the body does not produce ketones.

(For additional information, see <http://diabetes.niddk.nih.gov>)

Insulin is a hormone produced by the beta cells in the islets of Langerhans in the pancreas. It is a powerful hypoglycemic agent and it lowers blood glucose in the following ways:

- Facilitates the passage of glucose across cell membranes
- Inhibits the production of glucose from glycogen (the stored form of glucose)
- Promotes the conversion of fatty acids to fat
- Inhibits the breakdown of adipose tissue
- Stimulates the synthesis of protein
- Inhibits the production of glucose from protein

Prior to 1997, diabetes was known by many names: "Juvenile Diabetes" or "Insulin-Dependent Diabetes (IDDM)," and "Adult-Onset Diabetes" or "Non-Insulin Dependent Diabetes (NIDDM)" based upon the typical age of onset and the primary treatment methodology. In 1997, an Expert Panel commissioned by the American Diabetes Association recommended changes in the classification of diabetes. The panel advised

that the former classification system that focused on the pharmacological management of diabetes be replaced by one that addressed disease etiology (Expert Panel, American Diabetes Association, 1997).

For all intents and purposes there are three categories or "types" of diabetes: diabetes type 1 (DMT1), diabetes type 2 (DMT2), and gestational diabetes (GDM).

One other form of diabetes that occurs among youth (typically those under the age of 25) is now recognized, but is exceedingly rare (occurs in less than 5% of children with diabetes). This form of diabetes is known as "maturity-onset diabetes of the young" or "MODY" and it is due to monogenetic (chromosomal) defects that influence beta cell function. It occurs in young, non-obese individuals who are not necessarily members of the ethnic groups known to be at high risk for DMT2. It is characterized by mild fasting hyperglycemia (100–150 mg/dL) and is differentiated from other types of diabetes through commercial genetic testing which is readily available (ADA, 2018, pg. S13].

This is not to be confused with DMT2 which can occur in obese children. Rather, it is a distinct entity characterized by impaired insulin secretion with minimal or no defects in insulin action (ADA, 2018). Treatment is usually with low-dose sulfonylureas (Hattersley, Bruining, Shield, Njolstad, & Donaghue, 2009, pg. 37).

Another entity which is not considered "diabetes," but is a very important condition, is "Pre-Diabetes." Pre-diabetes (or "High-Risk for Diabetes") encompasses two conditions: Impaired glucose tolerance (IGT) and impaired fasting glucose (IFG). IGT is defined as a two-hour post-load glucose of 140–199 mg/dL during a standard oral glucose tolerance test. IFG is defined as a fasting glucose of 100-125 mg/dL. While neither constitutes evidence of diabetes, each represents a risk factor for the development of diabetes, and as such is considered an intermediate stage in the progression toward overt disease.

A critical, long-awaited recommendation was adopted at the 2010 "70th Scientific Sessions" of the American Diabetes Association (an annual gathering of scientists focusing on diabetes care and research). The recommendation was made to recognize the standardized, laboratory-calculated A1c (i.e. not to be confused with those point-of-care A1c tests that may not be considered sufficiently accurate for diagnostic purposes) as a tool to diagnose diabetes and pre-diabetes. This conclusion was made after many years of study and debate about the role of this laboratory tool in the diagnosis of diabetes (American Diabetes Association (ADA), 2011). An A1c of 5.7%-6.4% (verified on a second occasion in the absence of unequivocal hyperglycemia) was determined to be diagnostic of pre-diabetes while an A1c \geq 6.5% (also verified on a second occasion in the absence of unequivocal hyperglycemia) was determined to be diagnostic of diabetes (ADA, 2011).

Many people have pre-diabetes and are completely unaware of their condition. As such, they are at great risk of developing DMT2. Since interventions are available to help reduce the likelihood that these individuals will develop DMT2, it is imperative that persons with pre-diabetes know who they are. Screening for diabetes and educating people about the signs and symptoms are the best ways to achieve this goal.

But who should be screened? More on this later with the discussion of "Risk Factors for Diabetes."

Type 1 diabetes (DMT1) which is more commonly found among younger people than among older persons, is a consequence of an absolute lack of insulin. Most cases of DMT1 are characterized by the presence of antibodies in the individual's blood that identify the autoimmune process that leads to beta-cell destruction. Clinical evidence of this condition is classic in that it creates polyuria (excessive urination), polydipsia (excessive, prolonged thirst), and polyphagia (excessive eating) as the body tries to cope with the underlying pathophysiology. Without exogenous replacement of insulin in this case, the inevitable result is the development of metabolic acidosis (diabetic ketoacidosis) and ultimately, if uncorrected, death.

Type 2 diabetes (DMT2) has typically been a condition of adults who are overweight, and is a consequence of insulin resistance. Epidemiological data and clinically based reports are now indicating that obesity is reaching epidemic proportions among children (Hughes & Reilly, 2008; James, 2008). It follows that DMT2 is also reaching epidemic proportions within this population particularly among Native Americans, African Americans, Hispanic/Latino Americans, Asians, and Pacific Islanders. Increasing rates of obesity among these groups have been blamed (and continue to be blamed), at least in part for this dramatic change (Adams & Lammon, 2007; Soltész, 2006).

Gestational diabetes (GDM) is defined as any degree of glucose intolerance during pregnancy, with the resolution of the glucose intolerance after pregnancy. GDM affects about 4% of all pregnant women. Once a woman has had GDM, her chances are two in three that it will return in future pregnancies. Many will go on to develop DMT2 later in life.

The cause of DMT1 is not known for certain. It is a primary subject of research. DMT1 is believed to be the result of both genetic and environmental factors: heredity, auto-immune reactions which effectively destroy islet cells, and possibly effects of viral infections. Current beliefs are that all factors must be considered.

The cause of DMT2 is believed to be a combination of many metabolic abnormalities. Insulin resistance is typically one of the first abnormalities seen. Others include impairment of insulin secretion and elevated glucose production by the liver. Most persons with DMT2 are overweight. Hence, there is a strong association of DMT2 with overweightedness and obesity. In some cases, weight reduction can ameliorate the metabolic problem. (Such an occurrence should not be misconstrued to reflect "cure" of diabetes, but rather, "control" of diabetes via educated changes in the way one eats and the incorporation of regular exercise into one's life. Discontinuation of the control regimen with resultant weight gain will likely result in a return of the clinical signs and symptoms of overt DMT2).

In the past, practice guidelines advised a two to three month trial of "lifestyle management" (changes in one's nutritional intake and exercise) when DMT2 was diagnosed, with the introduction of oral medications if these efforts were unsuccessful in attaining control of the blood glucose after that period of time. Practice guidelines recommended by the American Diabetes Association for the individual with newly diagnosed DMT2 changed within the past several years and now include both lifestyle management (medical nutrition therapy and regular exercise) and oral medication (metformin, unless contraindicated) from the time of diagnosis (American Diabetes Association, 2014). Intensive education about diabetes, medical nutrition therapy, and self-monitoring of blood glucose (SMBG) (and documentation of the results!) remains fundamental to success in the treatment of diabetes. "Continuing timely augmentation of therapy with additional agents (including early initiation of insulin therapy) as a means of achieving and maintaining recommended levels of glycemic control (i.e., A1c < (less than) 7% for most [non-pregnant] patients)" (pg. S23) and assuring follow up at regular intervals to verify blood glucose control are critical to reaching established goals (American Diabetes Association, 2014).

UNIT II: NORMAL PHYSIOLOGY AND PATHOPHYSIOLOGY

OBJECTIVES

- Explain the normal physiology of glucose metabolism.
- Explain the pathophysiology of uncontrolled/undiagnosed DMT1.
- List the signs and symptoms of uncontrolled/undiagnosed DMT1.
- List the signs and symptoms of uncontrolled/undiagnosed DMT2.
- Explain the differences between DMT1 and DMT2.
- Describe the correct procedures (American Diabetes Association's recommendations) to be used to diagnose diabetes.
- List risk factors for diabetes for adults.
- List risk factors for diabetes for children.
- Recognize the role of waist circumference in screening for metabolic syndrome (a condition related to DMT2).

NORMAL PHYSIOLOGY

Overall, insulin functions as an anabolic agent because it builds the body up as opposed to breaking it down (catabolic). It is essential for the metabolism of glucose for energy by the cells.

The normal stimulus for the release of insulin from the beta cells of the pancreas into the blood stream is an increase in the blood glucose. Glucose is the body's preferred fuel. Later, when blood glucose drops to a critical level, insulin is "shut off" and glucagon, a hormone that is a hyperglycemic agent, is secreted by the alpha cells of the pancreas. Glucagon facilitates the conversion of glycogen to glucose in the liver (gluconeogenesis), thereby raising the blood glucose level.

Another hormone secreted by the beta cells of the pancreas is "amylin." The function of this substance is to aid in the absorption of glucose by slowing the emptying of the stomach and promoting satiety through chemical receptors in the hypothalamous. In addition, amylin inhibits the secretion of glucagon by the liver.

In these ways, blood glucose levels are maintained within a normal range (homeostasis). Diagram 1 illustrates the normal relationships among blood glucose, insulin, amylin, glucagon, and other selected hormones in the body:

When one ingests food, the initial result is an increase in blood glucose. Simultaneously, the body responds by secreting insulin and amylin from the beta cells of the pancreas. If the blood glucose becomes too low, glucagon is secreted from the alpha cells of the pancreas to (ultimately) raise the blood glucose. Simplistically speaking, this is the body's way of maintaining homeostasis of the blood glucose. There is a normal, predictable rise and fall of the blood glucose after a meal.

