

Metabolic syndrome

<p>Metabolic Changes Observed in Obesity</p>	<ul style="list-style-type: none"> The metabolic abnormalities of obesity reflect molecular signals originating from the increased mass of adipocytes The predominant effects of obesity include: <ol style="list-style-type: none"> dyslipidemias glucose intolerance insulin resistance hypertension
<p>Metabolic Syndrome</p>	<p>Metabolic syndrome is a cluster of closely related medical conditions which increase the risk of developing heart disease and diabetes</p> <ul style="list-style-type: none"> Features comprising Metabolic Syndrome: <ol style="list-style-type: none"> Obesity (specifically visceral) High serum TGs Low HDL cholesterol Hypertension Hyperglycemia Hyperinsulinemia (insulin resistance)
<p>Effects of Insulin Resistance in obese individuals</p>	<ul style="list-style-type: none"> Reduction of glucose uptake or glucose utilization among muscle cells and reduction of glycogenesis- both lead to hyperglycemia increased production of insulin in an effort by the body to maintain blood glucose levels (Compensatory hyperinsulinemia, which causes down regulation of insulin receptors) increased activity of hormone-sensitive lipase, resulting in hydrolysis of stored TGs or fats, leading to elevation of plasma FFA
<p>Dyslipidemia</p>	<ul style="list-style-type: none"> These fatty acids are carried to the liver and converted to TGs and cholesterol Excess TGs and cholesterol are released as VLDL, resulting in elevated serum triacylglycerols Concomitantly, HDL levels are decreased <p>Dyslipidemia and the Metabolic syndrome an inseparable couple?</p> <ul style="list-style-type: none"> Dyslipidemia is an early and consistent component of insulin resistance Liver fat seems to be the unifying factor between dyslipidemia and insulin resistance
<p>Risk factors</p>	<ol style="list-style-type: none"> Obesity Alcoholism Sedentary Lifestyle Smokers Hypercortisolism (e.g. steroid use or Cushing's disease) Drugs (Rifampicin, Isoniazid etc) Mutation of insulin receptors

Metabolic Syndrome is Linked to:	<ol style="list-style-type: none"> Heart disease: 1.5-3 fold increase for atherosclerotic CVD Type 2 Diabetes Mellitus: 5 fold increase Kidney disease Reproductive abnormalities in women <ol style="list-style-type: none"> PCOS, difficulty with ovulation and fertility, irregular periods Nonalcoholic steatohepatitis (fatty liver), related to distorted lipid metabolism Cancer: <ul style="list-style-type: none"> Obesity is major risk factor for cancer of the esophagus; colon and rectum; liver; gall bladder etc Being overweight and obese accounts for 14% of all cancer deaths in men and 20% of those in women
Diagnosis	<ol style="list-style-type: none"> WHO criteria (1999) <ul style="list-style-type: none"> Impaired glucose tolerance, DM, or insulin resistance; along with at least two of the below mentioned components: <ol style="list-style-type: none"> Hypertension - BP > 140/90 mmHg Dyslipidemia - High plasma TGs (>1.7mmol/L)¹ - Low HDL cholesterol (men <0.9, women <1.0 mmol/L) Central or General Obesity - Waist to hip ratio >0.9 in men, >0.85 in women - And/or BMI > 30 Microalbuminuria - Urinary albumin excretion rate ≥ 20ug/min or - Albumin:creatinine ratio ≥ 30mg/g
	<ol style="list-style-type: none"> NCEP² ATP³ III Guideline (2002) <p>Diagnosis: ≥ 3 of these risk factors are present</p> <ol style="list-style-type: none"> Waist circumference: <ul style="list-style-type: none"> Men > 102 cm (>40 in) Women > 88 cm (>35 in) Triglycerides > 150 mg/dL HDL cholesterol: <ul style="list-style-type: none"> Men < 40 mg/dL Women < 50 mg/dL Blood pressure 130/ 85 mm Hg Fasting glucose > 100 mg/dL
	<ol style="list-style-type: none"> Markers <ul style="list-style-type: none"> Lipoproteins- LDL, HDL Adipokines: <ul style="list-style-type: none"> Leptin Adiponectin Inflammatory markers: CRP, TNF-a, IL-6, IL-8 Hemostatic marker (Plasminogen Activator inhibitor-1)
Managing	<ol style="list-style-type: none"> Primary intervention: Lifestyle changes <ul style="list-style-type: none"> Weight reduction (strive for BMI less than 25) <ul style="list-style-type: none"> Reduced caloric intake and dietary fat Increased physical activity Set realistic goals: 5-10% weight loss from baseline

