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Contact Hours: **2**

Metabolic Syndrome
Risk, Diagnosis, and Treatment

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LEARNING OUTCOME AND OBJECTIVES: Upon completion of this continuing education course, you will demonstrate knowledge of evidence-based guidelines related to caring for patients with metabolic syndrome. Specific learning objectives to address potential knowledge gaps include:

- Describe the group of patient characteristics defining metabolic syndrome.
- Identify parameters for the key characteristics for metabolic syndrome.
- Discuss the criteria used to diagnose metabolic syndrome.
- Review current treatment guidelines and management strategies for patients.
- Identify other diseases and health problems associated with metabolic syndrome.
- Explain the recommended lifestyle changes for controlling risk factors associated with metabolic syndrome.
- Identify serious comorbidities associated with metabolic syndrome and interventions utilized for their effective treatment.
- Discuss strategies for the prevention of metabolic syndrome.

WHAT IS METABOLIC SYNDROME?

Metabolic syndrome is not a disease in the usual sense. Instead, it is a condition including a group of characteristics that impact the body's ability to maintain circulation of useful but not excessive levels of energy molecules (i.e., glucose and lipids) in the bloodstream. These characteristics include a cluster of health problems associated with diabetes (i.e., glucose

intolerance, hyperinsulinemia); high levels of triglycerides, glucose, and cholesterol; and insulin resistance (Mandal, 2019).

Initially, when the resulting health problems arise, they interact to worsen each other. Eventually, the set of problems (i.e., hyperglycemia, hyperlipidemia) becomes severe enough to lead to serious health consequences. At this point, clinicians say that a person has metabolic syndrome (Durkin, 2019; Merck Manual, 2020). From studies of large populations of people, the most common cluster of characteristics of persons with metabolic syndrome has been found to include obesity, insulin resistance, dyslipidemia (i.e., increased fasting triglycerides or decreased fasting high-density lipoprotein), and hypertension (NHLBI, 2019).

Metabolic syndrome has become increasingly common in the United States, and it is a major public health problem. Metabolic syndrome increases the risk of cardiovascular disease, diabetes, stroke, and coronary artery disease.

The primary causes of metabolic syndrome include obesity, physical inactivity, and possible genetic factors. The primary treatment of choice for metabolic syndrome includes lifestyle modifications such as increasing physical activity; eating a heart-healthy diet; and lowering blood glucose, blood cholesterol, and blood pressure (AHA, 2016).

DEFINITION OF METABOLIC SYNDROME

According to the guidelines from the National Heart, Lung, and Blood Institute and the American Heart Association, a diagnosis of metabolic syndrome is made if at least three of the following are present:

- Abdominal obesity: Waist circumference >102 cm (>40 inches) in men, >89 cm (>35 inches) in women
- Hypertriglyceridemia: Blood triglycerides >150 mg/dL (or on triglyceride-lowering medication)
- Low high-density lipoprotein (HDL) cholesterol: Blood HDL cholesterol <40 mg/dL in men, <50 mg/dL in women
- High blood pressure: BP >130/85 mmHg (or already diagnosed with hypertension)
- High fasting glucose: Blood glucose >100 mg/dL

(AHA, 2016; NHLBI, 2019)

It is estimated that 47 million Americans have metabolic syndrome, but many may not even know they have it. Metabolic syndrome prevalence increased from 1988 to 2012 for every sociodemographic group, especially among non-Hispanic White women, non-Hispanic Black women, and people with low socioeconomic status. By 2012, 34% of all U.S. adults met the definition and criteria for metabolic syndrome (Sherif, 2017; Moore et al., 2017). However, more recently, prevalence of the syndrome is declining, with rates as low as 24% in men and 22% in women (Swarup et al., 2020).

CAUSES/RISK FACTORS FOR METABOLIC SYNDROME

Metabolic syndrome appears to result from the interaction of a number of disorders that can be initiated separately. The development of metabolic syndrome is related to three issues:

- **Weight.** It is estimated that approximately 22% of people who are overweight and 60% of people who are obese have metabolic syndrome. The risk is believed to be directly related to the amount of abdominal fat, which is defined by waist circumference. However, not everyone who is overweight or obese has metabolic syndrome, and people who are of normal weight can also develop metabolic syndrome.

- **Lack of exercise.** Lack of exercise has been shown to be linked to a variety of diseases, including heart disease, cancer, and diabetes. Additionally, lack of exercise contributes to weight gain, being overweight, and becoming obese.

- **Genetics.** Research indicates that there may be a genetic link for the development of metabolic syndrome among family members.
  (Merck Manual, 2020; Sherif, 2017)

Although the specific chain of events leading to the appearance of metabolic syndrome is still not clear, much is known about the development and interactions of its separate components. Here is a summary of the causes of the individual components of metabolic syndrome.

Intra-Abdominal Obesity

Abdominal obesity is a significant predictor of metabolic syndrome. This is because abdominal (visceral) fat tends to be more resistant to insulin than fat in other areas of the body (Merck Manual, 2020). The amount of visceral fat, which tends to accumulate more in women after menopause, is the most important risk factor for metabolic syndrome (Sherif, 2017).

Having a large waistline means that there is excess body weight around the waist. A waist measurement of 35 inches or more for women or 40 inches or more for men is indicative of risk for metabolic syndrome. A large waistline is also a risk factor for other health problems such as cardiovascular disease (NHLBI, 2019).

GENETIC FACTORS THAT CONTRIBUTE TO OBESITY

In the past few decades, obesity has reached epidemic proportions in the United States. Genetics can play a significant role in the development of obesity. Studies of comparisons among family members, twins, and adoptees provide evidence that a sizable part of the variations in weight among adults is linked to genetic factors. Additionally, studies have identified variants in several genes that may contribute to the development of obesity by increasing hunger signals and food intake. Rarely, inherited obesity is caused by a specific variant of a single gene. The research that focuses on the genetic factors that contribute to the development of metabolic syndrome is at an early stage (CDC, 2018).

NONGENETIC FACTORS THAT CONTRIBUTE TO OBESITY

Prenatal. There are a number of factors that increase the risk for obesity beginning during the period of fetal development. These include a history of:

- Maternal smoking during pregnancy
- Gestational weight gain
- Gestational diabetes
  (Harvard School of Public Health, 2017)

Stress and anxiety can lead to overeating in an attempt to control negative emotions and find comfort. Sometimes referred to as *stress eating,* this type of eating can lead to significant weight gain.

