

Secrets about Metabolic Syndrome

A Layman's Guide to the Metabolic Syndrome

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INTRODUCTION TO AN UNLIKELY VILLAIN

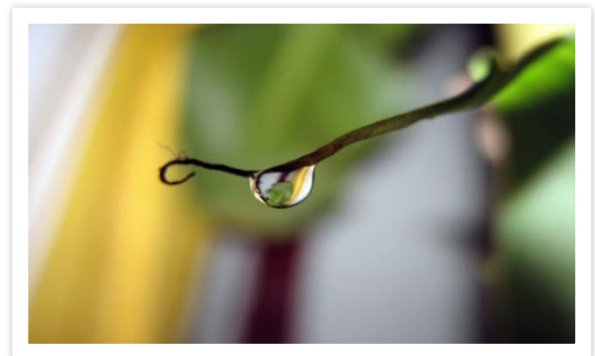
These modern days are fraught with endless problems, and we are witness to it. Despite the rapid progress made in various fields, especially medical advancements, we are fraught with newer and more complex problems. Take for example our diseases – looking 2 to 3 decades back, people were affected by diseases which seemed to be straightforward and clinically distinct, like the infectious diseases. More recently, we are drawn to a complex subset of diseases that are caused by our changing lifestyle and complex viral diseases that elude any form of therapy.

Ever since our understanding of Diabetes mellitus and Hypertension, and the circumstances in which they are common have been studied in detail, we have come to surmise that this is a new era of new diseases. Hardly had we digested these two monsters, when we had to prepare ourselves for Coronary artery disease and Hypercholesterolemia. Then, there was AIDS, the Mad Cow Disease and H5N1 flu, which have drained our resources and our minds. Finally, we are bulldozed with the concept of Metabolic Syndrome, a cluster of disorders which occur together and qualify as the number-one public health problem facing several Western Societies.

Jean Vague is credited with describing the Metabolic Syndrome in the 1940's, when he linked abdominal fat accumulation to metabolic abnormalities. More recently in 1988, Gerald Reaven described Metabolic Syndrome as we know it today, more or less, and coined the term Syndrome X. Ever since, much has been studied and reminisced about this peculiar condition that affects 47 million Americans, and is likely to affect 50 to 75 million by the end of this decade. This disorder is emerging as an epidemic in Western industrialized countries, affecting one out of every five individuals, and more seriously as a pandemic across the globe.

This calls for urgent action on our part – lifestyle modifications! Why so? The answer to this lies in the fact that this disorder is rife among sedentary, carbohydrate addicted and highly stressed individuals, which incidentally sound like all of us. So, what are you waiting for? Read on and know about this medical condition that could land you in a lot of trouble! The importance of diet and exercise in the prevention and treatment of Metabolic Syndrome cannot be undermined.

Most of the studies advocate that every individual whether young or old should be cautious and take all necessary steps to prevent this conundrum from wreaking havoc in our lives.



Hoping that this effort of ours comes in handy to inspire and guide you towards healthy living, and to keep your doubts at bay about this disorder which is turning out to be a prominent villain in our world today. Wishing you healthy living. Share this information with those that you care.

WHAT IS METABOLIC SYNDROME?

The Metabolic Syndrome, also called Syndrome X, Insulin resistance syndrome or Reaven Syndrome is described as a cluster of modifiable risk factors occurring in the same individual and associated with an increased risk of developing cardiovascular disease and Type 2 Diabetes Mellitus.

According to the NCEP ATP (National Cholesterol Education Program Adult Treatment Plan) III report, presence of 3 or more of the following modifiable risk factors constitutes the Metabolic Syndrome:

1. Abdominal obesity : Waist circumference >102 cm in men and >88 cm in women
2. Hypertriglyceridemia : High triglycerides in the blood (>150 mg/dL or 1.69 mmol/L)
3. Low High-density Lipoprotein (HDL) Cholesterol : <40 mg/dL (1.04 mmol/L) in men and <50 mg/dL (1.29 mmol/L) in women
4. High blood pressure : >130/85 mmHg
5. High Fasting Blood Glucose : >110 mg/dL (>6.1 mmol/L)

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Various definitions have been proposed with their own deficiencies, but the NCEP ATP III is simple to follow even for the lay person.

