**Metabolic syndrome**

### Definition
- Clustering of cardiovascular risk factors including HTN, hyperlipidemia, glucose intolerance, obesity & hyperinsulinemia.
- Other constituents include hyperuricemia, fatty liver and microalbuminuria.
- These factors were labelled syndrome X by Reaven in 1988 who suggested that Insulin resistance was its central characteristic, so it was also termed insulin resistance syndrome.

### Updated criteria for diagnosis of metabolic syndrome
At least 3 of the following 5 conditions:
- **Fasting glucose** ≥100 mg/dL (or receiving drug therapy for hyperglycemia)
- **Blood pressure** ≥130/85 mm Hg (or receiving drug therapy for hypertension)
- **Triglycerides** ≥150 mg/dL (or receiving drug therapy for hypertriglyceridemia)
- **HDL-C** < 40 mg/dL in men or < 50 mg/dL in women (or receiving drug therapy for reduced HDL-C)
- **Waist circumference**: According to population or country specific definitions.
  - USA > 102 cms in men and >88 cms in women
  - Europoid > 94 cms in men and >80 cms in women
  - Middle east are considered Europoid
  - South east Asia 90 cms in men and >80 cms in women

### Pathogenesis of the metabolic syndrome
**Potential etiologic categories**
1. Obesity and disorders of adipose tissue
2. Insulin resistance
3. genetic and acquired factors

**Other contributing factors**
- Lack of physical activity,
- Low cardio-respiratory fitness,
- Atherogenic diet,
- Smoking,
- Elevated LDL,
- Low household income,
- Family history of early coronary artery disease,
- Aging, post menopausal status,
- More exposure to work stressors.

### Treatment
Lifestyle change and weight loss are considered the most important initial steps in treating metabolic syndrome.
1. Dietary modification: inclusion of whole grains, fruits and vegetables and lean sources of animal proteins including low fat dairy products for insulin resistance.
2. Activity: exercise and weight loss improve hyperinsulinemia and BP.
3. Behavioural modification: Relaxation and Meditation was reported to improve glucose tolerance and lipid profile.
4. Smoking cessations

Mediterranean diet improved markers of vascular inflammation, endothelial dysfunction and insulin resistance in patients with metabolic syndrome.

**Pharmacotherapy:**
1. Metformin 500mg bid reported to improve insulin resistance and endothelial dysfunction
2. Antihyperlipidemic drugs:
3. Bezafibrate is beneficial in subjects with elevated TG
4. Statins in subjects with elevated LDL
5. Niacin in subjects with low HDL
6. Low dose aspirin: For prothrombotic state

Treatment of associated obstructive sleep apnea may also play a significant role in the management of metabolic syndrome.

### Weight loss

<table>
<thead>
<tr>
<th>Causes of weight loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
</tr>
<tr>
<td>Q2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nb</th>
<th>Q1</th>
<th>Q2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intentional (dieting)</td>
<td>With decreased appetite (anorexia + wt loss)</td>
</tr>
<tr>
<td></td>
<td>Unintentional (loss of 5% of body wt over 1-6 months should be investigated).</td>
<td>Inspite of good appetite</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1. GIT causes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malabsorption including celiac disease, inflammatory bowel disease.</td>
</tr>
<tr>
<td>Obstruction, dysphagia.</td>
</tr>
<tr>
<td>Gastric carcinoma, ulcer.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Malignancy</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>3. Endocrine disorders:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncontrolled diabetes.</td>
</tr>
<tr>
<td>Thyrotoxicosis.</td>
</tr>
<tr>
<td>Adrenal insufficiency (Addison's dis).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Infections: TB, HIV, Parasitic infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. Chronic inflammation: RA</td>
</tr>
<tr>
<td>6. Renal failure</td>
</tr>
<tr>
<td>7. Congestive heart failure</td>
</tr>
<tr>
<td>8. Psychiatric disorders:</td>
</tr>
<tr>
<td>9. Weight loss inspite of good appetite:</td>
</tr>
<tr>
<td>10. Anorexia with severe loss of weight usually denotes serious underlying cause as: Malignancies, Infections</td>
</tr>
<tr>
<td>11. In older patients The most common causes are: depression, cancer and benign GIT dis</td>
</tr>
<tr>
<td>12. Younger individuals: Diabetes, thyrotoxicosis, anorexia nervosa, infection including HIV should be considered.</td>
</tr>
</tbody>
</table>
Malnutrition and weight loss are usually present together in association with other disease conditions. Chronic protein energy malnutrition in adults is suspected through below criteria.