Pharmacologic. Many medications have weight gain as a side effect, and it is important to monitor persons taking these medications. They include:

- Psychiatric drugs (e.g., lithium, atypical antipsychotics such as clozapine and olanzapine, and antidepressants such as the tricyclics)
- Neurologic drugs (e.g., antiepileptic drugs such as valproate)
- Steroids (e.g., hormonal contraceptives, prednisone)
- Antidiabetic drugs (e.g., insulin)
- Antihistamines
- Beta-blockers
  (Comerford, 2017)

SUGAR-SWEETENED BEVERAGES AND WEIGHT GAIN

There is significant evidence that regular intake of sugar-sweetened beverages or foods that contain added sugars in the form of high fructose corn syrup or table sugar (sucrose) can lead to weight gain and an increase in risk of developing type 2 diabetes and cardiovascular disease. Research findings show that consuming one or more sugar-sweetened beverages a day is associated with greater weight gain and obesity (ACC, 2015).

Insulin Resistance

Insulin triggers the mechanisms that cells use to take up glucose from their surroundings. In addition, insulin tells cells to:

- Use their internal glucose for generating energy

- Store any excess internal glucose in the form of glycogen
- Stop releasing internal stores of glucose into the circulation

Under normal conditions, insulin molecules bind to the receptors on the cells of the body. When cell portals are activated by insulin, they open to allow glucose to enter the cell, where it is converted to energy. Insulin resistance exists when a given amount of insulin produces a less-than-expected biologic effect. In insulin resistance there is an increased insulin secretion to maintain normal glucose and lipid homeostasis.

Insulin resistance plays a major pathogenic role in the development of metabolic syndrome. Metabolic syndrome may include any or all of the following:

- Hyperinsulinemia
- Type 2 diabetes or glucose intolerance
- Central obesity
- Hypertension
- Dyslipidemia that includes high triglyceride levels
- Low HDL cholesterol level and small, dense low-density lipoprotein (LDL) particles
- Hypercoagulability
  (NHLBI, 2019)

GENETICS AND INSULIN RESISTANCE

As with many pathologic processes, insulin resistance develops most readily in people with a genetic predisposition for it. In predisposed people, it is possible that certain genes produce poorly functioning insulin receptor subunits or other molecules in the intracellular chain leading from the receptor to the actual glucose utilization machinery. It is still not clear, however, if any of these potential problems are common causes of the genetic predisposition to develop insulin resistance.

A family history of diabetes, lipid disorders, hypertension, or heart disease increases the risk for development of metabolic syndrome (NHLBI, 2019).

EXCESS VISCERAL FAT AND INSULIN RESISTANCE

Abdominal (visceral) obesity is a powerful predictor of metabolic syndrome because visceral fat tends to be more resistant to insulin than fat in other areas of the body. This resistance increases the release of free fatty acids into the portal system, which leads to increased apolipoprotein B, increased LDL, decreased HDL, and increased triglyceride levels. Because of elevated “bad” cholesterol and decreased “good” cholesterol, the risk of cardiovascular diseases also increases (Durkin, 2019).

Insulin resistance can be triggered by anything that causes high blood levels of free fatty acids, glucose, or insulin. Conditions that lead to insulin resistance through this mechanism include high levels of glucocorticoids (e.g., Cushing disease or long-term treatment with prednisone), nonalcoholic fatty liver disease, and treatment with protease inhibitors (e.g., for HIV).

Dyslipidemias

Dyslipidemia is an unhealthy amount of lipids circulating in the bloodstream. The specific dyslipidemias of metabolic syndrome include an increase in blood triglycerides and a decrease in blood HDL lipoproteins.

There are five types of lipoproteins:

- Chylomicrons: These are the largest and least dense of the lipoproteins and have the highest triglyceride content.
- VLDL (very-low-density lipoprotein): VLDL is composed of protein, fats, and cholesterol.
- IDL (intermediate-density lipoprotein): IDL is created by the metabolism of VLDL.
- LDL (low-density lipoprotein): This is the last remnant of VLDL and contains mostly cholesterol.
- HDL (high-density lipoprotein): HDL has the highest protein-to-lipid ratio and is the densest lipoprotein. It is referred to as *good cholesterol* because it transports cholesterol away from the tissues to the liver, which lowers blood cholesterol levels. (Ahmed et al., 2020)

GENETICS AND DYSLIPIDEMIAS

A number of different genetic mutations that affect fat cells will cause the dyslipidemias of metabolic syndrome. In addition, certain genetic mutations of apolipoproteins (e.g., familial combined hyperlipidemia) will cause high blood levels of triglycerides and low blood levels of HDL cholesterol.

Beyond direct genetic causes, the dyslipidemias of metabolic syndrome can result from a variety of problems.

METABOLIC DISORDERS AND DYSLIPIDEMIAS

The most common causes of dyslipidemias are other metabolic problems. Examples of such problems include:

- Diabetes
- Hypothyroidism
- Polycystic ovary syndrome
  (MedlinePlus, 2020a)

LIFESTYLE AND DYSLIPIDEMIAS

The same habits that tend to make a person obese will also cause lipid problems. Dyslipidemias can result from insufficient physical activity and a high-calorie diet with excess carbohydrates and excess saturated fats.

KIDNEY PROBLEMS AND DYSLIPIDEMIAS

Patients with chronic renal failure develop increased levels of triglycerides and decreased levels of HDL cholesterol. Later, if they receive kidney transplants, patients are put on immunosuppressive drugs, typically glucocorticoids and cyclosporine; these drugs also raise blood triglycerides and reduce blood HDL cholesterol (Comerford, 2017).

Hypertension

Hypertension develops when there is an increase in cardiac output, peripheral resistance, or both. There are a number of factors that play a role in the development of hypertension. These include:

- Family history
- Race (most common in African Americans)
- Stress
- Obesity
- Diet high in saturated fats or sodium
- Tobacco use
- Hormonal contraceptives
- Sedentary lifestyle
- Aging
  (Durkin, 2019)

GENETICS, RACE, AGE, AND HYPERTENSION

Hypertension has a tendency to run in families, especially in individuals with a family history from both parents. However, the genetic reasons for these patterns are not fully understood. In addition, the prevalence of the condition increases in people age 60 and over. African Americans are at highest risk to have hypertension starting at a younger age; often it is more severe and difficult to manage (Medline Plus, 2020b).