In 1964, scientists observed that plasma insulin levels rose more rapidly and for a more sustained period of time after the oral ingestion of glucose than after the intravenous infusion of the same amount of glucose. Such observations suggested that the gastrointestinal system played a role in glucose metabolism by stimulating insulin production. A study reported in the *Journal of Clinical Endocrinology* in 1964 verified these findings (Elrick, Stimmler, Hlad, & Arai, 1964) as did subsequent studies reported in the literature (McIntyre, Holdsworth, & Turner, 1965; Perky & Kipnis, 1967).

Further study led to a fuller understanding of the complexities of the underlying pathophysiology of type 2 diabetes and a clearer grasp of the relationship between hormones found in the small intestine (enteroendocrine cells) (Trujillo, 2006) and plasma insulin levels. The hormones discovered were labeled "incretins" – e.g. glucagon-like peptide-1 (GLP-1) and dipeptidyl peptidase-4 (DPP-4). Dysfunction of one or more of these was found to be related to the development of type 2 diabetes. However, it was not until 2005 when the first medication, *exenatide* – a GLP-1 receptor agonist -- was approved by the Federal Drug Agency (FDA) to treat type 2 diabetes. (More about this later.)

As studies continued, researchers noted that amylin – the hormone secreted along with insulin by the beta cells in the pancreas – was depleted in persons with DMT2 and virtually absent in those with DMT1. Accordingly, in 2005, the amylinomimetic (means, "imitates amylin") drug, pramlintide was approved by the FDA for treatment of both types of diabetes. Pramlintide slows emptying of the stomach and postprandial (refers to the period after a meal) glucagon secretion, and increases satiety. These effects can lead to weight loss (U.S. National Library of Medicine, Medline Plus, 2013).

Other hormones in the body influence blood glucose. They are adrenocorticotrophic hormone (ACTH) and epinephrine which are produced in response to stress, and which indirectly elevate the blood glucose. Consequently, emotional stress can result in elevated blood glucose levels. Chronic stress has been shown to be related to poor glucose control and thereby an increased incidence of complications.

In the person with normal glucose metabolism, fasting blood glucose (FBG) levels are maintained within a fairly narrow range of 65-110 mg/dL. Blood glucose levels typically rise with the ingestion of food, but are normally between 65 and 139 mg/dL at the two-hour post meal point (i.e. the "two-hour postprandial" blood glucose level).

PATHOPHYSIOLOGY

Diabetes mellitus is a condition resulting from a relative or absolute lack of insulin activity in the body. It is not simply always "too little insulin," and it is certainly not because the individual "ate too much candy" (a common misconception).

The graphs below show the typical glucose response to ingestion of food in the non-diabetic and the person with uncontrolled/undiagnosed diabetes mellitus. (Caution: The blood glucose values shown are not to be taken literally, but are used to reflect trends. Keep in mind the normal values of blood glucose in the fasting and postprandial states as you review the graphs). With insufficient insulin activity (DMT2) or, in the case of DMT1, an absolute lack of insulin, the blood glucose (BG) remains at excessively high levels. Like insulin, the hormone, amylin, normally secreted by the beta cells of the pancreas, is completely absent in DMT1.

Understanding the function of amylin (see "Normal Physiology"), one can appreciate the consequences in terms of blood glucose changes when amylin is absent (as in DMT1) or of insufficient quantity (as in DMT2).

The kidneys attempt to excrete the excess glucose in the urine leading to profound loss of fluid and insatiable thirst. Because the body cells cannot make use of the blood glucose due to insufficient (or absent) insulin, the metabolic processes effectively recognize a state of starvation and resort to the breakdown of fat (primarily, and eventually of) protein, and the hepatic production of glucose to meet energy needs.

UNCONTROLLED/UNDIAGNOSED DIABETES

Uncontrolled/undiagnosed diabetes is a life-threatening problem. Until 1921, when insulin was discovered by Dr. Frederick Banting and Charles Best (a medical student who was working with Dr. Banting), the diagnosis of diabetes (now identified as "DMT1") meant certain death. Death came slowly, essentially from metabolic acidosis and starvation, despite the presence of adequate food. The body simply broke itself down in an attempt to meet its energy needs. (See Best, 1964 for the exciting story of the discovery of insulin told first-hand by one of the discoverers!)

At the time insulin was discovered, the only kind of diabetes that was known was Type 1 – an absolute lack of insulin. The chemical changes that result from an absolute lack of insulin activity lead to the four cardinal signs (objective indications) of uncontrolled/undiagnosed DMT1:

1. polyuria (frequent urination)
2. polydipsia (insatiable thirst that leads to frequent, excessive drinking)
3. polyphagia (excessive eating due to insatiable hunger)
4. weight loss*

These signs generally appear together, but may not all be present simultaneously.

- * Note: These characteristics may present themselves in DMT2 as well except that weight loss typically does not occur. This is due to a basic difference between the underlying pathology of DMT1 and DMT2. A primary symptom of undiagnosed DMT2 is the complaint of fatigue.

LEARNER ACTIVITY

Capitalizing on your current understanding of normal human physiology, try to relate each of the above signs to the primary cause of the problem, insufficient insulin activity. Ask yourself, in the presence of hyperglycemia, why one might have excessive thirst, urination, hunger, and/or weight loss? Then, go on to read about it below.

The three "polys" can be explained from a pathophysiological basis as a direct response to the hyperglycemia: Because of the high concentration of glucose in the blood, water is drawn by osmosis from the cells into the blood thereby creating cellular dehydration and simultaneously increasing the blood volume. The excessive blood volume leads to excess urinary excretion (polyuria). The urine which is excreted has a high concentration of glucose (glucosuria -- a fifth sign) reflective of the high glucose concentration in the blood which exceeds the kidney's ability (threshold) to reabsorb the glucose back into the blood.

Renal threshold is individually determined. There is also evidence (Miller, 1986) that renal threshold levels are inconsistent with blood glucose levels due to the effects of disease, age, and certain drugs.)

The resultant dehydration leads to profound, insatiable thirst. If untreated, it can lead to severe dehydration, shock, and death.

The weight loss which can accompany uncontrolled/undiagnosed DMT1 is due to the virtual total catabolism of the body which occurs in an environment without insulin activity. What does the body do when it cannot meet its energy needs via glucose? The cells participate in a type of metabolism in which (initially) fats are broken down by a process called "lipolysis," and (eventually) proteins are catabolized to produce glucose, a process called "gluconeogenesis." (Note: This is the "desired" effect of those who purposely starve themselves to reduce weight. However, the results in the uncontrolled/undiagnosed diabetic are profound and can be fatal due to the high concentrations of the by-products of fat metabolism). This further increases blood glucose, raising the tonicity of the blood, and adding insult to injury. However, the body "knows" only that it is starving and is forced to meet its energy demands in any way it can. Polyphagia results from this faulty stimulus, further increasing blood glucose.

Breakdown of body proteins for energy leads to severe negative nitrogen balance, tissue wasting, and weight loss -- much more protein is being broken down than is being taken in through what is eaten. Growth cannot occur in this metabolic state and resistance to infection is reduced as well. In addition, the breakdown of fats results in the production of ketones and fatty acids, both of which markedly reduce the pH of the blood leading to metabolic acidosis. Ketonuria and an acidic blood pH are the sixth and seventh signs of uncontrolled/undiagnosed DMT1.

The kidneys compensate as long as they can by excreting hydrogen ions, in part, but if the aberrant metabolic process persists the kidneys cannot satisfactorily continue to maintain the normal range of blood pH. The individual subsequently develops diabetic ketoacidosis. The lungs respond to the acidic condition by trying to blow off more and more CO₂. The resulting respiratory pattern is a characteristic deep, rapid breathing (Kussmaul respirations). The presence of ketones is noted by the "fruity" odor to the breath. See the chart in Appendix A to review the pathophysiology of uncontrolled/undiagnosed diabetes.

The person who has reached this stage of uncontrolled/undiagnosed diabetes is in serious trouble and needs immediate, intensive care. Otherwise, profound metabolic acidosis will develop and, most likely, fatal coma will ensue.

In summary, the person in the early to middle stages of uncontrolled/undiagnosed diabetes mellitus due to an absolute lack of insulin (DMT1) will probably have the four cardinal signs as well as glucosuria and ketonuria. In addition, the blood pH will be lower than normal. (If untreated, the pH will drop to dangerous, lethal levels as metabolic acidosis ensues.) There may be complaints of fatigue and lethargy, muscle cramps due to electrolyte changes, and difficulty sleeping through the night (due to the frequency of the need to drink and urinate) -- symptoms (subjective indications) of diabetes when in conjunction with the above signs. This person may be more prone to illnesses than the average person and have skin rashes and/or infections which do not resolve. In undiagnosed DMT1 considerable weight loss may occur despite a voracious appetite. (Note: The person with uncontrolled/undiagnosed diabetes due to a relative lack of insulin (DMT2) may have few (if any) subjective indications of a problem. The primary subjective complaint is often "fatigue").

A hyperglycemic environment within the body provides an excellent medium for the growth of microorganisms. Consequently, females with uncontrolled/undiagnosed diabetes may be prone to stubborn

vaginal infections due to the presence of a high sugar concentration in the vaginal mucosa. Repeated vaginal infections in a patient should raise the health care provider's suspicions of diabetes.

The person in the late stages of uncontrolled/undiagnosed DMT1 (i.e. "diabetic ketoacidosis" (a specific type of metabolic acidosis) or "diabetic coma") will most likely exhibit each of the above symptoms, and will be in a comatose state. This does not typically occur as a consequence of uncontrolled/undiagnosed DMT2, however, due to a fundamental difference in the ongoing pathophysiology that occurs in this condition.