¹ Normal value ranges will be given

² National Cholesterol Education Program

³ Adult Treatment Panel

		<ul style="list-style-type: none"> Smoking cessation Lowering Blood pressure: <table border="1"> <thead> <tr> <th>Modification</th> <th>Recommendation</th> <th>Average drop on SBP</th> </tr> </thead> <tbody> <tr> <td>1. Weight Loss:</td> <td>Maintain normal body weight</td> <td>5-10 for every 22lbs loss</td> </tr> <tr> <td>2. Healthy eating plan:</td> <td>Meal plan rich in fruits, vegetables, low fat dairy and low in saturated fat and cholesterol</td> <td>8-14</td> </tr> <tr> <td>3. Sodium Restriction:</td> <td>Less than 2400 mg/day</td> <td>2-8</td> </tr> <tr> <td>4. Regular physical activity:</td> <td>30 min most days of the week</td> <td>4-9</td> </tr> </tbody> </table>	Modification	Recommendation	Average drop on SBP	1. Weight Loss:	Maintain normal body weight	5-10 for every 22lbs loss	2. Healthy eating plan:	Meal plan rich in fruits, vegetables, low fat dairy and low in saturated fat and cholesterol	8-14	3. Sodium Restriction:	Less than 2400 mg/day	2-8	4. Regular physical activity:	30 min most days of the week	4-9
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Secondary intervention: Pharmacotherapy; for Management of existing risk factors:																	
1. Blood pressure		<ul style="list-style-type: none"> Treat hypertension to goal (<130/80 mmHg) No particular anti-hypertensive agent is preferred for metabolic syndrome <ul style="list-style-type: none"> Low dose diuretic ACE inhibitor (if also have DM) 															
2. Lipids: Statins & Fibrates		Fibrates: <ul style="list-style-type: none"> Used to reduce the lipid levels Target for fibrates is a transcription factor- peroxisome proliferator activated receptor-α (PPAR-α), which when activated, leads to the transcription of genes involved in lipid degradation, or uptake by the cells. E.g. <ul style="list-style-type: none"> Carnitine palmitoyl transferase I, which enhances the uptake of FA into the mitochondria Lipoprotein Lipase Stimulates apoAI and apoAII protein synthesis (major proteins in HDL) 															
3. Blood glucose	Metformin	<ol style="list-style-type: none"> Metformin reduces blood glucose levels by inhibiting hepatic gluconeogenesis, which is active in patients due to liver's <u>resistance to the effects of insulin</u> Metformin also reduces lipid synthesis in the liver which aids in modulating blood lipid levels in these patients 															
	Thiazolidinediones (TZDs) e.g. pioglitazone	<ul style="list-style-type: none"> Used for the treatment of insulin resistance and type 2 diabetes mellitus TZDs activate PPAR-γ class of transcription factors expressed primarily in the adipose tissue <ul style="list-style-type: none"> Activates the transcription of adiponectin The increase in adiponectin reduces the fat content of the liver and enhances insulin sensitivity 															
4.CVD	Aspirin therapy	<ul style="list-style-type: none"> Aspirin to treat clotting disorders Daily low dose aspirin (81-325mg) for men over age 45 and postmenopausal women 															