### Changes of BMI (weight in kgs/height in square meters)  Weight loss in previous 3-6 months  Disease states that could lead to malnutrition

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Changes of BMI</th>
<th>Weight loss</th>
<th>Disease states</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 18.5 kg/m²</td>
<td>Probable PEM</td>
<td>&gt; 10%</td>
<td>High risk</td>
</tr>
<tr>
<td>18.5 - 20</td>
<td>Possible PEM</td>
<td>5-10 %</td>
<td>Possible risk</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>little or no risk</td>
<td>&lt; 5%</td>
<td>little or no risk</td>
</tr>
</tbody>
</table>

### Methods of Nutritional Assessment

#### Dietary assessment
- 24 hours dietary recall
- Food frequency questionnaire
- Dietary history
- Food dairy technique

#### Anthropometric data
- Weight, height, BMI, waist circumference, UMAC

#### Physical examination
- Muscle mass, or strength
- Evidence of chronic diseases e.g. liver dis.
- Evidence of vitamin deficiencies

#### Subjective global assessment
A systematic bedside assessment of nutritional status has been shown to accurately categorize patients as well nourished, moderately malnourished or severely malnourished.

#### Laboratory tests

### Assessment of malnutrition

1. Poor dietary intake:
   - Unavailability of food e.g. poverty, alcoholism,
   - Monotonous diets resulting in low micronutrient intake.
   - Poor dentures especially in elderly.
   - Dysphagia (e.g. esophageal stricture, achalasia or cancer)
   - Psychiatric disorders including anorexia nervosa

2. Malabsorption : all causes

3. Chronic infections: including T.B., AIDs , parasitic infest.

4. Malignancies

5. Increased demands : pregnancy and lactation

### Assessment of chronic underweight

<table>
<thead>
<tr>
<th>BMI (kg /m²)</th>
<th>Classification of chronic underweight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal &gt;18.5</td>
<td>Grade II 16.0-16.9</td>
</tr>
<tr>
<td>Grade I 17.0-18.4</td>
<td>Grade III &lt;=15.9</td>
</tr>
</tbody>
</table>

### Causes of malnutrition

1. Poor dietary intake:
   - Unavailability of food e.g. poverty , alcoholism, 
   - Monotonous diets resulting in low micronutrient intake.
   - Poor dentures especially in elderly.
   - Dysphagia (e.g. esophageal stricture, achalasia or cancer)
   - Psychiatric disorders including anorexia nervosa

2. Malabsorption : all causes

3. Chronic infections: including T.B., AIDs , parasitic infest.

4. Malignancies

5. Increased demands : pregnancy and lactation

### Assessment of malnutrition

1. General: Weight, Height, BMI, UMAC
2. Muscle status : muscle wasting : def of somatic proteins
3. Subcutaneous fat e.g. triceps skin fold thickness, hollow cheeks (loss of buccal pad of fat).
4. Skin:
   - Pallor (palmar, mucous membranes) → Iron, folic acid , vit B12 def
   - Hyper pigmentation → Niacin, protein def
   - Thickening and dryness → Essential FA
   - Bruising → Vit K, C
5. Eyes:
   - Pallor → iron , folic acid and vit B12 def
   - Bitot spots → vit A def
   - Corneal vascularization → riboflavin def

6. Hair → Sparse , thin : Protein and vit def
7. Nails:
   - Koilonychia → iron def
   - White nails → protein def

8. Oral cavity:
   - Glossitis: riboflavin, niacin, vit B12
   - Angular cheilitis: riboflavin
   - Bleeding gums: Vit K, C

9. Bones :
   - knock knees, widening of wrists → Vit D def

### B: Laboratory and imaging studies:

1. Complete blood picture and indices for diagnosis of the level and type of anemia.
2. Serum calcium , p and Alk p and electrolytes
3. Serum iron , ferritin and TIBC
4. Serum folic acid and vitamin B12

5. Blood glucose, liver and renal function.
6. BMD ( bone mineral density) for osteoporosis
7. Thyroid function
8. Urine analysis and chest X ray
9. Additional tests including Gi endoscopy, CT, MRI,HIV and chest CT

### Treatment of malnutrition

#### Goals of treatment:
1. Restoration of the body composition to normal by supply macronutrients (carbohydrates, proteins and fats) and micronutrients (vitamins and minerals).
2. Treatment of underlying causes of malnutrition.

#### Treatment of severe malnutrition is divided into 2 stages:
1. Correction of fluids, electrolyte and acid base balance and treatment of hypocalcemia, hypoglycemia.
2. 2- Supply nutrients to restore normal body composition, slowly and gradually. This is important to avoid (Refeeding syndrome).
### Vitamins deficiency