TYPES OF DIABETES – DETAILED DESCRIPTIONS

INTRODUCTION

After the discovery of insulin in 1921, people who were diagnosed with diabetes were successfully treated with insulin, though there was very little of it to go around, at first. The first such person to receive an injection of insulin was a 14 year old child named Leonard Thompson of Toronto, Canada, who had developed diabetes three years earlier. At the time he received the injection, he weighed 65 pounds and was "near death." His symptoms reversed and he lived until 1935 when he died of pneumonia.

In the 1920s, the pharmaceutical company, Eli Lilly and Company, collaborated with Dr. Banting and Charles Best to isolate and purify insulin to treat diabetes. In 1923, Lilly produced what was called at that time, "Isletin."

Over time, it became apparent that two different types of diabetes existed: "Juvenile Diabetes" which characteristically presented itself in younger people (under the age of approximately 24 years) and required the injection of insulin several times each day, and "Adult-Onset Diabetes," – a form of diabetes in which the victim was typically over the age of 40 and did not require exogenous insulin injections to survive. In 1959, this distinction was made official.

Eventually, Juvenile Diabetes became known as Insulin-Dependent Diabetes Mellitus or IDDM, for obvious reasons, and Adult-Onset Diabetes became known as Non-Insulin Dependent Diabetes or NIDDM. In time, it was found that people with NIDDM often benefited from the use of exogenous insulin. Consequently, the name "non-insulin dependent" became a misnomer.

In 1997, the decision was made by the American Diabetes Association to simplify and clarify, and to identify the two main types of diabetes as just Type 1 and Type 2. Current classifications of diabetes include four clinical classes as identified below: DMT1, DMT2, Other Specific Types of Diabetes -- due to other causes, e.g. genetic defects in beta-cell function or insulin action, diseases of the exocrine pancreas (e.g. cystic fibrosis), and drug- or chemical-induced (such as in the treatment of AIDS or after organ transplantation) – and, Gestational Diabetes Mellitus (GDM) – diabetes diagnosed during pregnancy that is not overt diabetes) (American Diabetes Association, 2011).

TYPE 1 DIABETES (DMT1)

Type 1 diabetes most often affects persons under the age of 24 (but this is certainly not the "magic age"). Of those with diabetes, only about 10% have DMT1. In this case, there is an absolute lack of insulin activity, either because the beta cells in the pancreas simply do not produce it or because, once they do, the body inactivates it in some fashion. Whatever the case, the critical point is that there is no effective insulin activity in the body. It is characterized by rapid onset of symptoms, especially thirst, frequency of urination, and lassitude. (See Appendix A: Pathophysiology of Diabetic Ketoacidosis.) Treatment consists of balancing exogenous insulin administered by injections (or continuous subcutaneous insulin infusions,

also called CSII or the insulin pump), nutrition/eating patterns, exercise, and self-monitoring of blood glucose.

TYPE 2 DIABETES (DMT2)

In contrast, Type 2 diabetes (DMT2) is by far the more common type of diabetes, comprising approximately 90% of all cases. The underlying problem in DMT2 is insulin resistance which creates a relative lack of insulin for the body's metabolic needs.

Until the past 15-20 years, DMT2 was a disease of older people (Adult-Onset Diabetes), the incidence of DMT2 among children is growing exponentially in this country. More information on that will be offered later in the self-study, but suffice it to say that there is an explanation for this phenomenon when one recognizes the growing incidence of obesity among the nation's children.

For reasons that are not clearly understood, the cells in the body of an individual with DMT2 become more and more resistant to the body's own insulin, thereby interfering with the transport of sugar across cell membranes to be used by the cells of the body. Initially, the body responds by producing more insulin to maintain normoglycemia. But, the pancreatic cells that produce insulin – the beta cells of the pancreas – can do only so much for so long and eventually they cannot keep up with the demand. Consequently, insulin resistance combined with diminished secretion of insulin results in subjective and objective symptoms of DMT2. The excess sugar collects in the blood and creates the objective and subjective indicators of diabetes: hyperglycemia, polydipsia, polyuria, and fatigue. Blood sugar rises significantly when the transportation of sugar into the cell is impaired.

Another defect complicating the above pathology is the fact that DMT2 is associated with elevations in glucagon secretion from the liver, leading particularly to postprandial (after meal) blood glucose elevations.

In Type 2 diabetes, the body is not forced to resort to abnormal pathways to meet its metabolic needs -- there is sufficient insulin for this. Consequently, the signs and symptoms of undiagnosed DMT2 are not as noticeable as they are in undiagnosed DMT1.

Early in the metabolic derangement characteristic of the DMT2, excess insulin is secreted to compensate for the reduced insulin activity. Glucose levels can be maintained in the normal range for some time in this hyperinsulinemic state. However, associations have been discovered between hyperinsulinemia and the development of obesity, hypertension, dyslipidemia, and atherosclerosis (a cluster of metabolic disorders previously referred to as Syndrome X but now called the metabolic syndrome) all of which are known to be related to cardiovascular disease (Fonseca, 2007; Li et al., 2006).

Type 2 diabetes characteristically does not produce ketones in the blood or urine. This is because the body does not have to resort to fat metabolism to meet its energy needs. Essentially, the problem is a result of a relative lack of insulin: excessive demands for insulin perhaps due to resistance to insulin by target tissues and/or defective secretion of insulin. Hyperglycemia and glucosuria are typical laboratory findings as well as polydipsia, polyuria, fatigue, and infections or wounds that do not heal. Acidosis, ketonemia, and ketonuria are typically not present. (Both may be present, however, in the individual with DMT2 who has an infection). Since symptoms are usually less severe, professional intervention may not be sought early. Consequently, damage may occur (retinal, renal, neurological, cardiovascular, cerebrovascular) before the condition is diagnosed.

When compensatory hyperinsulinemia fails to maintain normal glucose levels, pathophysiologic changes result in further compounding the hyperglycemia -- overproduction of glucose by the liver, increased insulin resistance, and dysfunction of pancreatic beta cells. This is the body's attempt to correct a perceived problem, but is, in fact, highly maladaptive.

Initially, attempts to control the blood glucose in the individual diagnosed with DMT2 will be made through nutritional instruction, exercise, and an oral agent, metformin (unless contraindicated). Some regimens include both oral agents and insulin. Insulin injections are nearly always necessary when the individual with DMT2 experiences pregnancy, unusual stress, infections, develops an allergy to oral hypoglycemic agents, and in all conditions which increase the metabolic demands on the body that result in loss of control of the blood glucose. A key to success requires frequent blood glucose determinations (and documentation) by the patient, as well as frequent re-evaluations with the patient's health care provider to determine the extent to which glycemic control is being obtained.

A caution is in order with regard to aggressive use of insulin in persons with DMT2. As stated above, evidence suggests an association between hyperinsulinemia (higher than normal levels of insulin in the blood) and cardiovascular disease (Fonseca, 2007; Li et al., 2006). On the other hand, the use of exogenous insulin in conjunction with oral agents that reduce resistance to insulin could lessen this problem by actually reducing the amount of insulin secreted. In fact, many persons with DMT2 are controlled in precisely this manner.

(Note: The presence of ketoacidosis strongly suggests the underlying problem is type 1 diabetes, not type 2 diabetes.) When improvement in glycemic control is achieved with insulin, it would then be appropriate to introduce oral agents and discontinue the use of insulin.

[This self-study is updated periodically, but is not updated every year. Throughout the self-study, references are made to the American Diabetes Association's standards of medical care. These are reviewed and published each year on the American Diabetes Association's (ADA) web page at <http://www.diabetes.org>. To see the most current standards, go to <http://www.diabetes.org>, click on "Research & Practice", and then click on "Clinical Practice Guidelines". It is in this way that you can remain current on the ADA's clinical practice recommendations.]

LEARNER ACTIVITY

Fill in the chart below with reference to characteristics of DMT1 and DMT2 described above.

<u>Comparisons of DMT1 and DMT2</u>		
	Type 1	Type 2
1. Previous name(s) for the condition:		
2. Typical age at onset:		
3. Underlying pathology:		
4. Causes:		
5. Treatments:		
(To verify the accuracy of your answers to the above, please review the previous content in the self-study.)		

GESTATIONAL DIABETES MELLITUS (GDM)

GDM refers to diabetes that is diagnosed during pregnancy (typically during the last trimester). Since even mild glucose intolerance is associated with a greater than expected incidence of perinatal mortality and morbidity of the neonate, it is important that the condition is promptly diagnosed and effectively managed. Management includes specific dietary modifications alone or, in some cases, dietary modifications plus insulin. Following delivery, glucose metabolism may change to normal, remain as impaired glucose tolerance, or become overt diabetes. It is highly likely that a woman who has GDM will develop DMT2 at some time in her future.

The American Diabetes Association recommends screening for GDM at the first prenatal visit in patients who have risk factors for diabetes, and then, if warranted, arranging for testing using standard diagnostic criteria (2014). Screening for GDM is performed at 24-28 weeks gestation in those not known to have had diabetes in the past. Among women who have had GDM, the recommendation is to screen them for diabetes every three years for the rest of their lives.

Other Conditions of Glucose Intolerance or Pre-Diabetes as defined by the American Diabetes Association:

- Impaired Fasting Glucose (IFG) – Diagnosed by results of a fasting blood glucose of 100 mg/dL to 125 mg/dL
- Impaired Glucose Tolerance (IGT) – Diagnosed by results at 2 hours in the standardized oral glucose tolerance test of 140 mg/dL to 199 mg/dL (American Diabetes Association, 2014, p. S16)

Either of the above has been identified as a risk factor for the future development of diabetes and for cardiovascular disease.

