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Metabolic syndrome

What is the metabolic syndrome?

Metabolic syndrome refers to the combination of obesity, hypertension, dyslipidaemia and insulin resistance. Metabolic syndrome results in a proinflammatory state. It at least doubles the chance of suffering from cardiovascular disease compared with the normal population. Those with metabolic syndrome have a 5 to 30 times greater chance of developing type 2 [diabetes](#).

The metabolic syndrome is also known as syndrome X. This is not to be confused with the cardiac syndrome X, which refers to angina-like chest pain with normal coronary arteries.

According to the National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATP III) definition, the metabolic syndrome is present if a person has three or more of the five health problems listed in the table below.

1. High blood sugar	<ul style="list-style-type: none"> • Glucose > 5.6mmol/L or >100mg/dL • Current drug treatment for diabetes
2. Reduced high density lipoprotein (HDL), so-called "good" cholesterol	<ul style="list-style-type: none"> • HDL <1.0mmol/L or <40mg/dL (men) • HDL <1.3mmol/L or <50mg/dL (women)
3. High triglycerides	<ul style="list-style-type: none"> • Triglycerides: >1.7mmol/L or 150mg/dL • Current treatment for elevated triglycerides
4. High blood pressure	<ul style="list-style-type: none"> • Blood pressure >130/85 • Current drug treatment for hypertension
5. Abdominal obesity	<ul style="list-style-type: none"> • Waist circumference >102cm (men) • Waist circumference >88 cm (women)

Metabolic syndrome is associated with:

- Raised C-reactive protein (CRP), interleukin 6 (IL-6) and tumour necrosis factor-alpha (TNF α), reflecting inflammation
- Raised fibrinogen or plasminogen activator inhibitor-1, which may result in blood clots
- Fatty liver, which may progress to non-alcoholic cirrhosis
- Gallstones
- Protein in the urine, due to kidney damage
- Elevated uric acid levels from dietary sugars, which may lead to gout
- [Haemochromatosis](#) (iron overload)
- Obstructive sleep apnoea
- [Polycystic ovary syndrome](#)
- Dementia with aging, and cognitive decline in the elderly.

The greater the number of risk factors, the greater the chance of developing heart disease, diabetes, or stroke. The risk for heart disease is also increased by raised high low-density lipoprotein (LDL) cholesterol, so-called "bad" cholesterol, and by smoking, but these factors are not part of metabolic syndrome.

What causes metabolic syndrome?

Important factors contributing to metabolic syndrome include:

- Genetic predisposition
- Aging i.e. men over 45 and post-menopausal women
- Hormonal imbalance
- Physical inactivity
- Excessive carbohydrates in the diet
- Certain medications that contribute to weight increase e.g. antidepressants
- Rarely, congenital [lipodystrophy](#)

It is slightly more common in those that consume an alcohol-free diet.

Metabolic syndrome is present in about 5% of people with normal body weight, 22% of those who are overweight and 60% of those considered obese, so clearly, obesity is a major risk factor for metabolic syndrome.

What does it mean to be insulin resistant?

Insulin is a hormone that transfers glucose (sugar) out of the bloodstream into the muscle, fat and liver cells. It is required to store glucose for future energy needs. Low insulin levels result in raised blood glucose.

Insulin resistance is defined as a subnormal response to insulin, in which the body cells resist its effects. Blood glucose may be high despite normal or increased amounts of insulin. Insulin resistance may be subclinical (where the patient does not have symptoms or signs) or result in overt type 2 diabetes.

There is debate regarding whether insulin resistance is the cause of the metabolic syndrome or a consequence of it.

In the earliest stage, insulin resistance can only be detected with the euglycaemic insulin clamp technique which is considered as the gold standard. This involves measuring insulin-induced glucose uptake whilst the blood glucose concentration is maintained at a steady concentration (via glucose infusion). However, this technique is impractical in everyday clinical practice. Raised blood sugar levels can be detected as insulin resistance increases.

Type 2 diabetes usually appears in adults over the age of 45 years, but may arise earlier in those with metabolic syndrome.

In contrast, type 1 diabetes usually arises in children and young adults. It often results from progressive destruction of insulin-producing cells in the pancreas by antibodies, and is not caused by insulin resistance. It is also associated with genetic factors but is not related to body fat or activity.