LIFESTYLE AND HYPERTENSION

Hypertension is a chronic condition that may be the result of lifestyle factors mentioned above, and it requires long-term management. Education and supportive resources to empower patients to make changes are the key to success for good control of blood pressure and prevention of complications. Changes including weight loss and management, increasing physical activity, encouraging the use of stress management strategies, reducing/limiting alcohol intake, and smoking cessation should be provided for patients with hypertension who are also at high risk for metabolic syndrome (Iqbal & Jamal, 2020).

DIAGNOSING METABOLIC SYNDROME

Diagnosing metabolic syndrome requires a physical examination and blood tests.

Medical History

The medical history offers important information that can help to confirm the diagnosis and determine the extent of the problem. A person who has metabolic syndrome may already have been diagnosed with some components of the syndrome, such as obesity, hypertension, or dyslipidemia. A major complication of the syndrome (atherosclerotic artery disease, ischemic heart disease, diabetes) may also be present.

In addition, the person may come with a diagnosis (or the signs and symptoms) of one of a number of other medical problems that occur especially frequently with metabolic syndrome. Diseases that often present with metabolic syndrome include:

- Obesity
- Polycystic ovary syndrome (PCOS)
- Cardiovascular disease
- Nonalcoholic fatty liver disease
- Chronic kidney disease
  (NHLBI, 2019; Durkin, 2019)

Any of these problems should alert clinicians to the possibility of metabolic syndrome.

Diagnostic Criteria

As stated earlier, metabolic syndrome is diagnosed if three or more of the following traits are present:

- Large waist circumference: Waist circumference >102 cm (>40 inches) in men, >89 cm (>35 inches) in women

- High blood triglyceride level: 150 mg/dL (1.7 mmol/L) or higher (or on triglyceride-lowering medication)
- Reduced high-density lipoprotein (HDL) cholesterol: <40 mg/dL (1.04 mmol/L) in men, <50 mg/dL (1.3 mmol/L) in women
- Increased blood pressure: 130/85 mmHg or higher (or already diagnosed with hypertension)
- Elevated fasting blood sugar: >100 mg/dL
  (NHLBI, 2019)

INTRA-ABDOMINAL FAT

Today, the standard physical examination of a patient includes height and weight, but it does not usually include a measurement that is essential for diagnosing metabolic syndrome: the patient's waist circumference. The specific aspect of obesity that best warns of future cardiovascular problems is the amount of fat concentrated inside the abdomen (AHA, 2016), and waist circumference is a good measure of intra-abdominal fat.

Measuring Obesity

The most commonly used measure of obesity is the **body mass index (BMI)**. This is measured using the formula:

BMI = weight in kilograms/height in meters squared
or
BMI = weight in pounds x 703/height in inches squared

BMI has been shown to be a good indirect indication of the percentage of body fat, and it is the most commonly used measure of total body fat. The BMI obesity definitions for adults are as follows (CDC, 2020a):

BODY MASS INDEX CLASSIFICATIONS		
Classification		**BMI (kg/m^2)**
Normal		18.5–24.9
Overweight		25.0–29.9
Obese	Class 1	30.0–34.9
	Class 2	35.0–39.9
	Class 3 (extreme obesity)	>40.0

Obese people are more likely than people of normal weight to suffer from certain medical problems, including diabetes, hypertension, dyslipidemias, polycystic ovarian syndrome, degenerative joint disease, sleep apnea, cancer (specifically, breast, colon, endometrial, prostatic), gastroesophageal reflux disease, fatty liver disease, and gallstones.

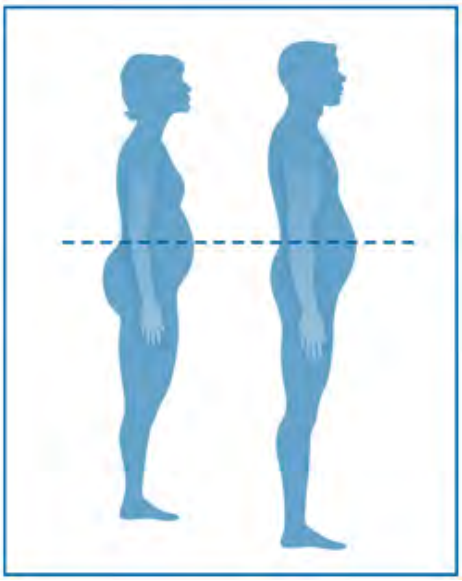
All overweight people have an increased risk of developing metabolic syndrome. In overweight and class 1 obese people, the risk of having or developing metabolic syndrome is much greater if their excess fat is located inside the abdomen (i.e., visceral). When excess fat is concentrated in the abdomen, a person will have a round, apple shape. This is called ***android obesity***, and of all shapes, it is the most strongly predictive of metabolic syndrome–related conditions such as diabetes, hypertension, dyslipidemias, and atherosclerotic cardiovascular disease. (Another common shape of obesity has excess fat concentrated lower on the body, in the hips and thighs. This gives a person a pear shape and is called *gynecoid obesity*.)

Measuring Waist Circumference

Many large studies have shown that simply measuring a person's waist circumference gives a good indication of the amount of excess body fat that is located inside the abdomen. A waist circumference of >94 cm (37 inches) in men and >80 cm (31.5 inches) in women is considered a warning sign, and a circumference of >102 cm (40 inches) in men and >89 cm (35 inches) in women puts the person in the high or very high risk category for developing metabolic syndrome and its serious health consequences.

The waist is the narrow band of the abdomen below the lowest margin of the ribs and above the top (iliac crest) of the hipbones. To measure the waist:

- Place the tape measure around the abdomen, just above the hip bone.
- Hold the tape measure snug to the skin and parallel to the floor.
- Measure with the patient relaxed and breathing normally.



Measuring tape position for waist circumference.
(Source: Adapted from CDC.gov.)

CASE

Sharon, Age 52

Sharon is a 52-year-old female patient who has come to the physician's office for an initial appointment to help manage her hypertension and joint pain. Sharon appears to be obese, with an android shape, prompting the nurse, Jennifer, to measure her waist circumference, which is 92 cm. After weighing Sharon and measuring her height, Jennifer calculates the patient's BMI as 35.2 kg/m^2. Sharon's blood pressure is measured today at 187/93 mmHg after resting for 5 minutes.

Jennifer draws the patient's blood and sends the samples to the lab for a fasting glucose level and total lipid panel. Jennifer then asks Sharon about her recent medical history. Sharon reports having pain in her joints, occasional difficulty breathing, excessive thirst, and having to get up several times during the night to urinate.