HOW TO DIAGNOSE DIABETES

Blood glucose levels are used to diagnose diabetes according to the following recommendations by the American Diabetes Association:

Criteria for the Diagnosis of Diabetes*	
A. A1c** > (greater than or equal to) 6.5% or	The test should be performed in a laboratory using a method that is NGSP (National Glycohemoglobin Standardization Program) certified and standardized to the DCCT assay.**
B. FPG >126 mg/dL or	Fasting is defined as no caloric intake for at least 8 hours.***
C. 2-hr plasma glucose > 200 mg/dL during an OGTT or	The test should be performed using a glucose load containing the equivalent of 75g anhydrous glucose dissolved in water.**
D. In a patient with classic symptoms of hyperglycemia (polyuria, polydipsia, and polyphagia) or in a hyperglycemic crisis, a random plasma glucose >200 mg/dL.	

*“The epidemiological studies that formed the basis for recommending A1C to diagnose diabetes included only adult populations. Therefore, it remains unclear whether A1C and the same A1C cut point should be used to diagnose diabetes in children and adolescents (American Diabetes Association, 2018, S15).

**One concern has been recognized with regard to using the A1c in the diagnosis of (or to assess blood glucose control in) diabetes. In the presence of the conditions listed below, the only test that should be used to diagnose diabetes is plasma blood glucose. These conditions have in common with one another the fact that they are associated with increased red blood cell turnover. The conditions are sickle cell

disease, 2nd and 3rd trimesters of pregnancy, recent transfusion or loss of blood, hemodialysis, or treatment with erythropoietin) (ADA, 2018).

***In the absence of unequivocal hyperglycemia, the result for each of these should be confirmed by repeat testing of the same test on a different day (ADA, 2018).

The following chart shows how the results of the FBG and the two-hour post-load BG (during the OGTT), and the hemoglobin A1c are used to diagnose diabetes (provided abnormal results on the same tests are obtained on two different days).

Normal, Pre-Diabetes, and Diabetes Blood Glucose (BG) Test Results		
Fasting Blood Glucose Results (Fasting means the individual has had no caloric intake for at least 8 hours before the test.)		
Normal < 100 mg/dL	Pre-Diabetes 100-125 mg/dL	Diabetes > 126 mg/dL
Two-Hour Post-Load BG Results in the 75g Oral Glucose Tolerance Test (OGTT)		
Normal < 140 mg/dL	Pre-Diabetes 140-199 mg/dL	Diabetes > 200 mg/dL
Hemoglobin A1c		
Normal < 5.7%	Pre-Diabetes 5.7%-6.4%	Diabetes > 6.5%
(American Diabetes Association, 2014, pg. S15)		

The American Diabetes Association (2014) recommends that testing for diabetes should be performed on all adults who are overweight (BMI = 25-29.9 kg/m²) or obese (BMI \geq 30 kg/m²) and have one or more risk factors for diabetes (P. S 16). (See "Risk Factors for Diabetes" below). However, if no risk factors are present, the American Diabetes Association recommends testing for pre-diabetes and diabetes starting at

age 45 years. If the results at that time are within normal limits, the recommendation is to repeat the testing at three-year intervals, or more often if test results and/or risk status warrant it (American Diabetes Association, 2018).

If on the other hand results are diagnostic of pre-diabetes, interventions are recommended. Such interventions include lifestyle changes (revisions in dietary intake and regular exercise) and starting metformin, if not contraindicated in the patient (American Diabetes Association, 2018).

Studies cited in the "Standards of Medical Care in Diabetes – 2014" (American Diabetes Association, 2014) demonstrated that individuals with pre-diabetes were able to "decrease the rate of onset of diabetes with...intensive lifestyle modification programs...[-- an approximate] 58% reduction after 3 years) and [the use of] pharmacological agents" (p. S20).

Due to the significant increase in obesity among children over the past years (and the associated increase in the number of children diagnosed with DMT2), the American Diabetes Association (2014 and 2018) recommend testing (using the hemoglobin A1c) for pre-diabetes and DMT2 in children (age 18 and younger) if the child is overweight (BMI > 85th percentile for age and gender, weight by height is > 85th percentile, or weight > 120% of ideal weight for height), and has any two of the risk factors listed below:

- Family history is positive for DMT2 in a first- or second-degree relative
- The child's race/ethnicity is any one of the following: Native American, African American, Latino/Hispanic, Asian American, or Pacific Islander
- Physical evidence of insulin resistance is present (acanthosis nigricans), or other conditions are present that are known to be associated with insulin resistance (hypertension, dyslipidemia, polycystic ovarian syndrome, or the child's birth weight was "small-for-gestational-age")
- Mother had gestational diabetes when pregnant with the child. (2018, pg. S19)

Because the rates of DMT1 are increasing in the United States as well, the American Diabetes Association recommends screening relatives of individuals with DMT1 for islet autoantibodies. Positive results would provide for follow-up of individuals and as such could increase the chance for earlier identification of DMT1 before the development of ketoacidosis (American Diabetes Association, 2018, pg. S17).

RISK FACTORS FOR DMT2

As explained in the American Diabetes Association's Standards of Medical Care in Diabetes -- 2018, individuals with one or more of the following should be considered at risk for the development of DMT2:

- Has a first-degree relative with diabetes
- Is a member of a high-risk race/ethnic population (African American, Latino/Hispanic, Native American, Asian American, Pacific Islander)
- Is physically inactive
- Has been diagnosed with GDM
- Has hypertension or is being treated for hypertension

- Has conditions associated with insulin resistance (e.g., obesity or acanthosis nigricans*) – this would include obese or overweight children and adolescents who have one or more risk factors for diabetes.

(American Diabetes Association, 2018, pg. S18)

*Acanthosis nigricans (AN) is a dermatologic condition characterized by symmetric brown thickening of the skin – of predominantly the neck and the axillae, the back of the neck and the groin. It is associated with insulin resistance and (consequently) hyperinsulinemia which occurs as a natural response to insulin resistance. As such, it may be a predictor of DMT2. Over time, the darkened area may become thickened and develop a leathery or warty surface. It should be considered a redflag for the presence or development of prediabetes or DMT2 in obese children and adults. It should also be noted, however, that the sudden appearance of AN after the age of 50 should be addressed immediately as such occurrences may be related to adenocarcinoma of the stomach (Trace, 2013). Prompt follow-up of this condition is warranted.

In 2018, the American Diabetes Association added the following recommendations for screening for diabetes among asymptomatic overweight and obese children and adolescents for diabetes:

Overweight or obese individuals under the age of 18 plus at least one of the following risk factors:

Maternal history of diabetes or gestational diabetes mellitus during the child's gestation

Family history of type 2 diabetes in first- or second-degree relative

Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander)

Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight). (ADA, 2018, pg. S19)

Waist Circumference, Metabolic Syndrome, and Diabetes

Any additional clinical evidence of metabolic syndrome (the clinical condition reflected by the presence of insulin resistance, hyperlipidemia, and hypertension) should be pursued because the presence of any of these is a risk factor for the development of DMT2. That said, waist circumference alone has been found to be a predictor of metabolic syndrome and of DMT2 (Janiszewski, Janssen, & Ross, 2007; Wang, Rimm, Stampfer, Willett, & Hu, 2005).

The American Heart Association defines metabolic syndrome as a group of risk factors that lead to the development of atherosclerotic heart disease and increase one's risk for the development of DMT2. The risk factors include hypertension, elevated blood glucose, elevated triglycerides and low-density lipoproteins (LDLs) as well as low levels of high-density lipoproteins (HDLs) in the blood. A clinical red flag is increased waist circumference in men greater than 40 inches (102 cm), and in women greater than 35 inches (88 cm) (American Heart Association, 2015).

In a study reported in *Diabetes Care* in 2007, the authors reported "WC [waist circumference] predicted diabetes...The findings lend critical support for the recommendation that WC be a routine measure for identification of the high-risk, abdominally obese patient" (Janiszewski, Janssen, & Ross, 2007, p. 3105). In this study, waist circumference was measured during minimal respiration to the nearest 0.1 cm at the level of the iliac crest.

Location of Measuring Tape to Determine Waist Circumference:

Place Tape at the Level of the Iliac Crest

The measurement should be made at the normal minimal respiration.

High Risk*

Men: >102 cm (>40 in.)

Women: >88 cm (>35 in.)

*This measurement is useful in predicting risks as described above in all adult ethnic or racial groups, but only in those with a BMI of less than 35 and those who are at least five feet tall (National Heart, Lung, and Blood Institute of the National Institutes of Health (NHLBI), 1998).

The findings of the Janiszewski, Janssen, and Ross (2007) study reinforced the conclusions of a previous study published in 2005 which compared measurements of abdominal adiposity and overall obesity with regard to predicting risk of DMT2: "In conclusion, the present study provides further evidence that abdominal adiposity measured with the use of WC [waist circumference]... is a strong risk factor for type 2 diabetes, independent of overall obesity assessed by BMI [body mass index]" (Wang, Rimm, Stampfer, Willett, & Hu, 2005, p. 562).

The cut points for WC measurements in the Wang, Rimm, Stampfer, Willett, and Hu (2005) study were exactly the same as those recommended in the 1998 NHLBI publication above.