Why is waist circumference important?

Abdominal obesity is more associated with metabolic syndrome and cardiovascular problems than accumulated fat in the buttocks and thighs. Hence the "apple-shaped" body is more likely to develop cardiovascular disease than the "pear-shaped" body.

In clinical practice, the waist to hip ratio is used to diagnose abdominal obesity, and appears to be more important than the body mass index (BMI).

Asian Indians have more abdominal fat than caucasians and blacks, due to β 3-adrenergic receptor polymorphism. Women tend to have fat distributed on buttocks and thighs, due to oestrogen. This is protective.

The lipotoxicity theory

Fat stored in the abdominal region is more likely than in other sites to break down into free fatty acids (lipolysis), which get deposited in the liver. These fat cells produce pro-inflammatory cytokines including $\text{TNF}\alpha$, which induce insulin resistance.

Saturated fats, sugars and fast digesting starches (carbohydrates) in the diet increase the blood levels of triglycerides, which induce fat to be laid down. So the most obvious way to prevent metabolic syndrome is to reduce the intake of saturated fats and carbohydrates.

Skin manifestations of the metabolic syndrome

Skin problems are common in patients with metabolic syndrome, associated with obesity, diabetes, hyperlipidaemia and chronic inflammation.

Obesity

Obese patients are prone to rashes in body folds (intertrigo) due to sweating, occlusion, the skin surfaces rubbing together, and inverse psoriasis. Adipose tissue increases the production of male hormones (androgens) and obese patients are also at greater risk of polycystic ovarian syndrome.

Skin infections	<ul style="list-style-type: none"> • Candida albicans • Tinea infections • Erythrasma • Folliculitis, furunculosis
Altered collagen structure and function	<ul style="list-style-type: none"> • Impaired wound healing
Sweating	<ul style="list-style-type: none"> • Hyperhidrosis • Bromhidrosis • Intertrigo
Polycystic ovary syndrome	<ul style="list-style-type: none"> • Acne • Hirsutism • Androgenetic alopecia • Hidradenitis suppurativa
Mechanical factors	<ul style="list-style-type: none"> • Prominent cellulite • Stretch marks (striae distensae) • Lymphoedema • Chronic venous insufficiency and leg ulcers • Corns, calluses and cracked heels
Miscellaneous	<ul style="list-style-type: none"> • Keratosis pilaris • Adiposis dolorosa

Diabetes / insulin resistance

High blood glucose levels result in infections, nerve damage and poor wound healing. Excess insulin causes the skin cells to grow abnormally.

Infections	<ul style="list-style-type: none"> • Bacterial infection • Fungal infection
Nerve damage	<ul style="list-style-type: none"> • Foot ulcers • Thermal burns
Poor wound healing	<ul style="list-style-type: none"> • Diabetic dermopathy • Bullous disease

Circulating growth factors	<ul style="list-style-type: none"> • Acanthosis nigricans • Skin tags • Diabetic thick skin • Scleroedema
Hypertriglyceridaemia	<ul style="list-style-type: none"> • Eruptive xanthomas

Psoriasis

There is a higher prevalence of [psoriasis](#) amongst obese patients than the general population. This is thought to be due to the chronic inflammation associated with metabolic syndrome.

- Cytokines including TNF α promote psoriasis
- Insulin resistance induces growth factors
- Persistent intertrigo may lead to [flexural psoriasis](#)

Obese patients with psoriasis have greater morbidity compared with those of normal weight.

- The psoriasis tends to be more severe
- It is more resistant to treatment
- Sweating makes the plaques more uncomfortable
- Treatment expenses are greater
- Ointments may be difficult to apply
- [Phototherapy](#) is more likely to result in burns as the lamps are closer to the skin surface

Weight loss and medications for diabetes have been shown to improve psoriasis in these patients.

Why is it important to treat the metabolic syndrome?

Early treatment of metabolic syndrome reduces the risk of developing type 2 diabetes and/or cardiovascular disease.

If type 2 diabetes and/or cardiovascular disease have already developed, aggressive lifestyle modifications improve the outlook.

How is metabolic syndrome treated?

The first line treatment is change of lifestyle but drug treatment is frequently required.