According to the WHO (World Health Organization), a diagnosis of Metabolic Syndrome is imminent in the presence of insulin resistance with two or more other features, such as antihypertensive medication and/or high blood pressure, high plasma triglycerides, Low HDL (high-density lipoprotein) levels, obesity and changes in urine albumin excretion or albumin/creatinine ratio.

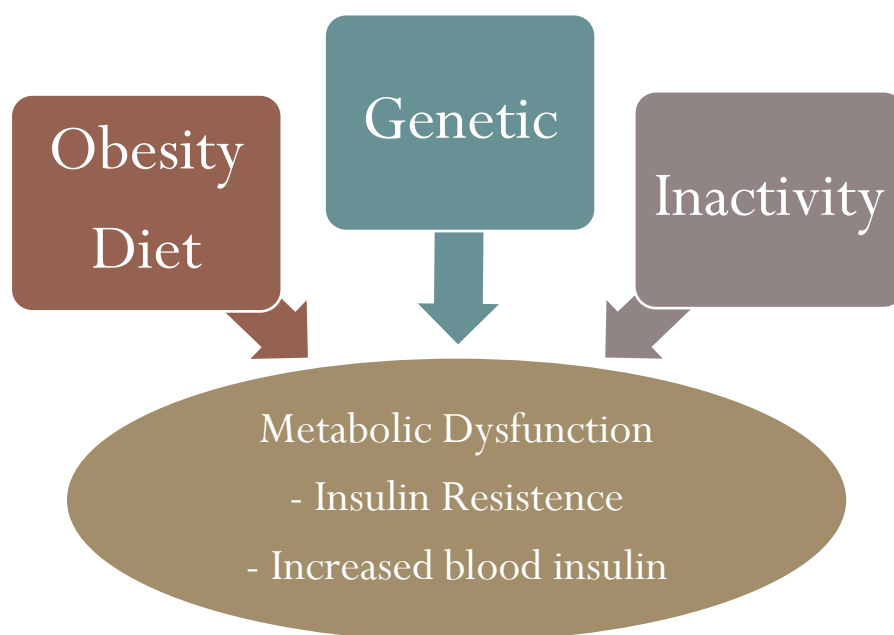
Insulin resistance is said to be present if the individual concerned cannot maintain a particular level of glucose in the blood, despite the presence of proportionately normal insulin levels. This is seen in patients with Type 2 diabetes, those with impaired fasting glucose or glucose tolerance.

Insulin resistance is the single most important metabolic change that leads to the other features such as Type 2 diabetes mellitus. Hence, Metabolic Syndrome is now increasingly being referred to as pre-diabetes

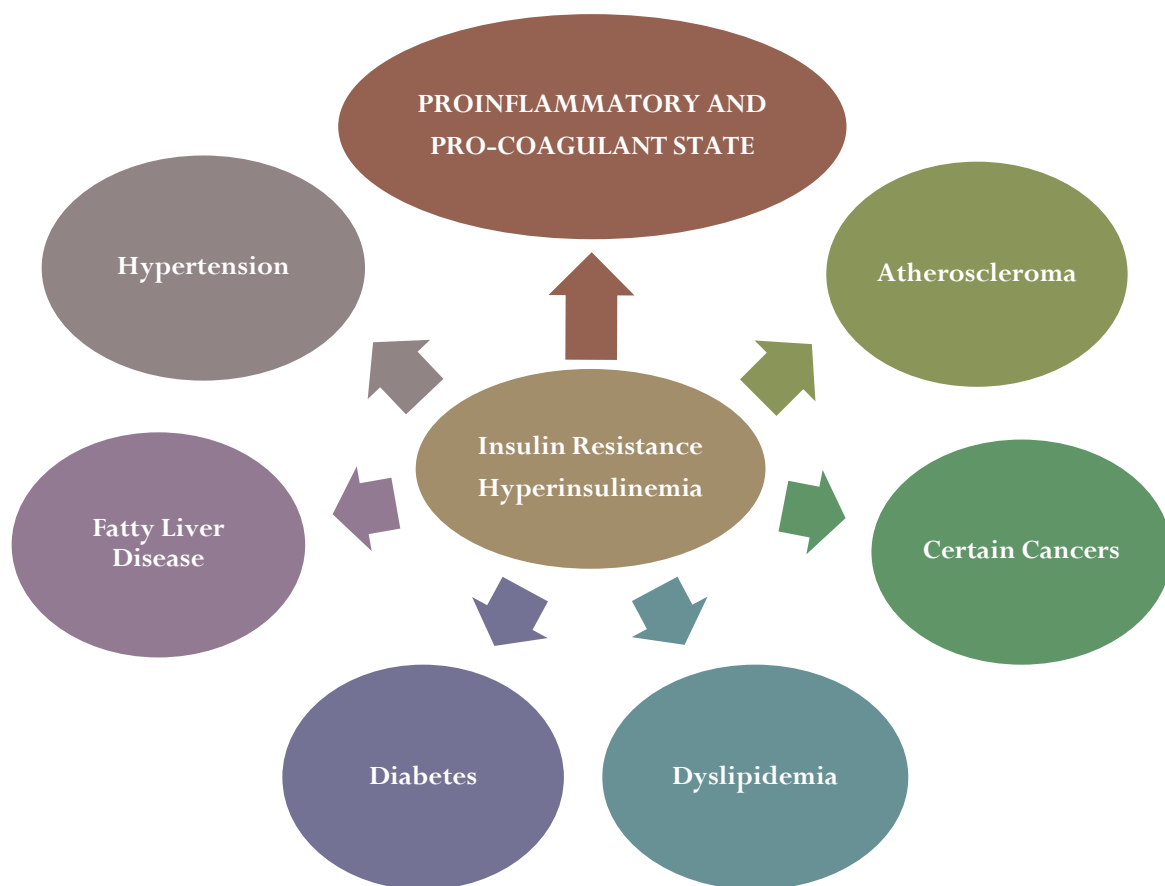
A person with Metabolic Syndrome has a greatly increased risk of cardiovascular disease, Type 2 diabetes and as a consequence, an early or premature death.