Unfortunately, inconsistency exists relative to measuring waist circumference among health care providers. Different anatomical landmarks have been used to determine the exact location for measuring WC in different clinical studies, including: 1) midpoint between the lowest rib and the iliac crest; 2) the umbilicus; 3) narrowest (minimum) or widest (maximum) waist circumference; 4) just below the lowest rib; and 5) just above the iliac crest. The specific site used to measure WC influences the absolute WC value that is obtained (Klein et al., 2007, pg. 1648).

HISTORY OF DIABETES AND THE DISCOVERY OF INSULIN

Diabetes has probably always been a part of human life. Historically, treatments ranged from near starvation diets that included foods high in fat and protein and low in carbohydrate. In spite of the best medical treatments known until 1921, however, diabetes always resulted in death.

The term, diabetes, comes from a Greek word meaning something which passes through (siphons), and the Latin word, mell which translates as honey. Mellitus refers to sweet urine – a fact determined by the observation that the urine of those with diabetes attracted flies and smelled sweet. The syndrome has been recognized since history has been recorded. Ancient Sanskrit literature includes descriptions of a disorder with honeyed urine. Papers from 1550 B.C. in Egypt describe dietary treatments for victims of the disease. In 170 A.D., Aretaeus, a Greek physician described "this mysterious affection . . . being [an inevitable] melting down of flesh and limbs into urine . . ." (Bloom & Ireland, 1980, p. 9). The tremendous significance of Banting and Best's discovery (described below) can be understood more clearly when one recognizes that in 1921, diabetes was a long-standing, terminal disease which was especially virulent among children. Treatment regimens recommended before the discovery of insulin took a huge toll on the quality of life.

According to historical documentation, diabetes was treated in the pre-insulin era (i.e. prior to 1921) by diets of fat, rancid meat, boiled vegetables, and bran, or any combination thereof. In 1796, Dr. John Rollo, building on earlier revelations that the urine of persons with diabetes contained sugar, devised the first effective treatment of some people with diabetes. (We now know his treatment helped those with Type 2 diabetes, only.) The treatment was a diet high in animal foods (fats and meats) and low in vegetable foods (breads and grains). Until insulin was discovered in 1921, this was the only treatment for diabetes.

In 1921 (3,473 years from the first documentation of diabetes) Frederick G. Banting, MD (1891-1941) and Charles Best (1899-1978), a 22-year old medical student in need of a summer job, conducted research in Toronto, Canada that led to the discovery of, what was thought at the time to be a cure for diabetes: insulin. While it was soon discovered that insulin was not a cure, the discovery of insulin was a life-saving event met with considerable relief by the medical community of the time, not to mention by the public as well. Toronto was deluged with people who needed insulin to save their lives. Resources in Toronto produced insulin, but by July of 1922, a severe shortage of insulin had occurred. Soon thereafter, the pharmaceutical company, Eli Lilly and Company produced and distributed insulin for most western countries. Later, European pharmaceutical companies took on the challenge to mass-produce insulin.

In 1923, Dr. Banting received the Nobel Prize in Physiology or Medicine for the discovery in 1921 of insulin. The award was split with John James Richard Macleod, a Scottish physician and physiologist whose work in carbohydrate metabolism led to his involvement in the research that led to the discovery. The award for Dr. Macleod was controversial. Dr. Banting publicly insisted Macleod's involvement in the discovery was nominal, and that Charles Best should have received the other half of the prize. Consequently, Banting voluntarily shared half of his award money with Best. While Charles Best did not receive public recognition for his part in the discovery, his name will forever be associated with it. Dr. Best died in 1978.

In 1934, Dr. Banting was knighted for his discovery of insulin, and thereafter known as Sir Frederick G. Banting. In 1941, Banting was killed in an airplane crash in Newfoundland while in route to England.

History of the Development of Insulin

At the time of the discovery of insulin (and ultimately its mass production from animal pancreases – bovine and porcine), there was known to be only one kind of diabetes. In this type of diabetes, the individual had lost his/her ability to produce insulin, thus rendering the individual entirely dependent on exogenous insulin (insulin by injection). Diabetes at that time was simply, diabetes; not Type 1 or Type 2 or anything else.

It was quickly discovered that insulin could not be administered orally due to the destructive effects of the gastric and intestinal juices on the insulin molecule. The only practical way to administer insulin was found to be by injection.

The first insulin was a fast- (onset within 30 minutes), short-acting insulin with a peak of activity in 2-4 hours, and a relatively short duration of action (6-8 hours) called simply regular insulin. It required twice daily intramuscular injections of 5-18 ml, and patients were not happy with it because of the pain and abscesses often associated with the injections and impurities in the insulin. Impurities in early insulin were mainly due to pancreatic peptides which were present in tiny concentrations. (In 1982, the problem was resolved with the development of recombinant DNA (rDNA) synthesis of insulin whereby purified insulin was produced. Recombinant DNA synthesis is the technology that allows biochemists to insert genes from one organism into another to make it produce a protein product – in this case, insulin from a harmless strain of a bacterium. Eli Lilly and Company produced the first rDNA insulin at that time).

It did not take long in the late 1920s and early 1930s for the public to clamor for a longer acting insulin that would provide extended coverage of the body's metabolic needs for insulin, and could be injected just once daily. In 1936 "Protamine Zinc Insulin" (PZI) was introduced, followed by "NPH" (Neutral Protamine Hagedorn) insulin in 1946, and the Lente insulins (Lente, Semilente, and Ultra-Lente – each with different action profiles) in 1951. Each of these preparations provided one peak time for insulin activity and long durations of actions, making them less than optimal for treatment (Bloomgarden, 2006), but the public appreciated the simpler approach to taking insulin.

Pre-mixed formulations of regular insulin or rapid-acting insulin and intermediate-acting insulin provide for convenience and improved accuracy of mixing than those mixed by patients, though there is less flexibility in dosing with these formulations. Such pre-mixed insulins available in the United States are 70/30 and 50/50 mixtures of NPH and Regular insulin, a 75/25 and 50/50 mixture of lispro insulin in its NPH-like formulation (insulin lispro protamine/insulin lispro), and a 70/30 mixture of insulin aspart with its NPH-like (insulin aspart protamine/insulin aspart).

Neither PZI nor any of the Lente insulins are on the market at present. NPH is the only intermediate-acting insulin now available. After subcutaneous injection, its onset of action is one to four hours, peak of activity is at six to twelve hours, and duration of activity is 18-28 hours (Deglin & Vallerand, 2001).

Faster in action than regular insulin, the first rapid-acting insulin analogue, insulin lispro (Humalog®) (sometimes referred to as "ultra rapid-acting"), was introduced in 1996, followed in 2000 by another ultra rapid-acting insulin, insulin aspart (Novolog®). The third rapid-acting insulin analogue, insulin glulisine (Apidra®) came on the scene in 2004. The onset of this rapid acting class of insulin is 5-15 minutes -- approximately twice as fast as that of Regular insulin. The peak time is about one hour, and the duration of activity is approximately four hours. Each of these is made by rDNA synthesis.

In 2000, a 24 hour-acting rDNA synthesized insulin entered the market in the form of insulin glargine (manufactured by Sanofi-Aventis as Lantus®). Insulin glargine was far different from prior intermediate- or long-acting insulins. A distinct advantage of insulin glargine was that it had no discernible time of peak activity. Hence, it became known as the peakless insulin. Insulin glargine has a duration of action of approximately 24 hours so is administered subcutaneously just once per day. It is considered a basal insulin.

Not long after insulin glargine became available, insulin detemir (manufactured by Novo-Nordisk as Levemir®) came on the market. Also considered a basal insulin, this medication has no peak and is administered once every 24 hours, much like insulin glargine. Other basal insulins have come along (and will undoubtedly continue to come along) and are available for treatment of diabetes in some individuals.

Unit III: Overview Of The Cornerstones Of Control Of Diabetes

OBJECTIVES

- List the four cornerstones of control of diabetes.
- Explain the effect each cornerstone has on blood glucose.

INTRODUCTION

The professional health care provider must recognize that successful treatment of diabetes depends upon knowledgeable, accurate self-care by the individual with diabetes. All the good intentions and the wealth of knowledge provided by the health care provider are for naught if the individual cannot or will not learn. "Nurses who encourage patients...to play an integral role in planning care 'empower' them by incorporating them into the health care team" (Callaghan & Williams, 1994, p. 138). While the previous quote is taken from a publication that is over twenty years old, it remains true now and, no doubt always will.

Check out this link for opportunities to receive regular e-newsletters about diabetes and diabetes-related topics from the American Diabetes Association:
http://main.diabetes.org/site/PageServer?pagename=EM_signup&WTLPromo=PK_eneews (This web address was current and functional as of 03/24/18.)

Four Cornerstones of Control of Diabetes

Treatment of diabetes requires the careful balancing of PROPER NUTRITION, EXERCISE, MEDICATION and SELF-MONITORING OF BLOOD GLUCOSE (SMBG) -- the four "cornerstones" of diabetes control. In the cases of proper nutrition, exercise, and medication, both hyperglycemia and hypoglycemia can occur with relative ease when any one of these is disrupted. Problems ensue, also, if the person experiences severe stress (physical or emotional) which produces an outpouring of epinephrine and glucocorticoids. These are hormones produced in the body that fuel the "fight or flight" response to a stressor. Glucocorticoids specifically increase the blood glucose. (Review the "stress response" or the "General Adaptation Syndrome" in any physiology text to learn more about this, if necessary.)

The ingestion of carbohydrates – sugars and starches – leads to an increase in the blood glucose in the body. (Take a look at the amount of carbohydrate (reported in grams) listed on the "Nutrition Facts" label included on the packaging of foods). Insulin causes a decrease in blood glucose. Exercise leads to a decrease in blood glucose as the body's cells use it for energy.