Sharon also reports that her mother has a diagnosis of type 2 diabetes and her father has heart disease; additionally, both of her parents have high cholesterol and taking medication for it. She states that for the past 10 years, she has had increasing problems keeping her weight under control and even more so now that she has gone through menopause. She states that she would like to exercise more, but with the excess weight and joint pain, she has not been able to perform any regular exercise.

Jennifer suspects that Sharon may have metabolic syndrome, with possible coexisting hypertension, osteoarthritis, diabetes, dyslipidemia, and asthma, and discusses her beliefs with Sharon's physician. They also discuss Sharon's desire to incorporate exercise into her normal routine. Jennifer helps Sharon with scheduling an initial appointment with a physical therapist for an evaluation and exercise recommendations with a focus on weight loss.

Sharon is scheduled for a return visit to review the results of her blood tests and discuss possible therapeutic recommendations, including both lifestyle changes and medications to control her blood pressure and manage her other coexisting conditions.
(continues)

HIGH BLOOD PRESSURE

The second component of metabolic syndrome that can be picked up in a physical exam is high blood pressure. To be used as a diagnostic condition for metabolic syndrome, a person's blood pressure must be >130/85 mmHg. (If a person is already taking antihypertensive medication, it is assumed that their blood pressure would normally be >130/85 mmHg.)

BLOOD PRESSURE RANGES (mmHg)		
Level	**Systolic**	**Diastolic**
Normal	<120	<80
Elevated	120–129	<80
Hypertension, stage 1	130–139	80–89
Hypertension, stage 2	>140	>90
Hypertensive crisis	>180	>120
(AHA, 2017)		

CASE

Sharon, Age 52 *(continued)*

Sharon returns for a follow-up appointment with her physician. At her previous appointment, her blood pressure was 187/93 mmHg. The nurse, Jennifer, measures the patient's blood pressure once again; this time the reading is 189/94 mmHg.

At this time, Sharon's blood test results have come in, and they show a blood triglyceride level of 155 mg/dL and an HDL cholesterol level of 43 mg/dL. Her fasting blood glucose level is 142 mg/dL.

Based on the previous visit's assessment of an abnormal waist measurement and hypertension, the nurse suspects that Sharon has metabolic syndrome. The physician confirms the diagnosis of metabolic syndrome and outlines a treatment plan for Sharon, including appropriate diet and exercise as well as adhering to her prescribed medication regimen to control her blood sugar, lipid, and blood pressure levels. The physician refers Sharon to a dietitian for nutrition recommendations, as well as instructs her to continue to see the physical therapist for an individualized exercise program.

At the next follow-up appointment, Jennifer reviews with Sharon her new treatment recommendations for following a Mediterranean diet from the dietitian and her current therapeutic exercise program from her physical therapist to make sure that she understands and is incorporating the recommendations from these providers. Sharon reports that she is scheduled to see the physical therapist again soon, who will continue to progress her therapeutic regimen and monitor any changes over the next four weeks. Jennifer then reminds the patient to schedule another follow-up visit in one month with the physician and herself to monitor Sharon's symptoms and progress.

Laboratory Tests

It is important to measure two other factors that contribute to metabolic syndrome: insulin resistance and dyslipidemias. In evaluating a patient who is at risk for metabolic syndrome, laboratory testing includes both fasting glucose levels and fasting lipid profiles.

ASSESSING INSULIN RESISTANCE

Among the various measurements of the body's ability to produce and use glucose, the blood level of glucose after an 8-hour fast is probably the simplest. Fasting glucose levels are a well-calibrated standard that is now widely used to screen for insulin resistance, a common cause of diabetes.

Diabetes

Diabetes mellitus is an endocrine disease that disrupts the body's energy metabolism. In diabetes there is an insufficient amount of insulin available to the cells, and therefore glucose is not used efficiently throughout the body. Diabetes is diagnosed when any one of the following hyperglycemic conditions is present:

- Fasting blood glucose level ≥126 mg/dL
- Hemoglobin A1C level ≥6.5% (an index measuring the amount of glucose sticking to hemoglobin inside red blood cells, and which indicates a person's average blood glucose level over the past two to three months)
- Two-hour plasma glucose level ≥200 mg/dL in an oral glucose tolerance test
- Random plasma glucose level ≥200 mg/dL, accompanied by classic symptoms of hyperglycemia or hyperglycemic crisis

(Durkin, 2019; ADA, 2020a; Mayo Clinic, 2020a)

Hyperglycemia

Hyperglycemia can result from a variety of causes. A fasting blood sugar >100 mg/dL is one of the primary indicators of metabolic syndrome (Mayo Clinic, 2019a). The two most common causes are decreased secretion of insulin and insulin resistance.

ASSESSING DYSLIPIDEMIAS

Dyslipidemias are conditions in which the bloodstream contains unhealthy amounts of lipids. The dyslipidemias of metabolic syndrome are: 1) elevated blood levels of triglycerides and 2) reduced blood levels of high-density lipoproteins. Metabolic syndrome is often accompanied by additional dyslipidemias, although these abnormalities are not necessary for the diagnosis of the syndrome.

Classification of blood lipid levels are given in the table below:

CLASSIFICATION OF BLOOD LIPID LEVELS	
Type	**Blood Concentrations (mg/dL)** (Measured after an 8-hour fast)
Triglycerides	• Normal: <150 • Borderline high: 150–199 • High: 200–499 • Very high: ≥500
HDL cholesterol	• Poor: <40 (men), <50 (women) • Better: 40–59 (men), 50–59 (women) • Best: ≥60
LDL cholesterol	• Best for people with existing heart disease: <70 • Optimal: <100 • Near optimal: 100–129 • Borderline high: 130–159 • High: 160–189 • Very high: ≥190
(Labtestsonline.org, 2020; Mayo Clinic, 2016a)	

Metabolic syndrome is characterized by fasting blood triglycerides >150 mg/dL and fasting blood HDL cholesterol <40 mg/dL in men and <50 mg/dL in women (NHLBI, 2019).

CASE

George, Age 45

George is a 45-year-old male patient who comes to the clinic for his annual physical. After stepping onto a scale, he is found to have gained 10 pounds over the previous year. His blood pressure has gradually been increasing over the past two years as well, with a current measurement of 145/88 mmHg.