A SIMPLIFIED APPROACH TO THE METABOLIC SYNDROME

The metabolic disarray of insulin resistance and increased blood insulin is caused by a complex interaction of diet, obesity, sedentary lifestyle and genetic factors. This leads to a proinflammatory and pro-coagulant state in the body, which in turn predisposes to hypertension, Atherosclerosis, Diabetes mellitus, dyslipidemia, fatty changes in the liver, and certain cancers.



The prevailing theory is that in most people with metabolic syndrome, the development of obesity and physical inactivity leads to insulin resistance and compensatory increase in insulin levels in the blood. This response of the body helps maintain body glucose levels. However, if pancreatic insulin secretion fails, the person develops diabetes or impaired glucose tolerance. Genetic factors also influence an individual's insulin sensitivity.



The Lipid Hypothesis: Alteration of cellular lipid metabolism is closely associated with insulin resistance and hyperinsulinemia. According to the lipid hypothesis, cellular dysfunction and insulin resistance result from an increase in the intracellular concentration of long-chain fatty acyl CoA secondary to an increase in plasma free fatty acids levels or a decrease in mitochondrial fatty acid oxidation.

Adipose tissue not only stores fat but also is an active endocrine organ which responds to signals from many sources, including the central nervous system. Adipose tissue is a source of metabolically active substances including elevated levels of free fatty acids. These in turn affect parallel insulin-signalling pathways in the liver, skeletal muscle, and blood vessels, leading to increased blood sugar levels and dysfunction of the lining of blood vessels. Abnormalities following this include the following:

- Increased synthesis of glucose
- Decreased glucose uptake in skeletal muscle
- Blood vessels are prone to narrowing due to constriction
- Aggregation of platelets
- Increased oxidative stress
- Formation of advanced glycation end products

Persons with metabolic syndrome tend to have central obesity or abdominal obesity which is associated with greater amount of visceral fat i.e. subcutaneous fat. This fat is metabolically active and produces free fatty acids and inflammatory cytokines that enter

into the liver. Finally, fat deposits in the liver leads to overproduction of very-low-density lipoprotein (VLDL), elevated triglycerides, low-density lipoprotein (LDL) which constitute the “Bad Fat” which cause atherosclerosis. It also leads to lowering of high-density lipoproteins (HDL) which is the “Good Fat” and helps neutralize the bad fat. In addition to all these factors, the insulin resistant state favors the development of hypertension.

In simple terms, it is a complex cluster of risk factors that predispose a person to hypertension, diabetes, lipid abnormalities and certain cancers. It is the bane of the coming generations as we fight against this silent and quite innocuous villain. The mechanisms involved in the genesis of this syndrome are not fully understood and many studies are being focused on various aspects of this menacing problem.