Lifestyle changes

Lifestyle changes are required lifelong. They may include:

- Low calorie diet (800–1200kcal/day) to reduce weight and achieve desirable weight (BMI less than 25 kg/m²)
- Healthy eating habits: low intake of saturated fat, trans fat and cholesterol
- Physical activity: at least 30 minutes of moderate–intensity activity on most days of the week
- Stopping smoking

A healthy weight loss is 0.5kg to 1.0kg a week. Amounts greater than this often involves loss of body water instead of fat. A dietician is important to provide advice on regular meal times, the avoidance of snacking, reducing portion size and identifying foods that are high in energy. Fad diets are generally avoided as they work in the short term but lack the compliance for the long term.

A detailed discussion of diet therapies, pros and cons of various diets etc. is beyond the scope of this article. However, there is now a trend toward the use of a Mediterranean diet – one that is rich in “good” fats (olive oil) and contains a reasonable amount of carbohydrates and proteins (such as from fish and chicken).

The Mediterranean diet is palatable and easily sustained. In addition, recent studies have shown that when compared to a low fat diet, people on the Mediterranean diet have a greater decrease in body weight, and also had greater improvements in blood pressure, cholesterol levels, and other markers of heart disease.

Exercise has been shown to be of benefit regardless of whether weight loss is achieved or not.

- Lowered blood pressure
- Reduced total cholesterol and improved LDL/HDL cholesterol ratio
- Lowered triglyceride levels
- Improved insulin sensitivity

The aim is to increase energy expenditure. This can be by avoiding sitting down (less television) as well as by deliberate visits to a personal trainer at a gym, or by walking, running or participating in sports.

Drug treatment

Drug treatment may include:

- Statins to raise HDL and reduce triglyceride and LDL cholesterol levels
- Diuretics and ACE inhibitors to reduce blood pressure below 130/80
- Antidiabetic agents to reduce glucose levels
- Drugs to assist with weight loss.

The aim of prescribing cholesterol lowering agents is to primarily to reduce the LDL cholesterol, but lower triglycerides and higher HDL cholesterol are expected benefits as well.

ACE inhibitors have also been shown to reduce the levels of insulin resistance and actually deter the development of type 2 diabetes.

Metformin and thiazolidinediones (pioglitazone, rosiglitazone) are used to reduce blood sugar in type 2 diabetes. They also decrease insulin resistance and may prevent the onset of diabetes in people with metabolic syndrome although their use for this is controversial. Thiazolidinediones also reduce the thickness of the walls of the carotid arteries, reducing the risk of heart disease.

The role of vitamin D

[Vitamin D](#) normally helps maintain adequate insulin levels. It also reduces cell proliferation (particularly in the skin) and has immunosuppressive effects.

Vitamin D deficiency is common in obese individuals and in those with metabolic syndrome. This is because fat retains vitamin D and because obese patients tend to have less sun exposure. In these patients, vitamin D supplements may be helpful.

- Insulin levels may increase, reducing blood sugar in diabetics
- HDL cholesterol levels may increase
- Blood pressure may reduce
- Heart disease may improve
- Psoriasis may improve

Surgery

Surgery such as laparoscopic banding of the stomach may be offered to well-motivated morbidly obese patients with a BMI >40 kg/m². These patient are at high risk of surgical complications. However, weight loss may be dramatic after surgery resulting in marked improvement in diabetes, hypertension, hyperlipidemia, and obstructive sleep apnoea.

Cosmetic surgery including tummy tuck (abdominoplasty) and [liposuction](#) may be performed to reduce sagging skin and achieve a smooth, firm contour. Best results are seen in those who are in good health and have reached target weight. Unfortunately, removal of large amounts of abdominal fat does not seem to improve insulin sensitivity, blood pressure, or cholesterol.

Maintaining weight loss

The final step of treatment involves maintenance of weight loss. See your health professional(s) regularly.

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Draft 12 May 2008

Related information

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On DermNet NZ:

- [Diabetes](#)

Other websites:

- [What Is Metabolic Syndrome?](#) National Heart Lung and Blood Institute

Books about skin diseases:

See the [DermNet NZ bookstore](#)

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DermNet does not provide an on-line consultation service.

If you have any concerns with your skin or its treatment, see a [dermatologist](#) for advice.

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