As his medical and family history is taken, George mentions that his mother has type 2 diabetes and that his uncle was diagnosed with heart disease after suffering a heart attack at age 55. The nurse takes a measurement of his waist circumference, which is 105 cm (41 inches).

After discussing George's physical assessment findings with the physician, a lipid panel is ordered. Three days later, the results of George's lipid panel show a blood triglyceride level of 156 mg/dL and a HDL cholesterol level of 38 mg/dL.

George is diagnosed with metabolic syndrome; he is started on appropriate therapy, instructed on incorporating lifestyle interventions (e.g., diet, exercise), and referred to a dietitian at his request. A follow-up appointment is scheduled for three months later to assess how he is doing with initial management of his condition.

When George returns for his follow-up visit, he reports that he has been following his diet and exercise plan and feels that this has made a difference in how he is feeling. He has lost 8 pounds, his blood pressure is now 124/68, his triglycerides have improved to 130 mg/dL, and his HDL cholesterol has increased to 52 mg/dL.

George continues to be motivated to make changes in order to improve his health and states that he feels better than ever. He adds that his wife has been very supportive. Together they joined the local Weight Watchers to support a healthy diet and weight loss program, and they are exercising on a regular basis.

Two Possible Coexistent Diagnoses

Patients with intra-abdominal obesity, high fasting glucose levels, high blood pressure, high blood levels of triglycerides, and low blood levels of HDL cholesterol have metabolic syndrome and should be treated. Yet it is important to remember that a patient may simultaneously have other diseases with similar or overlapping symptoms. Two specific disorders to keep in mind are Cushing's syndrome and hypothyroidism.

CUSHING'S SYNDROME

Cushing's syndrome is caused by excess glucocorticoid, either excess intrinsic cortisol (as is produced by the adrenal glands in Cushing's disease) or excess extrinsic glucocorticoids (e.g., prednisone), which might have been prescribed to treat another disorder. Typically, a person with Cushing's syndrome has weight gain, skin striae (stretch marks), hirsutism, and proximal muscle weakness (Durkin, 2019).

As in metabolic syndrome, Cushing's syndrome leads to central (as opposed to peripheral) obesity. Cushing's syndrome also includes hypertension, elevated blood glucose levels, and dyslipidemias, including an elevated level of blood triglycerides. Moreover, patients with Cushing's syndrome are more susceptible to cardiovascular disease (Durkin, 2019).

HYPOTHYROIDISM

Hypothyroidism is caused by a decreased secretion of thyroid hormone from the thyroid gland, slowing metabolic processes throughout the body. As in metabolic syndrome, people with hypothyroidism tend to be overweight and inactive. They also have dyslipidemia and, sometimes, mild hypertension. Moreover, patients with hypothyroidism are more likely than normal to have cardiovascular disease. On the other hand, unlike metabolic syndrome, low blood glucose levels are typical of hypothyroidism (Durkin, 2019).

Comorbid Diseases Associated with Metabolic Syndrome

People with metabolic syndrome are at risk for a long list of health problems. It is not always clear whether metabolic syndrome is the cause or whether the related disorders share common causes with the components of metabolic syndrome. Two serious comorbidities that may result from long-term metabolic syndrome are coronary heart disease and type 2 diabetes.

CORONARY HEART DISEASE

The most striking risk posed by metabolic syndrome is coronary heart disease (also known as *coronary artery disease* or *atherosclerotic cardiovascular disease*). By themselves, the dyslipidemias of metabolic syndrome (i.e., high triglycerides and low HDL cholesterol levels) encourage plaque to form along the walls of arteries. When combined with the other components of metabolic syndrome, these atherogenic dyslipidemias (i.e., those that tend to cause atherosclerotic plaque) put a person at high risk for developing serious atherosclerotic vascular disease with coronary artery blockage.

People who have metabolic syndrome often also have low-level inflammation throughout the body and blood clotting defects that increase the risk of developing blood clots in the arteries. These conditions contribute to increased risk for cardiovascular disease (NHLBI, 2019).

TYPE 2 DIABETES

Metabolic syndrome is a precursor to type 2 diabetes. The mechanism is as follows: The insulin resistance of metabolic syndrome forces the pancreas to secrete higher than normal amounts of insulin. Meanwhile, some hyperglycemia persists even with the excess circulating insulin. The continuous hyperglycemia and hyperinsulinemia are toxic to the beta cells in the pancreas, and over time these cells weaken and the amount of insulin that they produce decreases. Eventually, the pancreas cannot cope with hyperglycemia, and the patient develops diabetes.

TREATING METABOLIC SYNDROME

The individual components of metabolic syndrome—abdominal obesity, high triglycerides, low HDL cholesterol, high blood pressure, and high fasting glucose—would not always be treated if found in isolation. When found together, however, metabolic syndrome is typically diagnosed, indicating the need for treatment. That is, **metabolic syndrome lowers the threshold for the treatment of its components.**

Treatment goals for metabolic syndrome are:

- Treat underlying causes
- Prevent the development of type 2 diabetes
- Treat cardiovascular risk factors (i.e., manage hypertension, lower LDL cholesterol and triglyceride levels)
  (NHLBI, 2019)

Treatment for metabolic syndrome consists of the following **main therapeutic strategies**:

1. Weight loss and increased physical activity focused on reversing the direct causes of the condition

2. Medications designed to treat the condition's various components, such as dyslipidemia, hypertension, prothrombic conditions, and insulin resistance
3. Dietary management focused on lowering cholesterol and restricting calories from simple carbohydrates (i.e., emphasis on low-fat dairy, whole grains, and fresh fruits and vegetables)
   (NHLBI, 2019)

Treatment of the components of metabolic syndrome begins with lifestyle changes. Because lifestyle changes are easy to prescribe but difficult to carry out, often medications must be added to ensure that the treatment regimens succeed.

Therapeutic Lifestyle Changes

Lifestyle modification is the preferred treatment of metabolic syndrome. Therapeutic lifestyle changes—such as increased physical exercise, eating a heart-healthy diet, and weight management—are the cornerstones of the treatment of obesity, hypertension, insulin resistance, and most dyslipidemias. Reducing dietary calories and fats (especially saturated and trans fats) and increasing exercise can significantly reduce the risk of developing diabetes and atherosclerotic cardiovascular disease (NHLBI, 2019).