Even as we read this, new research keeps pouring in from across the globe in an attempt to lay bare the facts of metabolic syndrome and to create awareness about it.

DIAGNOSTIC GUIDELINES THAT MATTER

Various scientific panels and researchers have been working to create guidelines that could help in the diagnosis of Metabolic Syndrome. Which diagnostic criteria to adapt are based on individual preferences of the health professional and local and regional guidelines take precedence. There is no definitive diagnostic test for the Metabolic Syndrome as yet.

Although attributed to the diabetologists, the concept of Metabolic Syndrome has been widely accepted, debated, and run into numerous controversies among the medical fraternity. Recently, the cardiologists have taken keen interest in this disease process. There is also widespread approval among health professionals that whatever the diagnostic guidelines, the management of Metabolic Syndrome follows the same principles with special emphasis on diet and exercise.

The three commonly used definitions for the diagnosis of Metabolic Syndrome are the World Health Organization (WHO) Criteria, the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), and the International Diabetes Federation (IDF) definitions.

For all practical purposes, the NCEP ATP III is simple and is commonly used in the US.

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TABLE 1. Comparison of WHO, NCEP ATP III, and IDF Definitions of the Metabolic Syndrome*

| Risk factors | WHO ³ | NCEP ATP III ^{6,7} | IDF ⁸ |
|------------------------|---|---|---|
| | DM/IFG or IGT or IR plus any ≥ 2 risk factors | Any ≥ 3 risk factors | Increased WC (ethnicity-specific) plus any ≥ 2 risk factors |
| Obesity | Waist-to-hip ratio >0.90 in men and >0.85 in women and/or BMI >30 kg/m ² | WC ≥ 102 cm (40 in) in men or ≥ 88 cm (35 in) in women | WC criteria dependent on ethnicity |
| Triglycerides | ≥ 150 mg/dL | ≥ 150 mg/dL or drug treatment for elevated levels | ≥ 150 mg/dL or drug treatment for elevated levels |
| HDL cholesterol | <35 mg/dL in men and <39 mg/dL in women | <40 mg/dL in men and <50 mg/dL in women or drug treatment for reduced levels | <40 mg/dL in men and <50 mg/dL in women or drug treatment for reduced levels |
| Blood pressure | $\geq 140/90$ mm Hg | ≥ 130 mm Hg systolic or ≥ 85 mm Hg diastolic or drug treatment for hypertension | ≥ 130 mm Hg systolic or ≥ 85 mm Hg diastolic or drug treatment for hypertension |
| Fasting plasma glucose | IGT, IFG, or type 2 DM | ≥ 100 mg/dL or drug treatment for DM | ≥ 100 mg/dL or drug treatment for DM |
| Microalbuminuria | >30 mg albumin/g creatinine | | |

*Criteria for the diagnosis of diabetes mellitus (DM) (each must be confirmed on a subsequent day): symptoms of DM plus casual plasma glucose level >199 mg/dL or fasting plasma glucose level >125 mg/dL or 2-hour plasma glucose level after 75-g glucose load >199 mg/dL. BMI = body mass index; IDF = International Diabetes Federation; IFG = impaired fasting glucose (fasting plasma glucose level, 100-125 mg/dL); IGT = impaired glucose tolerance (2-hour plasma glucose level after 75-g glucose load, 140-199 mg/dL); IR = insulin resistance; NCEP ATP III = National Cholesterol Education Program Adult Treatment Panel III; WC = waist circumference; WHO = World Health Organization.

The diagnosis is made by a trained medical person with the assistance of various diagnostic investigations indicated. The diagnosis of Metabolic Syndrome in an individual does not vindicate the individual’s health status. It is to indicate that the individual should seek help to contain the hyperinsulinemia, obesity, altered fat metabolism and any other features of the syndrome. For those who escape it even by a whisker, it is a warning and should be taken seriously. As the age old adage goes, “Prevention is better than cure”, we should all wake up to this call and take necessary precautions.

Whichever the diagnostic criteria, the numbers are increasing at an alarming rate, begging for our attention.

IS THERE A THRIFTY GENE?

During the second half of the twentieth century, obesity progressed from being a minor health problem to a major risk factor and into an epidemic of massive proportions. This closely correlates to the increased availability of food and reduced physical activity in industrialized countries during this period. Obesity is now linked as a causal factor of Type 2 diabetes and the metabolic syndrome.

