

The Major Source of All Illnesses

Insulin Resistance Syndrome

Insulin is a major hormone that is required to develop proper tissues, to maintain glucose homeostasis, and to also increase hepatic and adipose lipid synthesis in order to affect lipid metabolism.

Insulin Resistance Syndrome (IRS) is decreased cellular sensitivity to insulin, and it directly affects various cells, organs, and a specific metabolic pathway. IRS is also associated with **inflammation** in the body and eventually leads to the Metabolic Syndrome.

As a result, IRS in muscles causes a reduced glucose process from the bloodstream, and IRS in liver causes increased glucose production. Impairment of insulin secretion by pancreatic beta cells is a critical element of the metabolic syndrome that leads to a diabetic condition due to defective insulin secretion and timing of the insulin response to glucose.

Data from Corona G, Monami M, Rastrelli G, et al. Testosterone and metabolic syndrome: a meta-analysis study. *J Sex Med.* 2011;8:272-283 and Reaven G. Metabolic syndrome: pathophysiology and implications for management of cardiovascular disease. *Circulation.* 2002;106:286-288.

Some Degree of Glucose Intolerance

- Impaired fasting glucose
- Impaired glucose tolerance

Abnormal Uric Acid Metabolism

- ↑ Plasma uric acid concentration
- ↓ Renal uric acid clearance

Dyslipidemia

- ↑ Triglycerides
- ↓ High-density lipoprotein cholesterol
- ↓ Low-density lipoprotein particle diameter
- ↑ Postprandial lipemia

Hemodynamic Changes

- ↑ Sympathetic nervous system activity
- ↑ Renal sodium retention
- ↑ Blood pressure (50% of patients with hypertension have insulin resistance)

Hemostatic Changes

- ↑ Plasminogen activator inhibitor-1
- ↑ Fibrinogen

Endothelial Dysfunction

- ↑ Mononuclear cell adhesion
- ↑ Plasma concentration of cellular adhesion molecules
- ↑ Plasma concentration of asymmetric dimethyl arginine
- ↓ Endothelial-dependent vasodilatation

Reproductive

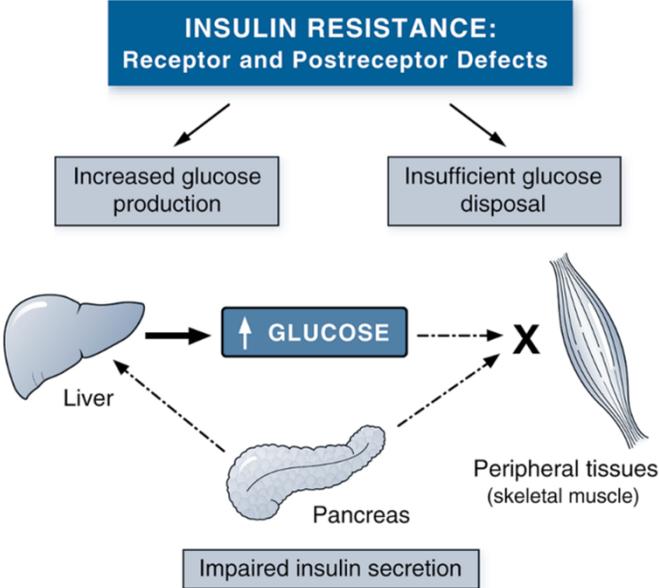
- Polycystic ovarian syndrome
- Low testosterone in men

Abnormalities Associated With Insulin Resistance Syndrome

Metabolic Syndrome includes several symptoms such as atherosclerosis, type 2 diabetes mellitus (DM), elevated fasting glucose, elevated triglycerides, reduced high-density lipoprotein (HDL) cholesterol, hypertension, and central obesity (increased waist circumference).

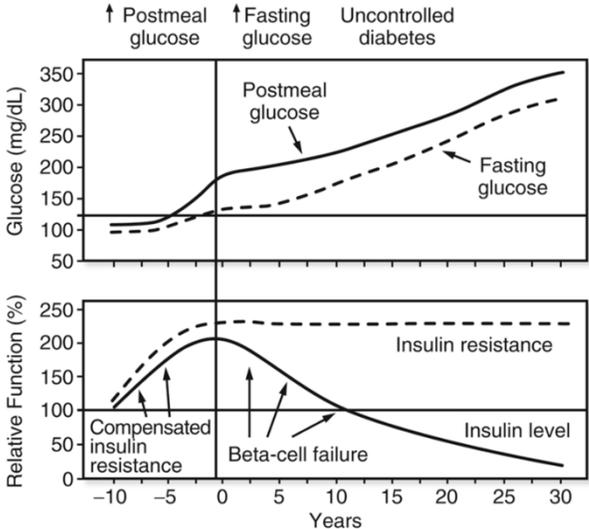
Especially visceral fat (fat inside the belly) has a great role of putting metabolic, endocrine, and even immune functions at risk, increasing the risk of type 2 DM and cardiovascular disease, which is the number one cause of death.