EXERCISE

All aspects of metabolic syndrome benefit from increased physical activity. Physical exercise helps in losing weight and in maintaining weight loss, and it has additional independent metabolic effects that directly reduce insulin resistance. Physical activity is usually a safe and beneficial treatment for people with metabolic syndrome and its associated consequences of atherosclerotic cardiovascular disease and type 2 diabetes.

The American Heart Association (2018) recommends the following physical activity for adults:

- For overall cardiovascular health:
  - Get at least 30 minutes of moderate-intensity exercise at least 5 days per week for a total of 150 minutes**.**
  - Get at least 25 minutes of vigorous aerobic activity at least 3 days per week for a total of 75 minutes, or a combination of moderate-and vigorous-intensity aerobic activity.
  - Do moderate- to high-intensity muscle-strengthening activity at least 2 days per week for additional health benefits.
  - Spend less time sitting. Even light-intensity activity may balance some of the risks of being sedentary.
  - Get even more benefits by being active at least 300 minutes (5 hours) per week.
  - Start slowly and increase the amount and intensity of activity gradually over time.

- For lowering blood pressure and cholesterol:
    - Get an average of 40 minutes of moderate- to vigorous-intensity aerobic activity 3 or 4 times per week.

For high-risk patients with comorbidities who are deconditioned or have had recent cardiac events, careful supervision of physical rehabilitation is recommended. Referral to a physical therapist or exercise physiologist to evaluate, plan, and monitor the patient's progress with his or her exercise program is an important consideration (AHA, 2018).

Patients may also benefit from partnering with others in activities such as swimming, biking, or walking groups to motivate and support each other to reach their goals.

SUPERVISED EXERCISE

Patients with metabolic syndrome are at risk of developing neuropathy (i.e., peripheral pain, numbness) characterized by a loss of unmyelinated cutaneous axons. Unmyelinated axons are susceptible to both physical and metabolic injury. However, they are also capable of rapid regeneration. Supervised exercise has been found to improve cutaneous reinnervation capacity in patients with metabolic syndrome. In a study conducted by Singleton and colleagues (2015), a relatively brief but intensive exercise program designed to improve glucose, insulin, and lipid metabolism resulted in a clear increase in the ability of cutaneous axons to regenerate following controlled denervation.

DIETARY MODIFICATIONS

Exercise alone rarely leads to significant weight loss. A heart-healthy diet is usually necessary, and nutrition planning is the second critical component of the initial treatment of metabolic syndrome.

Even a modest weight loss makes a difference for an overweight or obese person, and losing 5% to 7% of the original weight and keeping the weight off is a realistic goal. The ADA (2020b) recommends that patients aim for a weight loss of 7% of body weight, noting that a small but consistent weight loss of 1/2 to 2 pounds per week is the safest way to accomplish this.

Simply reducing the overall calories in the diet will improve the lipid profile. Reducing the amount of unhealthy fats and sugars improves the lipid profile even further. It is especially important to remove foods that are high in simple carbohydrates, refined grains, and saturated or trans fats (ADA, 2020c). It may also be important to restrict sodium intake to <2,300 mg/day.

Following a Mediterranean diet rich in nutrient-dense foods such as whole grains, vegetables, fruits, legumes, low-fat dairy, lean meats, nuts, and seeds is recommended for body weight management (ADA, 2020b).

MEDITERRANEAN DIET

The Mediterranean diet food pyramid is recognized as the "gold standard" eating pattern that promotes good health and prevention of cardiovascular risks:

- High consumption of monosaturated fatty acids (primarily from olives and olive oil)
- Daily consumption of fruits, vegetables, whole grain cereals, and low-fat dairy products
- Weekly consumption of fish, poultry, tree nuts, and legumes
- A relatively low consumption of red meat (approximately twice per month)
- Moderate daily consumption of alcohol (normally with meals)

Additionally, studies suggest that adherence to the Mediterranean diet can positively affect individual components of metabolic syndrome such as waist circumference, dyslipidemia, hypertension, and hyperglycemia.

(Foodpyramid.com, 2015; Mayo Clinic, 2019b)

Some research shows that insulin resistance can be reduced by following low-carbohydrate and ketogenic diets (Diabetes.co.uk, 2019). Ketogenic diets are high-fat, adequate protein, and low-carbohydrate. This type of diet alters the way energy is used in the body. Fat is converted into fatty acids and ketone bodies. This helps to lower glucose levels and reduces insulin resistance. Others caution the use of a ketogenic diet due to the high fat content (especially unsaturated fats), combined with eating fewer nutrient-rich fruits and vegetables for long-term cardiovascular health (Abbasi, 2018).

CASE

Angela, Age 52

The nurse, Lashay, enters the examination room to check the blood pressure and take a blood sample from the patient, Angela, who is a 52-year-old female recently diagnosed with metabolic syndrome. After removing the blood pressure cuff from Angela's arm, Lashay asks how well she has been managing her weight, and the patient replies that she has been having "difficulty losing weight" on her own and asks for more information about what strategies she should try at home. A discussion of diet and exercise ensues, during which Angela reveals that she has continued to struggle with healthy food choices and regular exercise.

Lashay discusses the benefits of the Mediterranean diet in managing the various components of metabolic syndrome. While reviewing the components of the diet, they look together at an educational booklet that outlines how to follow the Mediterranean diet model, with practical menu suggestions and a baseline assessment about knowledge of the healthy food choices

included in the model. Angela mentions that the diet seems easier than she imagined to follow and states that she will start to shop and plan her meals better with this information.

Lashay helps the patient make an appointment with a registered dietitian with the aim of establishing an individualized diet and exercise plan based on Angela's needs. Lashay also helps facilitate a referral to a physical therapist for an evaluation and treatment plan to address Angela's strength and endurance. They plan to have a follow-up visit in six weeks to monitor Angela's progress.

SMOKING CESSATION

When associated with metabolic syndrome, smoking increases the chance of developing insulin resistance, type 2 diabetes, and dyslipidemias. In addition, smoking contributes to the development of a variety of cancers, atherosclerotic cardiovascular diseases, lung diseases, gastrointestinal diseases, reproductive problems, osteoporosis, cataracts, age-related macular degeneration, and hypothyroidism.

Medications

HYPERTENSION MEDICATIONS

When lifestyle changes in diet and exercise are insufficient, persistent hypertension requires medication. For metabolic syndrome, antihypertensive drug therapy usually begins with an angiotensin-converting-enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB). Beta-blockers are avoided in metabolic syndrome because they tend to cause weight gain, increased triglyceride levels, and reduced HDL cholesterol levels (ADA, 2020c).