In 1962, Neel proposed the existence of a “thrifty gene” that predisposed people to obesity, and subsequently diabetes. During olden times, when the feast or famine environment was the rule, “individuals exceptionally efficient in the uptake and utilization of food and its storage as fat” were at a selective advantage. In the context of our modern generation where food is plentiful and we are addicted to carbohydrates, anyone who has the thrifty gene tends to accumulate the excess calories as fat, predisposing the individual to obesity, diabetes and the Metabolic Syndrome.

THE THERAPEUTIC JARGON UNRAVELED

So, the doctor at the hospital conveyed you the sad news, “You have high blood sugar readings, a high blood pressure reading and your body fat seems to stick to you. You have the Metabolic Syndrome.” You cannot believe your ears. The doctor tells you, “Sooner or later, you will have hypertension or even a heart attack or stroke, if you do not take necessary action.” This could not have sounded any more devastating.

This situation is commonplace with the increasing number of persons being affected. There is significant evidence that Metabolic Syndrome increases the risk for developing coronary heart disease, with or without other risk factors, and hence the need for organized therapy.

Simple tips that could save you from serious consequences of Metabolic Syndrome:

- Remember to visit your physician at regular intervals.
- Take your medications regularly.
- Do your exercises regularly, increasing it gradually.
- Check your weight regularly. Do not be disappointed if it does not decrease all at once. Be patient.
- Remember, we are addicted to carbohydrates. Keep them at bay.
- Fat is not necessarily bad. Our body needs essential fatty acids. Read up about them and prepare a list of food stuff which is edible and those which should be avoided.
- Those with a family history of diabetes, hypertension or Metabolic Syndrome should make efforts to know about the disease and prevent it from taking root in them.
- Awareness is the key to prevention of this dreaded disorder. Ask your physician about it.

So, what are the options available to a person who has Metabolic Syndrome? Do medications and other holistic methods have any role in the treatment of Metabolic Syndrome? Are surgical methods of obesity reduction safe and without risk? Let’s find out as we discuss the various options available to an affected individual.

The simplistic cliché, “Eat less, Exercise more” is outdated. Of course, obesity is the driving force of Metabolic Syndrome and should be dealt with seriously. However, a more integrated approach is advocated as it is a lifestyle-based disease.

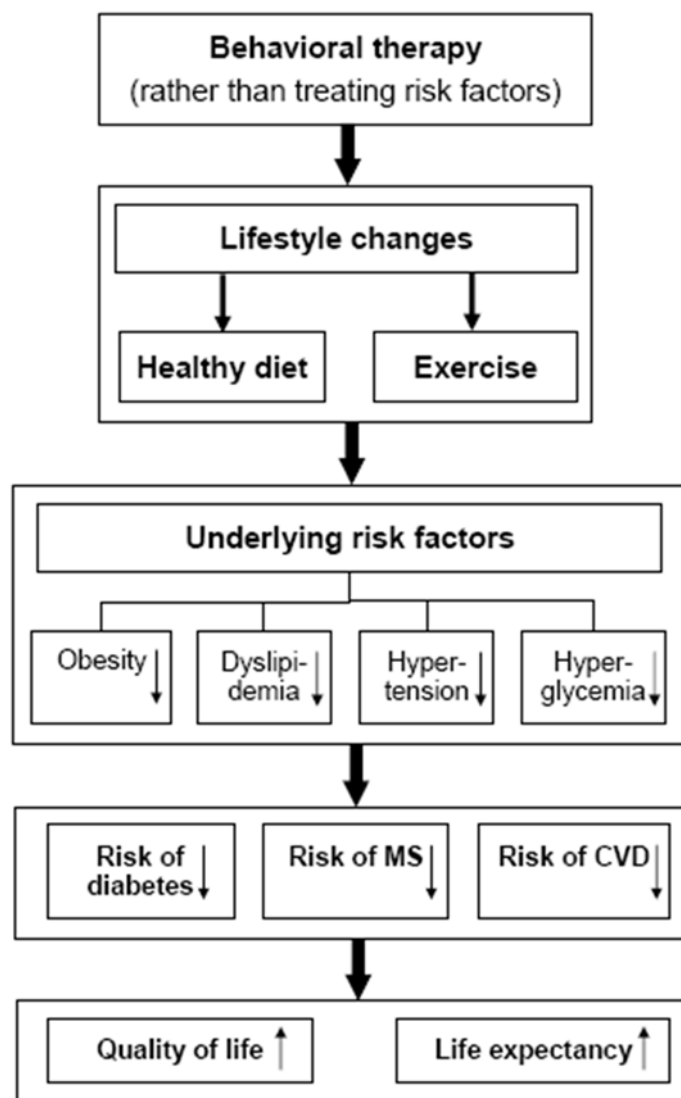
Lifestyle modification, including weight loss, healthy diet, and increased physical activity, is the cornerstone of therapy for the Metabolic Syndrome as well as for its components.