<table>
<thead>
<tr>
<th>Water soluble vitamins</th>
<th>B1 Thiamine</th>
<th>Beriberi, Wernicke- Korsakoff syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>B2 Riboflavin</td>
<td>Angular stomatitis</td>
<td></td>
</tr>
<tr>
<td>Niacin</td>
<td>Pellagra</td>
<td></td>
</tr>
<tr>
<td>B6 Pyridoxine</td>
<td>Polyneuropathy</td>
<td></td>
</tr>
<tr>
<td>B12 cobalamin</td>
<td>megaloblastic anemia, neurological disorders</td>
<td></td>
</tr>
<tr>
<td>Folate</td>
<td>megaloblastic anemia</td>
<td></td>
</tr>
<tr>
<td>C Ascorbic</td>
<td>Scurvy</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fat soluble vitamins</th>
<th>A (Retinol)</th>
<th>Xerophthalmia, night blindness, keratomalacia, follicular hyperkeratosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>D (Cholecalciferol)</td>
<td>Rickets, osteomalacia</td>
<td></td>
</tr>
<tr>
<td>K</td>
<td>Coagulation defects</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>(α-Tocopherol)</td>
<td></td>
</tr>
</tbody>
</table>

#### Thiamine B
- **Beri beri**
  - TPP A COFACTOR IN CHO METABOLISM
  - Dry: Symmetrical polyneuropathy
  - Wet: Oedema, tachycardia
  - High output heart failure
- **Wenicke-Korsakoff** especially in alcoholics
  - Confusion, lack of coordination

| Sources of vit B1 | Gereals, grains, beans, Nuts, ducks, pork |

#### Riboflavin B2
- **Deficiency**
  - 1. Angular stomatitis
  - 2. Red inflamed tongue
  - 3. Seborrheic dermatitis
  - 4. Anemia (impaired iron utilisation)
- **Dietary source**
  - Dairy products, Leafy vegetables
- **Def caused by**
  - Low intake of animal and dairy products.
  - Chronic alcoholism

#### Niacin
- **Deficiency**
  - Pellagra
  - Dermatitis: redness, cracks, ulceration, exposed areas, Collar, necklace.
  - Diarrhea: usually glossitis, angular stomatitis.
  - Red raw painful tongue.
  - Dementia: depression, apathy.
- **Sources**
  - Low intake of animal proteins
  - Rare
  - Raw egg intake contain Antagonist
  - Long term parenteral nutrition without vit supplement

#### Vitamin B6
- **Deficiency**
  - Polyneuropathy (occurring with isoniazide responds to vit B6) / Sideroblastic anemia
  - In cases of:
    - 1. Intake of drugs as INH, hydralazine, Penicillamine
    - 2. Rarely dietary deficiency
- **Def caused by**
  - Low intake of fruits and vegetables and dairy products
  - Malabsorption and intestinal parasites infections e.g. giardiasis
  - Disorders of folic acid metabolism
- **Def leads to**
  - 1. Megaloblastic anemia
  - 2. Risk factor for neural tube defects in fetus
  - 3. Elevated homocysteine, heart disease, stroke
  - 4. Impaired cognitive function, depression

#### Folic acid deficiency
- **Def caused by**
  - Low intake of animal proteins e.g. strict vegetarians
  - Malabsorption causing gastric Atrophy (insufficient intrinsic factor production = Pernicious anemia)
- **Def leads to**
  - Megaloblastic anemia
  - Risk factor for neural tube defects in fetus
  - Elevated homocysteine, heart disease, stroke
  - Impaired cognitive function, depression

#### Vitamin B12 Cobalamin
- **Def caused by**
  - Low intake of animal proteins e.g. strict vegetarians
  - Malabsorption causing gastric Atrophy (insufficient intrinsic factor production = Pernicious anemia)
- **Def leads to**
  - Megaloblastic anemia
  - Risk factor for neural tube defects in fetus
  - Elevated homocysteine, heart disease, stroke
  - Impaired cognitive function, depression

#### Biotin deficiency
- **Sources**
  - Rare
  - Raw egg intake contain Antagonist
  - Long term parenteral nutrition without vit supplement

#### Vitamin A
- **Due to**
  - Low intake of dairy products and carotenoids from fruits and vegetables.
  - Parasitic infestations e.g. ascariasis
- **Cp**
  - Hyperkeratosis, dry skin
- **Severe deficiency**
  - Scurvy
  - Swollen spongy gums with bleeding
  - Swelling and infection, arthritis
  - Spontaneous bruising
  - Weakness, fatigue, arthralgia
  - Subperiosteal hemorrhage
  - Poor wound healing

#### Vitamin C
- **Source**
  - Fresh fruits, Potatoes
  - But destroyed by cooking storage easily leached out of vegetables
- **Symptoms**
  - Weakness and muscle pain
  - Anemia usually hypochromic occasionally normochromic or megaloblastic
  - In people who do not eat vegetables

#### Vitamin D
- **Osteomalacia**
  - Adult, rickets
- **Children**

#### Vitamin K
- **VITAMIN K**
  - Cofactor in synthesis of coagulation factors: II, VII, IX, X
  - and inhibitors: protein C, S
  - Found in green leafy vegetables
  - Synthesised by intestinal bacteria
  - **DEFICIENCY**
  - Bleeding
  - Prolonged PT (INR)
- **Caused by**
  - * Cholestatic jaundice
  - * Vitamin K antagonists
  - * Antibacterial drugs