To review, for most people, the increase in blood glucose that occurs during and after a meal stimulates the release of precisely the right amount of insulin to make use of the glucose in the blood, and to bring it, eventually, back to normal. In people with diabetes, this does not happen quite as smoothly as that. As a matter of fact, in people with DMT1, there is no production of insulin at all and the blood glucose rises to extremely high levels and eventually metabolic acidosis ensues. Death will result if insulin is not administered.

In those with DMT2, while insulin is produced, the body's cells are in varying degrees resistant to it. Consequently, more and more insulin must be produced to metabolize glucose until the body can no longer meet the demand. Blood glucose rises uncontrollably. As noted in previous content of this self-study, the individual with DMT2 typically does not develop metabolic acidosis, but the signs and symptoms associated with hyperglycemia will undoubtedly appear and the individual will feel ill. Exercise leads to a decrease in blood glucose.

LEARNER ACTIVITY

Cover the column labeled "Answers". Identify the effects on blood glucose of changes in the following factors associated with diabetes treatment. (For the sake of discussion, only insulin is listed as a medication used in treatment of diabetes, but other drugs that stimulate insulin production can have the same effect on blood glucose.) Place an arrow in the blank space to indicate either an expected increase or decrease in blood glucose. Remove the cover and assess your understanding:

(Cover answers on the right and then compare with your answers.)

			Answers
1.	↑ Carbohydrate intake leads to _____	blood glucose	↑
2.	↓ Carbohydrate intake leads to _____	blood glucose	↓
3.	↑ Insulin leads to _____	blood glucose	↓
4.	↓ Insulin leads to _____	blood glucose	↑
5.	↑ Exercise leads to _____	blood glucose	↓
6.	↓ Exercise leads to _____	blood glucose	↑
7.	↑ Emotional stress leads to _____	blood glucose	↑

Note: Remember that, in some cases, exercise can reduce the blood glucose without the influence of insulin or oral medications. Exercise must be considered as a catalyst of diabetes medications when one attempts to balance the cornerstones.

Consider the possibility of effects "canceling" one another out or enhancing the effects of one another. It is important to understand this so that you can teach patients the effects of doing their own "manipulations." Also, if patients have had DMT1 for a long period of time, they will most likely have already figured out and used ways they think will "beat the system": how to eat more or less, ski all weekend without stopping for medication or meals, or sleep all weekend without waking for medication or meals. Each of these is accomplished by altering one or more of the "cornerstones" and can be very dangerous. It is much better to discuss the effects of such manipulations than to hope that patients will not attempt them.

LEARNER ACTIVITY

Consider the effects of the indicated changes below:

1.	↑	Carbohydrate intake	↑	insulin, maintain same exercise.	Could these balance?
2.	↓	Carbohydrate intake	↓	insulin, maintain same exercise.	Could these balance?
3.	↑	Carbohydrate intake	↑	exercise, maintain same insulin.	Could these balance?

Now, what is likely to happen in the following situations?

4.	↑	Exercise	↓	Carbohydrate intake, maintain same insulin.	Could these balance?		
5.	↓	Carbohydrate intake	↑	insulin	↓	exercise.	Could these balance?
6.	↑	Carbohydrate intake	↓	exercise, maintain same insulin.	Could these balance?		
7.	↑	Carbohydrate intake	↑	insulin	↓	exercise.	Could these balance?

Answers:

- (Answer: Yes, they could, but hyperglycemia or hypoglycemia could also result.)
- (Answer: Yes, they could, but hyperglycemia or hypoglycemia could also result.)
- (Answer: Yes, they could, but hyperglycemia or hypoglycemia could also result.)
- (Answer: This would cause hypoglycemia.)
- (Answer: This would cause profound hypoglycemia.)
- (Answer: This could cause hyperglycemia, and, if high enough, could result in Hyperosmolar Hyperglycemic State, also referred to as "HHS" – a severe state of hyperglycemia which requires emergency intervention and hospitalization. See this term in the glossary).
- (Answer: This could lead to hyperglycemia and metabolic acidosis as could ↓ carbohydrate intake, ↓ exercise, and ↓ insulin.)

People with diabetes must understand that taking and recording blood glucose values at regular intervals (to include fasting, before meals, two-hours after meals, at bed time and, if necessary, one or two times in the night on occasion to determine changes through the night) are necessary activities to obtain the information needed to determine effectiveness of the treatment regimen. Sharing the documentation of the values (and times obtained) is an important component of every visit with the health care provider, so it is absolutely critical that the individual writes the information on paper and shares it with the health care provider at the time of the visit.

The reason this information is necessary is that decisions relative to the degree of blood glucose control must be made based on *patterns* of blood glucose changes, not on one or two isolated events. One can make sound decisions about whether the regimen a patient is following is effective in maintaining blood glucose control only on the basis of patterns of blood glucose changes.

Even as the importance of the results of SMBG is emphasized, one must recognize that blood glucose testing requires equipment and materials – a meter, lancets, alcohol swabs, and blood glucose strips – that could represent a financial hardship for some individuals. Failure to comply with SMBG activities may reflect financial constraints more than unwillingness to cooperate. It is important to determine if this is the case in those patients who regularly do not bring results with them to their regular visits. It may be possible for the manufacturing company to provide some remedies for this situation.

This is the end of the content of the Home Study Program, Diabetes Fundamentals. Please complete the post-test and the evaluation form. Thank you.

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Resources – all links current as of 08/15/18

- **American Camp Association**

- 5000 State Road 67 North
Martinsville, IN 46151-7902
1-800-428-2267
1-765-342-8456
Fax: 765-342-2065
- Web: <http://www.acacamps.org>
- Contact the above for information on summer camps for children with diabetes in the U.S. At this web site go to "Find a Camp." Click on "Search by camp name" and write in "diabetes" at the next screen.

- **American Diabetes Association**

- 1701 North Beauregard St.
Alexandria, VA 22311
1-800-DIABETES (1-800-342-2383)
- Web: <http://www.diabetes.org>
- Publishes *Diabetes Forecast* (\$28 for a full year's subscription which is suitable for lay people). Search for "Diabetes Forecast" on the front page of the web site.

- **Academy of Nutrition and Dietetics** (formerly, "The American Dietetic Association")

- The Chicago-based Academy of Nutrition and Dietetics is the world's largest organization of food and nutrition professionals, with nearly 75,000 members. "Visit the **Academy of Nutrition and Dietetics** online 24 hours a day, seven days a week, at your convenience and discover a wealth of information at your fingertips!"
- Web: <http://www.eatright.org>
- Headquarters
Academy of Nutrition and Dietetics
120 South Riverside Plaza, Suite 2000
Chicago, Illinois 60606-6995
Call 1-800-877-1600 for information
- Washington, D.C. Office
Academy of Nutrition and Dietetics
1120 Connecticut Avenue NW, Suite 480
Washington, D.C. 20036
Phone: 1-800-877-0877

- **Children With Diabetes**

- On-line community for children, families, and adults with diabetes:
- Web: <http://www.childrenwithdiabetes.com>

- **Joslin Diabetes Center**
 - One Joslin Place
Boston, MA 02215
 - Web: <http://www.joslin.harvard.edu>
 - This web site has a wealth of information about diabetes.

- **Juvenile Diabetes Research Foundation International (JDRFI)**
 - 26 Broadway
New York, NY 10004
Phone: 1-800-533-CURE (2873)
Fax: (212) 785-9595
 - Web: <http://www.idrf.org>
 - Main objectives of JDRFI are finding a cure for DMT1 and providing resources for individuals with DMT1.

- **Medic Alert Foundation**
 - Web: <http://www.medicalert.org>
 - Call 1-888-633-4298 for information.
 - MedicAlert Foundation is a nonprofit organization providing 24-hour emergency medical information and identification service. For more than 50 years, Medic Alert Foundation International has been available to relay vital medical information to emergency care providers about members' medical conditions, allergies, medications and dosages. Membership requires an annual fee.

- **Medtronic Diabetes**
 - Information about insulin pump therapy and continuous glucose monitoring
 - Web: <http://www.medtronicdiabetes.com>

- **National Institute of Diabetes and Digestive and Kidney Diseases**
 - 9000 Rockville Pike
 - Bethesda, MD 20892
 - Telephone: 1-800-860-8747
 - Web: <http://diabetes.niddk.nih.gov/>

GLOSSARY

alpha cells of the pancreas -- secrete glucagon in response to decrease in blood glucose

beta cells of the pancreas -- secrete insulin in response to increase in blood glucose

compliance -- adherence to prescribed treatment regimen

DPP-4 -- dipeptidyl peptidase 4 -- This is an intestinal enzyme that blocks the action of hormones such as GLP-1 (see "glucagon-like peptide-1" below).

DPP-4 inhibitors -- a class of drugs used to treat DMT2 (and, in conjunction with insulin, DMT1) which block the action of DPP-4 and thereby lead to an increase in GLP-1. The end result of the actions of DPP-4 inhibitors is the enhanced secretion of GLP-1 (glucagon-like peptide-1). Two examples of DPP-4 inhibitors are sitagliptin and saxagliptin.