1. Lifestyle modification (Weight loss and Physical activity):

Metabolic Syndrome is closely related to the lifestyle changes that have taken place over the centuries. Hence, lifestyle modification and behavioral therapy take precedence in the management of this disorder.

A joint consensus of the American Heart Association; National Heart, Lung and Blood Institute; and the American Diabetic Association is that lifestyle modifications consisting of diet and physical activity for the treatment of obesity and overweight constitute the first line of therapy.

A flow diagram showing the benefits of Behavioral therapy resulting in improvement of quality of life and increase in life expectancy as the end result.



The duo of diet and exercise delays the onset of diabetes in individuals at risk. Physically active individuals show a 30% to 50% reduction in coronary heart disease risk as compared to those with a sedentary lifestyle.

Diet and lifestyle modification strategies have been central to the management of diabetes, hypertension, obesity and more recently, dyslipidemia, which all together

constitute the tenets of Metabolic Syndrome. The Greeks were the pioneers in advocating diet and lifestyle modifications in the management of high blood sugar levels. And, before the discovery of insulin and oral hypoglycemic agents, it was the only treatment option available for diabetes. The dietary guidelines have changed over the years – from the “high-fat and low-carbohydrate diet” of yester years to the recently advocated, more healthy, “low-fat and high-carbohydrate diet”. Diets rich in monounsaturated fat are known to reduce total and low-density lipoprotein (LDL) cholesterol, with no reduction of High-density lipoprotein (HDL) cholesterol. Low glycemic index carbohydrates and foods rich in monounsaturated fat are promoted.



There is less emphasis on cereal fiber diet and the precise effects of antioxidants are uncertain. Protein intake is generally restricted because of increased risk of nephropathy. It should be limited to <10 - 20% of total energy.

The benefits of physical activity for people with Metabolic Syndrome are increasingly being cited in reports and researches across the world. Regular, moderate intensity exercise is associated with decreased risk of developing Type 2 diabetes mellitus in men, women and overweight individuals. Exercise can produce a reduction in plasma triglycerides, increase in high-density lipoprotein (HDL) and can also aid weight loss. The overall impact of exercise on blood pressure is also beneficial. It reduces insulin resistance and negates the effect of the “thrifty gene” in predisposed individuals.

Metabolic Syndrome and Physical Activity: Physical activity fosters multiple benefits which are ideal for the prevention and management of individual components of the Metabolic Syndrome. The following benefits are increasingly being cited in various studies:

- a. Reduction in all-cause mortality
- b. Reduction in cardiovascular diseases including, but not limited to coronary artery disease, stroke and heart attack.
- c. Blood pressure reduction
- d. Improved weight loss in the obese and weight maintenance in those of normal weight.
- e. Prevention of Type 2 diabetes mellitus and improved glucose control.
- f. Prevention of osteoporosis, which is weakening of the bones.
- g. Improved flexibility and strength.
- h. Most important of all, increased self-esteem and confidence.

These benefits apply to all people irrespective of whether they have Metabolic Syndrome or not. Physically fit people are less likely to develop Type 2 diabetes. Recent research shows benefit in changing from a sedentary lifestyle to a moderately active lifestyle.

Exercise causes changes in the individual which promote insulin sensitivity. It benefits the diabetic or the overweight individual in achieving good control over glucose levels. It also benefits the normal individual by preventing the deposition of fat and its utilization from the body. This improves the cardiovascular function and health and a reduction in the blood pressure.

Physical activity is well documented in the prevention of heart disease in the general population. It causes decrease in the low-density lipoproteins (LDL), triglycerides and total cholesterol.