Sites of the Three Major Pathogenic Defects That Lead to Type 2 Diabetes Mellitus.



In fact, scientists have found out that impaired fatty acid metabolism causes abnormal build-up of fat in muscle tissues, the liver, and other organs. **Lipo-toxicity**, associated with increased plasma free fatty acid levels, is a symbol of IRS. Consequently, these lipids are correlated with not only an unnecessary accumulation but also increased **fat oxidation** with further damage to the cells.

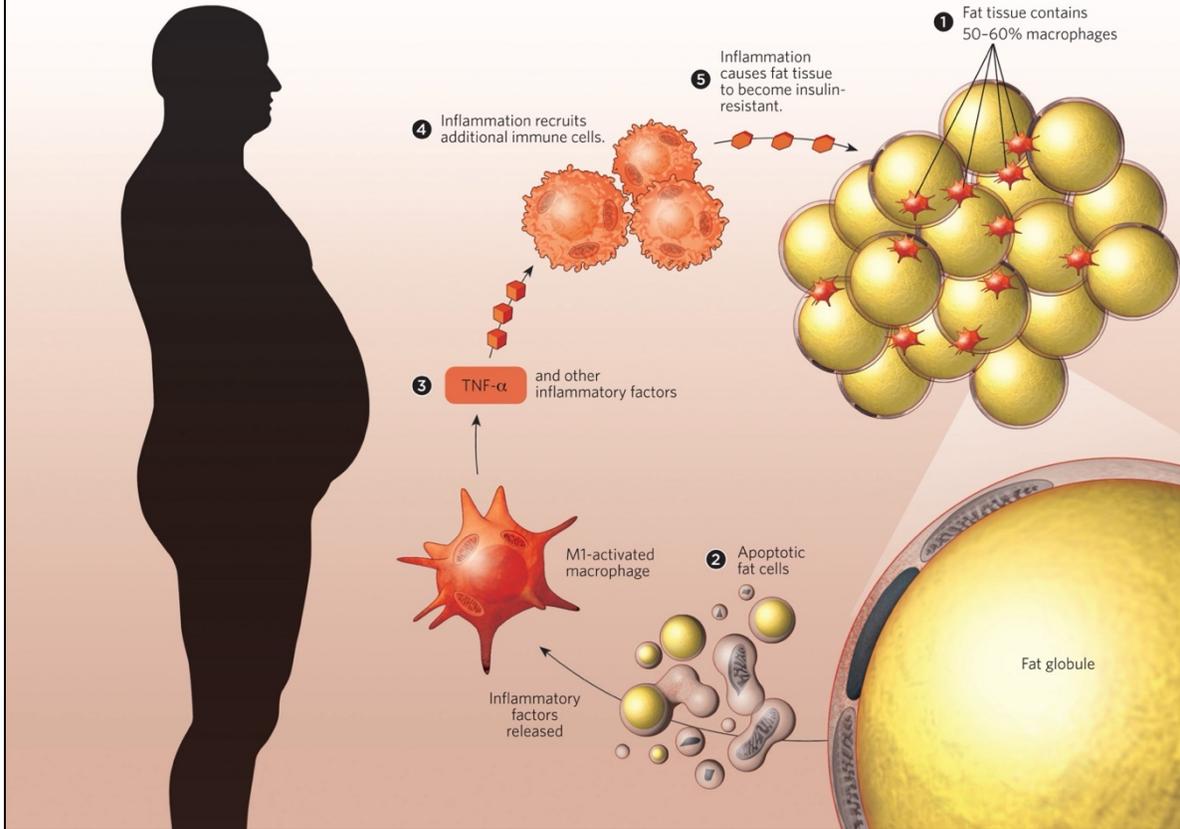
Chronic low-grade inflammation, which eventually causes **chronic fatigue** due to the immune response in the whole body, has also been posited to have a central pathogenic role in IRS. Research has shown that proinflammatory cytokines and acute-phase reactants are associated with many features of the metabolic syndrome.



