MANIFESTATIONS OF THE METABOLIC SYNDROME: PART 1

The metabolic syndrome (Met-S) is a concept that has evolved over the past 20 years, describing a complex combination of metabolic, malignant, fatty liver and cardiovascular risk factors.

Due to its multi-complexity, this overview of the metabolic syndrome is divided into two articles. Part one, in this issue (3 CPD points), and the next article in the March issue of Medical Chronicle (also 3 CPD points). The first section will deal with definition, investigations, epidemiology and aetiology. The second section will follow on with pathophysiology and management.

This syndrome has been known by many names:
- The metabolic syndrome
- The dysmetabolic syndrome
- Obesity-associated syndrome
- Syndrome X
- Hypertriglyceridaemic abdominal waist syndrome
- CHAOS (coronary artery disease, hypertension, atherosclerosis, obesity and stroke) in Australia.

The core of the syndrome is insulin resistance and the insulin resistance syndrome was coined and eponymously called Reaven’s syndrome.

It is now termed the cardiovascular-metabolic syndrome and in the presence of diabetes, it is a cardio-equivalent. This means it is equal in risk as having pre-existing cardiac disease for further cardiac events. The abbreviation is Met-S and its ICD-10 code: E88.9.

WHY IS IT METABOLIC?
The core of the syndrome is insulin resistance and the resultant glucose and free fatty acid energy utilisation and storage resulting in progressive abnormalities.

WHY IS IT A SYNDROME?
As there is no single definition, no precise cause with multiple pathogeneses and numerous clinical presentations, it is termed a syndrome. It is an amalgamation of signs, symptoms and measurements correlated with each other.

The Met-S is growing global pandemic. It is the most rapidly expanding disease in adults over the age of 45 years with a prevalence of up to 60% and also rapidly increasing in the paediatric population to over 20%.

It is vital to recognise the syndrome, as it is the commonest non-communicable disease and the commonest cause of premature death. It is preventable, treatable and the progress is stoppable. At the core of its management are the fundamental pillars of wellbeing: Diet, exercise and sleep.

Most of this disease is asymptomatic and so it must be screened for. Its diagnosis is based on numbers (see Figure 1). Certain nuances exist, such as ranges unique to age, ethnicity and gender.

DEFINITIONS
Due to the multi-complexities, numerous international groups have brought up their own definitions for the metabolic syndrome. This makes the diagnosis a bit confusing, and so it can be difficult to interpret various studies and trials.

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Ref: 1. Impact Rx. Script Data – October 2015. 2. Duomine 15 mg & 30 mg Capsule; Sustained action ion-exchange resin beads granules, available as capsules containing phentermine 15 mg and 36 mg, A11.3. Anorexigenics: 15 mg: B657; 30 mg: B658 [Act 101/1965]; iNova Pharmaceuticals (Pty) Limited. Co. Reg. No. 1952/1001640/07, 15e Riley Road, Bedfordview. Tel +27 11 087 0000. www.inovapharma.co.za For further information is available on request from iNova Pharmaceuticals. IN2248/16.

It is the most rapidly expanding disease in adults over the age of 45 years with a prevalence of up to 60%

Figure 1

60% adults affected
85% type 2 diabetes mellitus

A small loss of 5% body weight dramatic decrease in risk

HDL-c
-<1 men
-<1.2 women

Triglycerides-<1.7

Fasting blood glucose = 5.1 mmol/l

Abnormal circumference
Men=<94cm
Women=<88cm

Blood pressure=<130/85mmHg

At least 3/5 criteria

Dr Gary Hudson, Physician in private practice, Randburg
1. **International Diabetic Foundation.** This is the simplest definition. If you are obese BMI ≥30kg/m² then you have the metabolic syndrome.