Exercise plays a central role in weight reduction in the obese and overweight, and weight maintenance in those with normal weight. This is especially beneficial for diabetics, 80% of whom are overweight or obese.

The Physiology of Exercise:

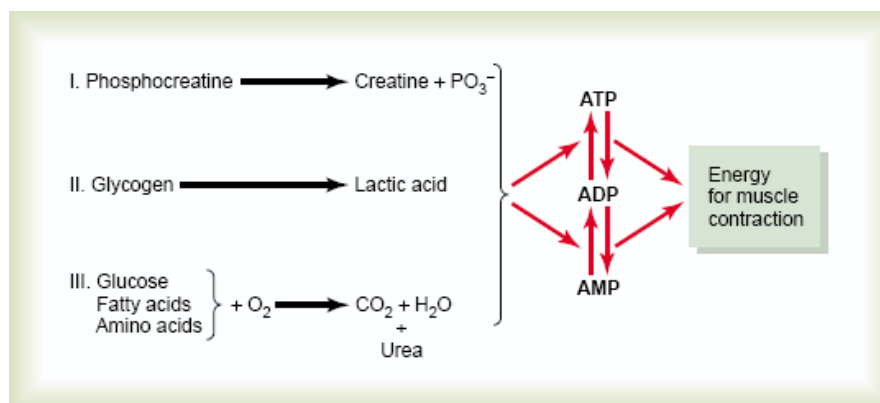
Metabolic changes provide the energy required for exercise. Glucose uptake by the exercising muscle increases and at the onset of exercise, muscle glycogen is converted to lactate to provide the energy substrate. When muscle glycogen is exhausted, energy is provided by glucose from the liver following glycogen breakdown. Eventually, when even the liver stores are exhausted, the energy required is derived from free fatty acids in fatty tissues of the body. This is what we refer to when we say, “burn the fat”.

In 1994, the UK Health Education Authority (HEA) adopted an international consensus statement and recommended the following:

Moderate intensity activity;

Of 30 minutes or more;

At a frequency of 5 or more days each week.



Hormonal responses to exercise are the action of insulin and its counter regulatory hormones glucagon, cortisol and catecholamines.

The key response to exercise is the suppression of insulin secretion, accompanied by a rise in hormones that cause breakdown of body fat and glycogen. This stimulates release of glucose from the liver and free fatty acids and maintains energy levels during exercise. At the same time, the utilization of glucose and fatty acids, and suppression of insulin leads to decrease in fat and glucose from the body and the beneficial effect of decreasing insulin resistance. There is continued oxidation of fat which limits the use of glucose as energy substrate. This undermines the principle of exercise in the management of Metabolic Syndrome.

However, the risk of hypoglycemia should be kept in mind in Type 1 diabetic patients.

| Glycemic Index (GI) | Examples of food | Timing |
|---------------------|---|--|
| Low | Pasta, Basmati rice, couscous, instant noodles, barley, wholegrain products, porridge, muesli, All-Bran, oat-based cereal bars, lentils and pulses including baked beans, chick peas and kidney beans, dried apricots | 2-3 hours before exercise, especially endurance events |
| High | Isotonic sports drinks, fruit juice, ordinary squash, jelly beans, ripe bananas, honey sandwich | During exercise session (If required) |
| High | Corn flakes, Rice Krispies, sugared cereals, white bread, rice (other than Basmati), potatoes | Within 30-60 minutes of completing an exercise session |

Here are guidelines for people with diabetes wishing to exercise (applicable to Metabolic Syndrome as well):

Before exercise:

- Monitor blood glucose regularly – before, during and after exercise.
- Eat a low glycemic index (GI) meal 2-3 hours before an endurance event.
- Reduce insulin by 30-50% for strenuous or endurance training.
- Optimum blood glucose levels are 6-13 mmol/l
- If blood glucose < 6 mmol/l, take 10-20 g fast-acting carbohydrate.
- If blood glucose > 13 mmol/l, delay exercise.

During exercise:

- 20-30 minutes of light to moderate activity should not require extra carbohydrate.
- 30-60 minutes of moderate activity may require an extra 10-20 g high glycemic index (GI) carbohydrate.
- 30-60 minutes of strenuous activity may require an extra 30-50 g high GI carbohydrate.
- Endurance training may require an additional 10-20 g high GI carbohydrate for each 30 minutes of exercise.
- Remember to consume adequate fluid to prevent dehydration.