Natural history of diabetes, depicting rising blood glucose levels with progressive beta cell dysfunction

ADIPOSE TISSUE METABOLISM IN OBESE INDIVIDUALS

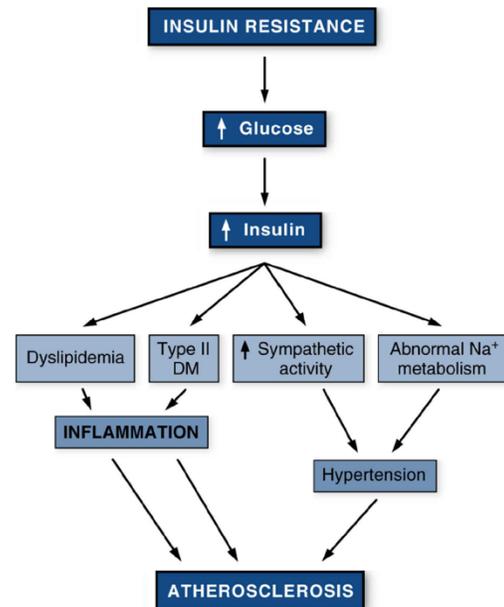
The adipose cells in obese individuals are both greater in number and size than in lean individuals, and the tissue contains a much higher percentage of macrophages **1**. As a result of storing excessive amounts of fat, the stressed adipose cells release inflammation-inducing factors and undergo apoptosis **2**. Both outcomes activate macrophages in a traditional M1 inflammatory state **3** in which they release tumor necrosis factor- α (TNF- α), which recruits and activates additional immune cells to the site **4**. This low level sustained inflammation causes tissues to become resistant to insulin **5**, the first step in developing diabetes.



The Scientist Magazine (Justin Odegaard and Ajay Chawla Dec 12, 2012)

Comorbidities of the Metabolic Syndrome

1. Alzheimer's disease
2. Atrial fibrillation
3. Baldness
4. Breast cancer
5. Cardiovascular risk
6. Chronic fatigue syndrome
7. Chronic kidney disease
8. Cognitive impairment
9. Colorectal cancer (men)
10. Coronary artery disease
11. Depression
12. Endometrial cancer
13. Erectile dysfunction
14. Gestational diabetes
15. Gout
16. Hypothyroid and subclinical hypothyroidism
17. Kidney stones
18. Nonalcoholic fatty liver disease
19. Pancreatic cancer
20. Peripheral artery disease
21. Psoriasis
22. Sleep apnea
23. Thyroid cancer



Summary of Insulin Resistance and Its Effects (David Rakel's Integrative Medicine, 4th ed.)

Therefore, IRS manifests as a reduction in insulin-stimulated glycogen synthesis resulting from decreased glucose transport. Once this occurs, lipid accumulates in many cells, most importantly in the liver and pancreas, causing **oxidative stress** and harmful changes to cellular metabolism. These multiple defects in insulin signaling trigger downstream impaired glucose metabolism in most tissues. That is why IRS is known as ***the major source of all illnesses and might be a key to the aging process.***

Obviously, environmental toxins such as the organic compound bisphenol A (BPA) in plastic, persistent organic pollutants (POPs), air pollution, and inorganic arsenic either trigger or make IRS conditions worse.

Although many supplements or medications are available in the market to improve IRS, lifestyle intervention offers the most promising prevention and management of both IRS and the metabolic syndrome.

Not surprisingly, a body has natural healing mechanisms, and a muscular system is one of them on its own. Muscles release very special proteins, called myokines. A myokine is one of several hundred cytokines or other small proteins and proteoglycan peptides that are produced and released by muscle cells in response to muscular contractions. They induce anti-inflammatory and have a profound effect on the immune system, increasing basal metabolic rate to let the body consume more fat as an energy source. Muscles tend to diminish as one's age is getting advanced, so ones must do their best to keep a decent amount of muscles ***minimizing fat*** in their body.

Recommendable exercises are push-ups(pectoralis muscles), sit-ups(core muscles), and squats(quadriceps muscles), which can be done without any equipment. To build up muscles, one must reach for the submaximal point. For instance of squatting, when reaching at the point of total exhaustion, just doing it one more time will make microscopic lesions in the muscles. Thus, alternating the regions of exercise every other day gives time for muscles to build up while they are healed.

Most of all, one who has potential IRS must ***simplify*** his or her diet. Medical professionals say that over 70% of illnesses are directly caused by food. Some foods actually cause inflammation - processed carbohydrates (flour), meat, eggs, trans fat, dairy products, etc. ***Simple diet refers to anti-inflammatory, anti-oxidant, and low-protein food*** - brown rice, veggies, and fruits. ***Changing one's diet will change one's life!***

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