HYPERGLYCEMIA MEDICATIONS

Antidiabetic drug therapy may be considered for high-risk patients with metabolic syndrome or prediabetes who are unable to control their blood sugar with weight loss and exercise. Research shows that drugs such as metformin (Glucophage) or acarbose (Precose) can delay the onset of type 2 diabetes in people with prediabetes, but not nearly as effectively as lifestyle changes (ADA, 2020b).

DYSLIPIDEMIA MEDICATIONS

The dyslipidemias of metabolic syndrome have two characteristics: high blood levels of triglycerides and low blood levels of HDL cholesterol. Both of these problems can lead to atherosclerotic cardiovascular disease. Metabolic syndrome is often worsened by the presence of another dyslipidemia, hypercholesterolemia (high blood levels of LDL cholesterol), which by itself is a major contributor to the development of coronary (atherosclerotic) heart disease.

When a three- to six-month trial of therapeutic lifestyle changes does not sufficiently improve these heart-threatening features of a patient's lipid profile, medications such as statins may be added.

OBESITY MEDICATIONS

Lifestyle changes and counseling are the first steps in treating patients with obesity and metabolic syndrome. When these steps do not lead to sufficient weight loss, antiobesity medications can be tried. Pharmacotherapy for the treatment of obesity may be combined with lifestyle changes and can result in loss of 5% to 10% of body weight. Each medication has risks and benefits and should be used under close medical supervision (ADA, 2020b).

PROTHROMBOTIC STATE THERAPY

Metabolic syndrome may be accompanied by a prothrombotic state, an increased tendency of the blood to form clots. Some clinicians prescribe daily low-dose aspirin as part of the therapy for metabolic syndrome for those patients who are at high risk or who have a history of heart disease or stroke (AHA, 2019).

Cognitive Behavioral Therapy

Changing one's lifestyle requires guidance and determination. Losing weight and making other lifestyle changes, for example, takes encouragement, self-monitoring, and practical advice. Cognitive behavioral therapy (CBT) focuses on helping a person understand how their actions and behaviors, including how someone thinks about an action or behavior change, can have a direct impact to the body.

People who engage in CBT often are guided by a trained psychologist or professional health coach who helps them understand their readiness and motivation to make a change by:

- Setting specific goals
- Outlining strategies for positive self-talk and self-monitoring
- Providing regular feedback and reinforcement
- Understanding the positive impact of the behavior change
- Outlining incentives and strategies for motivation

Research has shown that CBT can have a positive effect for patients with metabolic syndrome, including reducing waist circumference, fasting triglyceride levels, and hypertension. Participants have also reported an improved quality of life as a result of CBT (Zhang et al., 2016).

Surgery

Therapeutic lifestyle changes and medications work least often in severely obese patients. For these patients, bariatric surgery is an option. Surgery is considered if the patient has tried monitored dieting, exercise regimens, and medications.

It is important that persons who undergo bariatric surgery receive life-long lifestyle support and medical monitoring.

BARIATRIC SURGERY ACCREDITATION

The best hospitals for bariatric surgery are those that perform a significant number of the surgeries and that use a team (physician, psychologist, physical and occupational therapists, and dietitian) to treat patients. Patients making the decision to have surgery should be aware of quality and standards for centers that perform bariatric surgery.

The American College of Surgeons and the American Society for Metabolic and Bariatric Surgery combined their respective national bariatric surgery accreditation programs into a single, unified program to achieve one national accreditation standard for bariatric surgery centers: the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP). MBSAQIP accreditation is important because it provides an objective and measurable way by which a center demonstrates that it offers high-quality care to patients in the setting of a multidisciplinary team approach (MBSAQIP, 2020).

TYPES OF BARIATRIC SURGERY

Bariatric surgery assists with weight loss in two ways: restriction of the amount of space in the stomach (limiting intake of food) and malabsorption by shortening or bypassing the small intestine (reducing absorption). Examples of bariatric surgery are listed below (Merck Manual, 2019):

- **Roux-en-Y gastric bypass** (gastric bypass) is one of the most common bariatric surgical procedures, in which the surgeon creates a small pouch at the top of the stomach and attaches a narrow portion of the small intestine directly to the pouch, limiting the amount of food a person can eat as well as the amount of calories and nutrients absorbed.

- **Laparoscopic adjustable gastric banding** (lap banding) is a procedure that involves placing a band with an inflatable balloon around the upper part of the stomach. The band restricts the size of the stomach as well as narrows the opening to the rest of the stomach. A port placed under the skin in the abdominal area is connected and used to inflate or deflate the band to adjust the size. This procedure restricts the amount of food intake, with an early feeling of fullness.

- **Sleeve gastrectomy** (gastric sleeve) is a procedure involving the surgical removal of a section of the stomach. The remaining part of the stomach is formed into a smaller tube-like structure. The smaller stomach restricts the amount of food intake and decreases the production of ghrelin (a hormone that regulates the appetite).

- **Duodenal switch with biliopancreatic diversion** begins with the removal of a large part of the stomach, leaving the connection to the first part of the small intestine (duodenum). The middle section of the small intestine is closed off and reattached to the end of the intestine, allowing the bile and pancreatic juices to flow normally. As a result, the patient

has a smaller stomach, restricting food intake as well as limiting absorption because food bypasses most of the small intestine.

POSTSURGICAL CARE

Clinical guidelines have been developed for nutrition care after bariatric surgery, with an emphasis on detection and management of complications such as vitamin and mineral deficiencies, osteoporosis, and hypoglycemia. The goals of nutrition care after surgery are to provide adequate energy and nutrition to support lean body mass during extreme weight loss, support tissue healing, and encourage foods and liquids that maximize weight loss and promote weight maintenance while minimizing side effects of reflux, dumping syndrome, and early satiety (Franz & Evert, 2017).

After surgery, life-long lifestyle support and medical monitoring is necessary. Physical therapists and occupational therapists are an integral part of the rehabilitation team supporting patients in the postoperative and recovery period. Early mobilization, with assistance from occupational therapists who teach activities of daily living and physical therapists who create and monitor a regular exercise and strengthening program, is an important part of long-term recovery (ADA, 2020d).

PREVENTION OF METABOLIC SYNDROME

At each stage of life, strategies can be implemented to reduce the chance of developing metabolic syndrome, even for those individuals who have inherited a predisposition to it.