After exercise:

- Replenish glycogen stores by consuming high GI carbohydrate-rich foods within 30-60 minutes of exercise. After endurance training, monitor blood glucose levels, replenish glycogen stores with high GI carbohydrate and adjust insulin accordingly.

Very few studies have been done on Metabolic Syndrome. One of the epidemiologic studies that evaluated the association between physical activity and the prevalence of the metabolic syndrome was the ATTICA study. The results showed that even light-to-moderate leisure time physical activity expending <7 kcal/min was associated with a considerable reduction in the prevalence of the Metabolic Syndrome in 3042 men and women from the general population. Regular, intensive exercise was associated with a much greater decrease.

Physical exercise is also associated with decrease in the blood pressure, lowering of “bad fat” and increase of “good fat” in the body.

However, the benefits of lifestyle modifications can be a difficult choice for us who have become used to the sedentary lifestyle. Moreover, dietary restrictions are hard to follow.

Metabolic Syndrome and Diet: Protective health effects have been evidenced with the intake of diets rich in vegetables, fruits, legumes and whole grains, fish, nuts, and low-fat dairy products. Energy intake should not exceed the energy expenditure for a diet to be effective. This does not mean that we should cut down on our essential fats.

Weight gain, obesity, diabetes and other components of the Metabolic Syndrome are thought to be due to carbohydrate consumption. This is untrue. Excess ingestion of the wrong carbohydrates, such as simple sugars is instigated as the culprit, whereas complex carbohydrates contained in potatoes, bread and corn are recommended.

High fiber diets have received much of the limelight in recent years considering the decreased incidence of hypertension, diabetes, colon cancer and obesity.

Saturated fats have been proved to be causal in altered fat metabolism and atherosclerosis. Unsaturated fats contained in vegetable oils such as safflower, corn, olive and soya oil prevent atherosclerosis and hence, Metabolic Syndrome.

Dietary proteins are best restricted, especially in the obese and those with kidney disease as it can further damage the kidneys.

The Mediterranean diet is characterized by the use of olive oil, and large quantities of vegetables in the form of salads, and legumes in the form of cooked foods. It has drawn enough media and intellectual attention in the past decade. It also contains wheat, olives and grapes in their various forms. The ratio of monounsaturated to saturated fats is quite high in this diet which explains the health benefits. The vegetables, fresh fruits, cereals and olive oil provide high intake of beta-carotene, vitamins C and E, polyphenols and various important minerals. The benefits obtained by the Mediterranean diet are manifold. They include improvement in blood lipid profile, decreased risk of thrombosis, improvements in endothelial function and insulin resistance, a decrease in homocysteine levels and a decrease in total body fat.

Recently, Mediterranean diet was proved to be associated with 20% lower odds of having the metabolic syndrome, irrespective of age, sex, physical activity, lipids and blood pressure levels. This potential benefit could be explained by the presence of bioflavonoids from wild edible greens in the diet. Berries, particularly blueberries and acai berries are rich in flavonoids, which are natural antioxidants.

2. Drug Therapy

When recommended therapeutic goals elude with diet and exercise, pharmacologic therapy becomes essential, but not optional as most of might think.

In an individual at high risk for coronary heart disease and cerebrovascular disease, the use of statins is advocated and has a clearer role to contain plasma cholesterol levels.

In patients with diabetes, metformin and thiazolidinediones are routinely used because of their insulin-sensitizing and blood-glucose lowering activity.

Cigarette smoking should be discouraged in all individuals with the metabolic syndrome.

Low-dose aspirin is used to prevent coronary heart disease in Metabolic Syndrome in individuals with a 10% or greater risk for coronary heart disease.

CONCLUSION AND REMARKS

Metabolic Syndrome has taken the world by surprise. The magnitude of the problem is astounding and it requires a collective effort of the government, society and the individual at large to prevent this menace.

New inroads are being explored as newer findings are being evaluated for cornering and tackling this serious health problem.

If any one of you has a doubt about whether or not you have the Metabolic Syndrome, consult your physician. It is of utmost importance that this disease is rooted out from our society. The primary target to achieve this would be to prevent obesity and central adiposity by increasing physical activity and promoting healthy eating.

School and office based programs and awareness campaigns should be organized to sensitize people about this monstrous disorder that could dig holes in our resources.

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