DKA -- Diabetic KetoAcidosis; a form of metabolic acidosis due to insufficient insulin and the consequences of the chemical changes which occur as a result

endogenous -- from within the body

exogenous -- from outside the body; "exogenous insulin" is that insulin which is injected into the body from an outside source

GLP-1 -- glucagon-like peptide-1 -- a naturally occurring hormone that is secreted by intestinal cells in response to the ingestion of food. Such chemicals are called "incretins." GLP-1 stimulates the islet cells in the pancreas to produce insulin (possible in DMT2; not possible in DMT1). GLP-1 also slows gastric emptying, reduces appetite, increases the sense of satiety, and suppresses glucagon secretion. GLP-1 has a very short activity period because it is degraded by the enzyme, dipeptidyl peptidase 4 (DPP-4). An example of a GLP-1 is exenatide.

glucagon -- hormone secreted by alpha cells of pancreas; stimulates breakdown of glycogen and release of glucose by the liver

glucometer -- a device designed for self-monitoring of blood glucose

gluconeogenesis -- formation of glycogen from non-carbohydrate sources such as proteins and fats; occurs in liver under conditions of starvation or in any case when the body is deprived of sufficient glucose to meet its needs; occurs in uncontrolled/undiagnosed diabetes, despite hyperglycemia, because glucose cannot be used by the body due to the lack of insulin

glucose reagent strips -- materials treated with a substance which indicates varying amounts of glucose in the blood; usually **used** with a glucometer

glucosuria -- glucose in the urine

glycogen -- a storage form of glucose; converted into glucose when needed by the influence of the hormone, glucagon

glycosylated hemoglobin -- component of hemoglobin molecule which can be measured to indicate average blood glucose over past three months; also called "hemoglobin A1c," "HgbA1c," "HbA1c," and simply, "A1c"

HHS -- Hyperosmolar Hyperglycemic State; a pathophysiological state due to excessive blood sugar typically without ketonemia; previously called "HHNK" (Hyperglycemic Hyperosmolar Nonketotic" coma) until it was determined that it sometimes occurs in the presence of ketones

hyperglycemia -- high blood glucose

hypertonic -- having a higher osmotic pressure than a compared solution; a "concentrated" solution

hypoglycemia -- low blood glucose

immunosuppressive drug -- blocks the body's response to foreign tissue; also known as "anti-rejection" drug; examples are cyclosporine, Imuran, and FK506

ketonemia -- ketones in the blood

ketonuria -- ketones in the urine

metabolic acidosis -- abnormally low pH of the blood due to aberrant metabolic processes in the body

microalbuminuria -- protein elements indicative of kidney disease which appear in the urine at the earliest stages of the problem; detectable by a urine test

negative nitrogen balance -- metabolic state in which amount of nitrogen ingested is less than the amount excreted; could be the result of insufficient intake or excessive protein breakdown or both

neuropathy -- disease of a nerve; a complication which sometimes occurs in diabetes

oral hypoglycemic agents -- oral medications sometimes used to control DMT2; stimulate the pancreas to produce insulin

peripheral vascular disease/peripheral arterial disease -- disease of the small, distal arteries of the legs and feet; a complication which sometimes occurs in diabetes

polydipsia -- insatiable thirst that leads to frequent, excessive drinking; one of the cardinal signs of uncontrolled/undiagnosed diabetes

polyphagia -- excessive eating; one of the cardinal signs of uncontrolled/undiagnosed diabetes

polyuria --excessive urination; one of the cardinal signs of uncontrolled/undiagnosed diabetes

renal threshold -- blood glucose level at which kidneys can no longer reabsorb glucose into the blood and glucose spills into the urine

satiety -- physiological sense of being "full" to satisfaction (refers to state of body after eating)

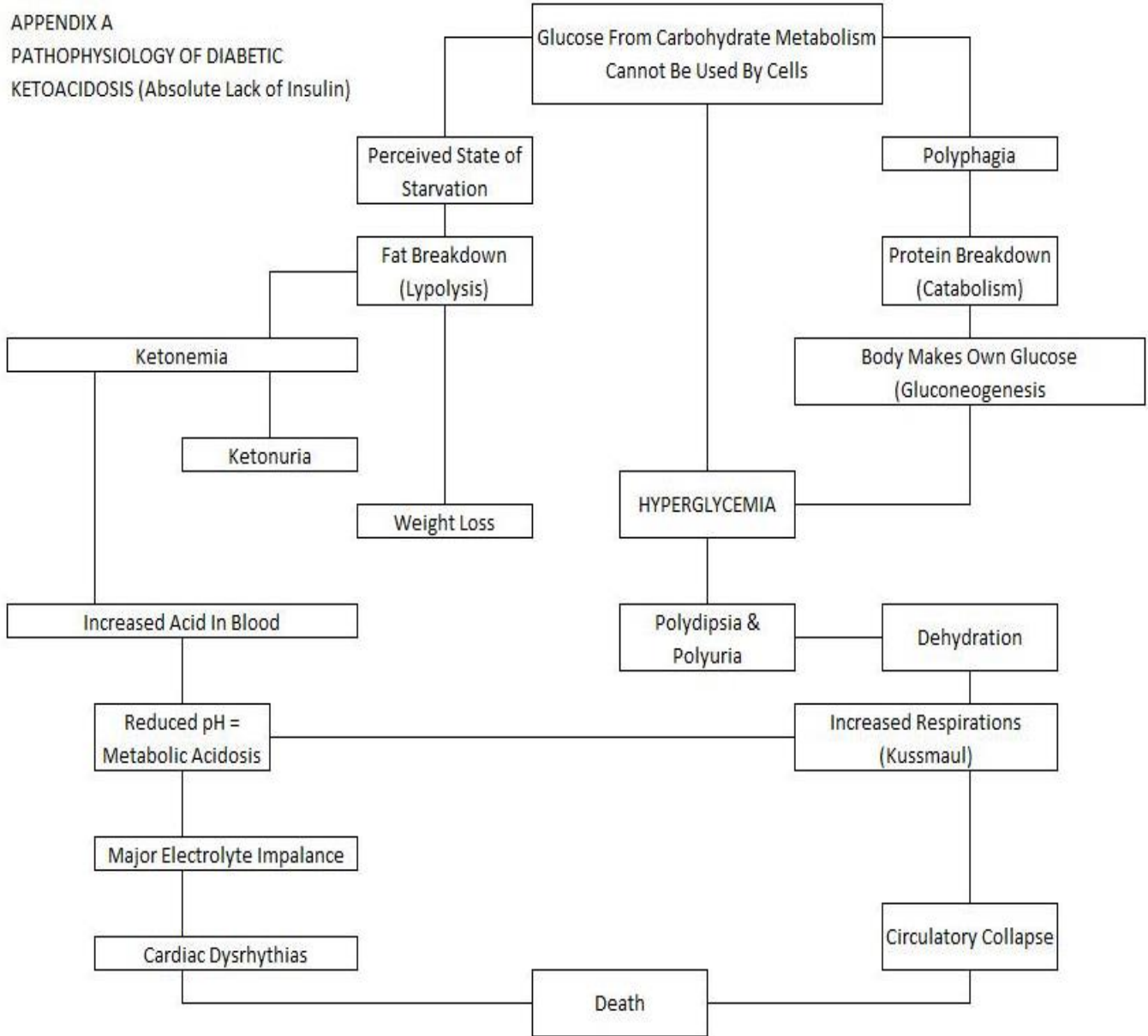
Somogyi Effect -- the occurrence of hyperglycemia after an episode of hypoglycemia; the result of a hypoglycemic reaction which stimulates body processes which raise the blood glucose

Type 1 diabetes (DMT1) -- previously known as type I diabetes, insulin-dependent diabetes, and juvenile diabetes; the type of diabetes that results from an absolute lack of insulin; usually occurs in persons under 24 years of age. Treatment is with insulin. Newer treatments may include pramlintide -- a synthetic reproduction of the hormone, amylin.

Type 2 diabetes (DMT2) -- previously known as type II diabetes, non-insulin-dependent diabetes, and adult onset diabetes; the type of diabetes that results from a relative lack of insulin -- from insulin resistance and impaired insulin secretion; treatment includes education about nutrition and eating patterns, exercise, and (usually) weight loss; treatment may also include oral anti-diabetic agents, injectable incretin mimetics, and/or insulin.

APPENDIX A: PATHOPHYSIOLOGY OF DIABETIC KETOACIDOSIS
(ABSOLUTE LACK OF INSULIN)

APPENDIX A
PATHOPHYSIOLOGY OF DIABETIC
KETOACIDOSIS (Absolute Lack of Insulin)



VGM/vgm 08/15/18

CE EXAM

DIABETES MELLITUS FUNDAMENTALS

1. Diabetes is:
 - A. Curable with weight loss
 - B. A fatal disease
 - C. A disorder of protein metabolism
 - D. A disorder of (predominantly) carbohydrate metabolism

2. Which of the following is **NOT** a cardinal sign of uncontrolled/undiagnosed type 1 diabetes?
 - A. Polyuria
 - B. Polyphagia
 - C. Polydipsia
 - D. Weight gain

3. A sign of uncontrolled/undiagnosed type 1 diabetes includes changes in the urine. Identify one such sign from the list below.
 - A. Absence of glucosuria
 - B. Presence of ketonuria
 - C. Presence of cloudy urine
 - D. Presence of albuminuria

4. A sign of uncontrolled/undiagnosed type 1 diabetes is that the pH of the blood:
 - A. Increases
 - B. Decrease
 - C. Is greater than 7.6
 - D. Does not change

5. A lab test used to diagnose diabetes is the:
 - A. Three-hour post-prandial blood glucose of 100 mg/dL
 - B. Fasting blood glucose > 126 mg/dL obtained on two different days
 - C. Tonicity of the blood
 - D. Test for glucosuria

6. Which of the following accurately describes the body's physiologic response when it is deprived of sufficient insulin to meet its metabolic needs?
 - A. Inability to metabolize glucose leads to an increased blood pH.
 - B. Protein anabolism leads to gluconeogenesis.
 - C. Breakdown of fat creates ketonemia which leads to acidosis.
 - D. Carbohydrate catabolism creates hyperglycemia.