Prenatal

Malnutrition of mother and child during pregnancy leads to low birth weight of the infant. Such a child may have a higher than normal risk of developing hypertension, abnormal glucose tolerance, and cardiovascular disease as an adult. A pregnant mother who gets good prenatal care and who eats a healthy diet will reduce her baby's chances of developing metabolic syndrome later in life.

Children and Adolescents

In the United States, approximately 19% (or 13.7 million) of children and adolescents aged 2–19 years are obese (CDC, 2019). Obesity in children increases the chance that they will have metabolic problems, high blood pressure, kidney problems, and cardiovascular disease as adults. It is therefore important that children be given guidance and encouragement to eat a healthy diet.

In addition, having a low level of physical exercise increases the chances that a child will develop metabolic syndrome as an adult even for children who are not overweight. Thus, children should be encouraged to be active, and sedentary pastimes, such as television-watching and video/computer games, should be limited.

Adults

SCREENING

General education programs can reduce the incidence of metabolic syndrome by making everyone aware of the benefits of staying at a healthy weight and exercising. People who already have metabolic syndrome can prevent many of the serious health problems by losing weight, eating a healthy diet, and exercising more. The first steps are to identify patients and then to advise them on the lifestyle changes that may benefit the condition. Carefully monitoring their condition over time is also important.

Healthcare providers should be aware of those who might have or be at risk for metabolic syndrome. Screening measures may include measuring waist size, blood pressure, and blood lipid and blood glucose levels.

EDUCATION

Without treatment, metabolic syndrome poses worsening risks with age. On the other hand, young adults with metabolic syndrome who lose weight and then maintain a stable weight can avoid the higher incidence of serious health problems that may come with advancing age.

Maintaining a healthy body weight is a key for preventing metabolic syndrome. Overweight people should be advised to maintain a healthy weight. People usually have the most success losing weight when they are part of a formal program that provides monitoring and counseling for continued support.

A second key preventive step is increasing physical activity. Although regular exercise can help a person lose weight, the most important benefits of physical activity are metabolic. Moderate exercise for >30 minutes four times a week can actually change the balance of biochemical processes in a person's body, reducing insulin resistance, lowering triglycerides, and lowering blood pressure. (See also "Exercise" above.)

CONCLUSION

Metabolic syndrome is the combination of:

- Insulin resistance
- Excess intra-abdominal fat
- Unhealthy levels of fats in the blood (too much triglyceride and too little HDL cholesterol)
- High blood pressure

Having metabolic syndrome makes a person more likely to develop diabetes and cardiovascular disease, especially men over 45 years of age and women over 55 years of age. Metabolic syndrome is a common health problem, especially in those parts of the world where obesity is on the rise.

Treatment of metabolic syndrome begins with therapeutic lifestyle changes. Weight loss, improved diet, and regular physical exercise are the elements of the initial treatment program. Medications may be recommended to treat those components of metabolic syndrome (e.g., high blood pressure, hypercholesterolemia) that do not improve sufficiently with therapeutic lifestyle changes alone.

RESOURCES

IDF Worldwide Definition of the Metabolic Syndrome (International Diabetes Federation)
http://www.idf.org/metabolic-syndrome

Metabolic syndrome (American Heart Association)
http://www.heart.org/HEARTORG/Conditions/More/MetabolicSyndrome/Metabolic-Syndrome_UCM_002080_SubHomePage.jsp

Metabolic syndrome (Mayo Clinic)
https://www.mayoclinic.org/diseases-conditions/metabolic-syndrome/symptoms-causes/syc-20351916

Metabolic syndrome (MedicineNet.com)
http://www.medicinenet.com/metabolic_syndrome/article.htm

Metabolic syndrome (National Library of Medicine)
http://www.nlm.nih.gov/medlineplus/metabolicsyndrome.html

What is metabolic syndrome? (National Heart, Blood, and Lung Institute)
http://www.nhlbi.nih.gov/health/health-topics/topics/ms/

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1. Characteristics of patients with metabolic syndrome include intra-abdominal obesity:

a. Hypoglycemia, and high HDL cholesterol.
b. Hypertension, and low HDL cholesterol.
c. Pulmonary hypertension, and insulin sensitivity.
d. Hypotension, and low LDL cholesterol.

2. In assessing a male patient who is obese and reports minimal physical activity, the clinician considers metabolic syndrome upon identifying which other key characteristic?

a. A blood pressure >130/85 mm Hg
b. A blood triglyceride level >100 mg/dL
c. A fasting blood high-density lipoprotein cholesterol level <60 mg/dL
d. A fasting blood glucose level >75 mg/dL

3. Which health condition directly causes insulin resistance and leads to increased triglyceride levels?

a. Ovarian cancer
b. Coronary heart disease
c. Excess visceral fat
d. Poor oral health

4. A criterion for the diagnosis of metabolic syndrome is a fasting blood sugar of:

a. 250 mg/dL or higher.
b. 200 mg/dL or higher.
c. 150 mg/dL or higher.
d. 100 mg/dL or higher.

5. Which clinical measurement or test is used to diagnose metabolic syndrome?

a. A blood urea nitrogen level
b. A coronary angiogram
c. A chest X-ray
d. A large waist circumference

6. A patient with metabolic syndrome is treated for diabetes when they have:

a. Higher-than-normal plasma glucose levels.
b. Higher-than-normal urinary albumin levels.
c. Symptoms of polyuria, polydipsia, and weakness.
d. Symptoms of retinopathy, neuropathy, or nephropathy.

7. Which fasting high-density lipoprotein (HDL) cholesterol level in a male patient is a risk factor for metabolic syndrome?

a. 38 mg/dL
b. 58 mg/dL
c. 68 mg/dL
d. 78 mg/dL

8. Which two comorbidities are most commonly associated with metabolic syndrome?

a. Colon cancer and stroke
b. Coronary heart disease and type 2 diabetes
c. Pulmonary hypertension and portal hypertension
d. Breast cancer and prostatic cancer

9. Physical exercise by patients with metabolic syndrome is associated with:

a. Increased blood levels of LDL cholesterol.
b. Reduced blood levels of HDL cholesterol.
c. Reduced insulin resistance.
d. Increased blood pressure.

10. The two key lifestyle changes that help prevent metabolic syndrome include:

a. Increasing calories and adding more dietary fats.
b. Drinking more fruit juices and taking a multivitamin.
c. Maintaining a healthy weight and doing regular exercise.
d. Avoiding alcohol and reducing salt intake.