2. **National Cholesterol Education Program** has strict criteria:
   - BMI ≥30kg/m²
   - Raised abdominal circumference 102cm in males and 88cm in females. In Asians 90cm males and 80cm females
   - Triglycerides (TG) >1.7mmol/L fasting or on treatment
   - HDL <0.9mmol/L in men and <1.0mmol/L in women or on therapy
   - SBP>130mmHg and DBP >85mmHg or on treatment
   - Fasting glucose concentration >5.6 mmol/L or on treatment.
   - Type 2 diabetes mellitus or on treatment
   - Impaired glucose tolerance
   - Abdominal : hip ratio >0.9 in men and >0.85 in women
   - SBP>130mmHg and DBP >85mmHg or on treatment
   - Micro-albuminuria >20µg/minute.
   These criteria are very strict, which is why so many people fulfil the criteria and the prevalence rate is so high. Notice that they take neither total cholesterol nor LDL cholesterol into account. The latter makes up the guidelines for target levels when treating dyslipidaemia, not HDL cholesterol.

3. **The World Health Organization’s** definition has a BMI >26, as well as:
   - Type 2 diabetes mellitus or on treatment
   - Impaired glucose tolerance
   - Abdominal : hip ratio >0.9 in men and >0.85 in women
   - TG >1.7mmol/L
   - HDL <0.9 mmol/L in men and <1.0mmol/L in women or on treatment
   - BP >=140/90mmHg or on therapy
   - Micro-albuminuria >20µg/minute.
   The criteria are more precise and include target organ damage, as measured by micro-albuminuria namely left ventricular dysfunction and renal dysfunction. It is also a prognostic marker.

4. **The European Group for Insulin Resistance measures** homeostatic model assessment (HOMA) >2 or quantitative insulin sensitivity check index (Quicki) index <0.35, plus two other criteria:
   - Waist circumference >94cm in men and >80cm in women
   - TG >2mmol/L or on therapy
   - HDL <1.0mmol/L or on therapy
   - BP >=140/90mmHg or on therapy
   - Fasting glucose >6.1mmol/L or on therapy.
   This measurement puts insulin resistance at the pathophysiologic core of the metabolic syndrome.

**AETIOLOGY**
Recent further associations are hyperuricaemia, non-alcoholic fatty liver disease, erectile dysfunction, polycystic ovarian syndrome in women, acanthosis nigricans, obstructive sleep apnoea, malignancies and even cognitive decline.

Obesity is one of the major aetiological risk factors. However, it is not necessarily generalised subcutaneous fat but the maldistribution to abdominal fat. Also termed ‘visceral ectopic fat’, the so-called apple-shape physique.

The maldistribution is the measurement of the abdominal girth measured with the person standing, at expiration, half way between the last ribs and the iliac crest. It is not necessarily the widest abdominal point - it is more supra umbilical.

More accurate measurement correlating with the Met-S, no matter age, gender or race is the abdominal:height ratio, which should be <=0.5.

**CAN A NON-OBESE PERSON HAVE Met-S?**
With a BMI over 25kg/m² it is in the pre-obesity overweight range, and three of five criteria are only needed for the diagnosis. There is a phenotype called thin outside, fat inside (TOFI).

**DO ALL OBESE HAVE Met-S?**
Obesity is the commonest association, up to 85%, but a person can be fat and fit. This phenotype is called fat outside, thin inside (FOTI).

The disease is progressive, so ultimately most would develop the syndrome.

**BACKGROUND**
The Met-S is a 20th Century, modern disease entity.

- **1947 Dr J Vague** recognised the association between upper body...
fat distribution with diabetes, hypertension, ischaemic heart disease, gout and renal calculi.

• 1955 Avegado and Crepaldi described six patients with moderate obesity, diabetes mellitus and dyslipidaemia, who all improved on a low calorie, low carbohydrate diet.

• 1977 Dr Haller coined the phrase ‘metabolic syndrome’ when describing the association between obesity, diabetes mellitus, dyslipidaemia, hyper-uricaemia and fatty liver as risks for ischaemic heart disease.

• 1977 Dr Singer added hypertension to the criteria.

• 1978 Dr Phelps stated that myocardial infarction was associated with glucose intolerance, hyper-insulinaemia, hypercholesterolemia, hypertriglyceridemia, hormone therapy, obesity and ageing, due to sex hormone abnormalities.

• 1988 Dr Gerald Reaven at the annual Banting lecture proposed the main pathophysiological factor was insulin resistance and coined the term Syndrome X.