7. Explain why body weight decreases in uncontrolled/undiagnosed DMT1.
 - A. Protein and fat catabolism occur to meet energy needs unmet by normal carbohydrate metabolism due to an absolute lack of insulin.
 - B. Since glucose cannot be transported across the cell membrane, fat cannot be manufactured resulting in a loss of body weight.
 - C. Hyperglycemia reduces the tonicity of the blood leading to excessive loss of fluid through excretion of urine resulting in a loss of body weight.
 - D. Hyperglycemia leads to loss of appetite resulting in less food eaten. Weight loss results from reduced intake of calories.

8. Physiologically, the underlying metabolic pathway utilized by the body in uncontrolled/undiagnosed DMT1 is similar to that used during periods of starvation.
 - A. True
 - B. False

9. Ketones are:
 - A. Responsible for kidney damage in diabetes
 - B. End-products of fat breakdown
 - C. Buffering agents in an acidic environment
 - D. Beneficial in high concentrations

10. Glycogen is defined as:
 - A. Abnormal products in the urine reflective of fat metabolis
 - B. A stored form of glucose
 - C. Excessive drinking
 - D. Hormone that leads to an increase in blood glucose

11. Polydipsia is defined as:
- A. Abnormal products in the urine reflective of fat metabolis
 - B. Stored carbohydrate
 - C. Excessive drinking
 - D. A hormone that leads to an increase in blood glucose
12. Ketonuria is defined as:
- A. Abnormal products in the urine reflective of fat metabolis
 - B. Stored carbohydrate
 - C. Excessive drinking
 - D. Hormone that leads to an increase in blood glucose
13. Glucagon is defined as:
- A. Abnormal products in the urine reflective of fat metabolis
 - B. Stored carbohydrate
 - C. Excessive drinking
 - D. A hormone that leads to an increase in blood glucose
14. Which of the following is a true statement concerning comparisons between diabetes type 1 (DMT1) and DMT2?
- A. Both typically include the development of ketones prior to effective treatment.
 - B. Obesity is a common element in both conditions.
 - C. DMT2 is treated with diet, exercise, and oral agents, only, whereas DMT1 is treated exclusively with insulin.
 - D. Ketonuria is typically not found in DMT2.
15. Insulin is a:
- A. Digestive enzyme produced by special cells in the pancreas
 - B. Hyperglycemic agent produced in the pancreas but stored in the liver
 - C. Hormone produced by special cells in the islets of langerhans
 - D. Hormone produced by the anterior pituitary gland

16. The hormone produced in the alpha cells of the pancreas which has opposite effects of insulin is:
- A. Glycogen
 - B. Lipase
 - C. Glucagon
 - D. Pancreatase
17. Insulin's functions include each of the following EXCEPT:
- A. Facilitating the passage of glucose across cell membrane
 - B. Inhibiting the conversion of glycogen to glucose
 - C. Promoting the breakdown of protein to glucose and inhibiting protein synthesis
 - D. Promoting the conversion of fatty acids to fat and inhibiting the breakdown of fat
18. The net effect of all of the functions of insulin is to:
- A. Decrease blood glucose
 - B. Increase blood glucose
 - C. Stimulate the breakdown of glycogen
 - D. Inhibit the development of metabolic alkalosis
19. Which of the following produces an increase in blood glucose?
- A. Insulin
 - B. Thyroxine
 - C. Calcitonin
 - D. Glucagon
20. Which of the following statements provides rationale for encouraging the diabetic to avoid excessive stress (physical and emotional) and/or coping with stress effectively:
- A. Excessive stress causes people to overeat leading to problems with glucose control.
 - B. The stress response leads to a systemic outpouring of glucocorticoids and epinephrine which lead to increased BG.
 - C. People with diabetes become forgetful when stressed, so may forget such things as medications and self-monitoring of BG.
 - D. Such stress leads to gastric ulcers which compromise diabetes control.

21. The four cornerstones of diabetes management are proper nutrition, exercise, insulin, and self-monitoring of blood glucose (SMBG).
- A. True
 - B. False
22. Weight loss can cure diabetes type 2.
- A. True
 - B. False
23. The net effect on the diabetic's blood glucose of ingesting more carbohydrate than recommended is:
- A. Increased BG
 - B. Decreased BG
 - C. Profound decrease in BG
 - D. No change expected
24. The net effect on blood glucose of increasing insulin and exercising more than usual is-
- A. Increased BG
 - B. Decreased BG
 - C. Profound decrease in BG
 - D. No change expected
25. If the type 1 diabetic reduces her/his usual dosage of insulin intake with no other changes, what outcomes might occur as a result?
- A. Hypoglycemia
 - B. Ketonemia
 - C. Glucagon production
 - D. Weight gain
26. Which of the following circumstances is likely to lead to hypoglycemia in the individual taking medication for diabetes?
- A. A meal contains more fat than is recommended.
 - B. Less carbohydrate is ingested than is recommended.
 - C. A dose of medication is missed.
 - D. Usual exercise is not performed.
27. Which of the following could result in hyperosmolar hyperglycemic state (HHS) in the person with diabetes? The person with:

- A. DMT1 forgets to take his insulin
 - B. DMT2 exercises more than usual
 - C. DMT1 takes too much insulin
 - D. DMT2 eats an entire cherry pie
28. Diabetic ketoacidosis can develop in the person with DMT2 when she/he:
- A. Overeats carbohydrates
 - B. Has an infection
 - C. Forgets to take his/her oral anti-diabetes medication
 - D. None of the choices is correct
29. Hospitalization is usually required for which of the following conditions in the person with diabetes:
- A. Hypoglycemia
 - B. Hyperosmolar hyperglycemic state (HHS)
 - C. Hyperglycemia
 - D. Infection
30. A primary complaint of people with undiagnosed DMT2 is often fatigue.
- A. True
 - B. False
31. Which of the following blood glucose values suggests impaired glucose tolerance (IGT)?
- A. Blood glucose of 190 mg/dL two hours after having ingested a specific amount of glucose in a standardized oral glucose tolerance test (OGTT)
 - B. Blood glucose of 135 mg/dL two hours after having ingested a specific amount of glucose in a standard OGTT
 - C. Fasting blood glucose of 120 mg/dL
 - D. Fasting blood glucose of 95 mg/dL
32. Which of the following blood glucose values suggests impaired fasting glucose (IFG)?
- A. Blood glucose of 190 mg/dL two hours after having ingested a specific amount of glucose in a standard OGTT
 - B. Blood glucose of 135 mg/dL two hours after having ingested a specific amount of glucose in a standard OGTT
 - C. Fasting blood glucose level of 120 mg/dL
 - D. Fasting blood glucose level of 95 mg/dL

33. The presence of gestational diabetes in a woman represents a risk factor for her later development of diabetes.
- A. True
 - B. False
34. A child is considered "overweight" when which of the following conditions is present?
The child's:
- A. Body mass index (BMI) is over the 5th percentile for age and gender
 - B. Weight by height is greater than the 8th percentile
 - C. Current weight is 150% of his/her ideal weight for height
 - D. Waist circumference exceeds 30"
35. The American Diabetes Association recommends testing overweight children for diabetes and pre-diabetes if they have at least two risk factors for diabetes.
- A. True
 - B. False
36. A child whose mother had gestational diabetes when she was pregnant with him/her is at risk for the development of diabetes.
- A. True
 - B. False
37. Which of the following testing methods is recommended for screening children for diabetes?
- A. Oral glucose tolerance test
 - B. Fasting blood sugar
 - C. Hemoglobin a1c
 - D. 2-hour post-prandial blood glucose
38. An adult male's waist circumference measures 46 inches. This has been found to be associated with what condition?
- A. Metabolic syndrome
 - B. Hypertension
 - C. Hyperosmolar hyperglycemic state (HHS)
 - D. No condition. This is within normal limit.
39. The American Diabetes Association recommends which of the following as the initial intervention for the patient diagnosed with DMT2?

- A. Life style management, only
 - B. Metformin, only
 - C. Rosiglitazone and life style management
 - D. Metformin and life style management
40. The American Diabetes Association recommends which of the following as the goal for A1c for non-pregnant adults with diabetes?
- A. Less than 8.5%
 - B. Less than 8.0%
 - C. Less than 7.5%
 - D. Less than 7.0%
41. Barry is a 62 year old male. He has not been feeling well for some time, so he sees his healthcare provider on Monday. The healthcare provider sends him to a standardized lab for a hemoglobin A1c. The result is 7.0%. On Friday, a second hemoglobin A1c is drawn at the same lab. The result is 6.8%. What conclusion can be drawn from these two results? Barry:
- A. Has diabetes
 - B. Has pre-diabetes
 - C. Must have a fasting blood glucose to confirm the results
 - D. Should return in three months to have the tests repeated
42. Researchers/authors cited within the self-study reported figures which indicated that between 2009 and 2034 the number of people with diagnosed and undiagnosed diabetes in the United States would _____.
- A. Nearly double
 - B. Increase by one million
 - C. Include 50% children
 - D. Stabilize at 30 million
43. There is an epidemic of obesity in this country at this time.
- A. True
 - B. False
44. There is an epidemic of DMT2 in this country at this time.
- A. True
 - B. False

45. Professional nurses have an obligation to assure that the newly diagnosed diabetic is effectively educated for self-care.
- A. True
 - B. False