WHO IS AT RISK?
1. Those over 45 years of age
2. A positive family history
3. Pregnancy, malnutrition and birth weight abnormalities over two generations
4. Genetics - 25% patients with >90 alleles with mainly single nucleotide polymorphisms. Measurable are FTO, PPAR, TC77L2. One needs the gene, foetal stresses and environmental factors to develop the metabolic syndrome phenotype.
5. Centro-pedal obesity
6. Sedentary lifestyle
7. Sleep disturbances
8. Inflammatory diseases especially psoriasis
9. Psychiatric diseases, notably schizophrenia and bipolar depression
10. HIV and other forms of lipodystrophy
12. Latrogenic: Due to highly active antiretroviral therapy, anti-epileptics, especially valproic acid, antidepressants, growth hormone, hormone replacement therapy, corticosteroids.

The recent question posed is: Can hypothyroidism cause the metabolic syndrome? Well, hypothyroidism causes weight gain and dyslipidaemic profile. In the study by Swetha K et al, none of the hypothyroidic patients fulfilled three out of five of the criteria as the lipid profile is different, glucose profile is normal and there is no direct association with hypertension.

The seven deadly sins are called the seven S’s of the metabolic syndrome:

1. Sugar
2. Sodas
3. Spirits
4. Salt
5. Sleep disturbances
6. Sitting
7. Sadness

MANIFESTATIONS OF THE METABOLIC SYNDROME

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<thead>
<tr>
<th>SURNAME</th>
<th>INITIALS</th>
<th>YOUR HPCSA REGISTRATION NO.</th>
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Address: ____________________________
Telephone: __________ Email: __________ Fax: __________

1. Choose the incorrect statement:
A. There are multiple definitions of the metabolic syndrome
B. There is a single cause
C. There are numerous clinical presentations
D. None of the above.

2. Choose the incorrect statement. Metabolic Syndrome:
A. Is the commonest non-communicable disease
B. Is the commonest cause of premature death
C. Is it non-preventable
D. Is treatable.

3. Choose the incorrect statement:
A. Progress of Met-S is unstoppable
B. Diet is key to its management
C. Exercise is key to its management
D. Sleep is key to its management.

4. Choose the incorrect option:
A. It is the most rapidly expanding disease in adults over the age of 40
B. It has a prevalence of up to 60% in adults over 45
C. It rapidly increasing in the paediatric population to over 10%.
D. A & C

5. According to the International Diabetic Foundation:
A. If you are obese BMI ≥10kg/m² then you have the metabolic syndrome.
B. If you are obese BMI ≥15kg/m² then you have the metabolic syndrome.
C. If you are obese BMI ≥20kg/m² then you have the metabolic syndrome.
D. If you are obese BMI ≥25kg/m² then you have the metabolic syndrome.

6. Choose the incorrect option:
A. The National Cholesterol Education Program has strict criteria.
B. LDL cholesterol is taken into account
C. Many people fulfil the criteria
D. Total cholesterol is not taken into account.

7. The WHO’s criteria:
A. Include target organ damage
B. Are more precise than the others
C. Include ventricular dysfunction and renal dysfunction
D. All of the above.

8. Choose the incorrect option. The European Group for Insulin Resistance measures:
A. Homeostatic model assessment >2
B. Quantitative insulin sensitivity check index index <0.35
C. Waist circumference >84cm in men and >70cm in women
D. TG ≥2mmol/L or on therapy.

9. Choose the incorrect option. Recent further associations are:
A. non-alcoholic fatty liver disease
B. Endometriosis
C. polycystic ovarian syndrome
D. erectile dysfunction

10. Choose the incorrect option:
A. The pear-shape physique is associated with the syndrome.
B. Obesity is one of the major aetiological risk factors.
C. Visceral ectopic fat is a greater risk factor than generalised subcutaneous fat.
D. The apple-shape physique is associated with the syndrome.

INSTRUCTIONS: 1. Go to www.medicalchronicle.co.za 2. Click the tab labelled ‘CPD Portal’ on the far right tab near the top of the page. 3. Select the relevant questionnaire from the list and complete the form at http://www.medicalchronicle.co.za/clinical_update Erectile Dysfunction/