

The evidence is showing that obesity, diabetes, alzheimer's (type 3 diabetes) and chronic and degenerative diseases, including cancer, are related to insulin resistance by predicting a variety of metabolic and age-related diseases. Insulin resistance defines an impairment in the biological response to insulin stimulation of target tissues, mainly the liver, muscles, adipose tissue and brain. The inability to carry out glucose disposal results in increased -cell insulin production and hyperinsulinemia. IR affects physiology in many ways, causing hyperglycemia, hypertension, dyslipidemia, visceral adiposity, hyperuricemia, elevated inflammatory markers, and endothelial dysfunction.

If it persists over time, it can lead to the development of metabolic syndrome, NAFLD, cardiovascular diseases (CVD), Alzheimer's disease (AD) and, more commonly, when cells cannot keep up and insulin production gradually decreases until stop. diabetes mellitus type 2. Insulin resistance precedes and causes inflammation in adipose tissue. Nutrients such as resveratrol, anthocyanin extracts from purple plants, curcumin or flavonoids play a relevant role in improving insulin resistance at molecular levels.

Calorie restriction is a non-pharmacological intervention known to improve metabolic defects associated with aging, including insulin resistance. miRNA expression levels may represent a predictive tool for aging-related alterations www.mdpi.com/.../208 (2022).---

www.sciencedirect.com/science/article/abs/pii/S1471489221001752 (2022).--- www.mdpi.com/.../4358 (2022).--- www.mdpi.com/.../779 (2023).--- onlinelibrary.wiley.com/.../acel.13919 (2023).---

## juststeve

Gui, we know insulin resistance causes inflammation, along with full blown diabetes. With a body already suffering the soreness, pain and other complications, when trying to exercise on its own temporarily creates discomfort. It's when the inflammation gets backed off and then the exercise discomfort gets scaled back to levels of less concern, unless one over does it. The longer someone is out of shape, the harder it is for them to get off the ground in a positive way. Not impossible but should be kept in mind, as things improve and get better, the benefits grow, and the discomforts are briefer.

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#### stoneharbor

Thanks Gui and Steve for pointing out that IR is not just a disability that effects the efficient utilization of glucose in all our cells, but is a compounding factor in health in that chronic IR leads to all the other disabilities that Gui mentions: all these life threatening degenerative diseases that once initiated, are more difficult to cure than just recovering from insulin resistance. So it's really best to start the recovery from IR way before any degenerative disease starts showing its symptoms. Start this intermittent fasting now, to prevent onset of the degenerative diseases later on in life, or to stop the worsening of any of these conditions such as metabolic syndrome or CVD before they get worse. And while we're at it, fixing our diet and eating window, yes, we better get our exercise routine tuned to optimize our health as Juststeve advises.

Thanks Just and stoneharbor. Yes, insulin resistance, chronic inflation and diseases. In this context, we also consider time-restricted feeding (TRE) as an instrument to combat dysbiosis of the intestinal microbiota that is closely related to metabolic diseases. Many intestinal microorganisms have been identified as being related to obesity. They induce the onset and development of obesity by increasing host energy absorption, increasing central appetite, improving fat storage, contributing to chronic inflammation, and regulating circadian rhythms. One third of the world's population is overweight and approximately 10% are obese.

By 2030, the number of obese people worldwide is expected to reach 1.12 billion. The health risk of obesity has caused widespread concern and has become a major global health problem. Obesity not only manifests itself as changes in appearance, but is also associated with disorders of lipid and glucose metabolism, chronic inflammation, oxidative stress and an increased risk of a variety of diseases, in particular cardiovascular diseases, diabetes and cancer. In this study TRF is positively associated with the richness of the gut microbiome. improving the serum and hepatic lipid profiles of individuals.

In the TRF group, gut microbial richness was significantly improved, with an enrichment of Prevotellaceae and Bacteroideaceae. Time-restricted restriction (TRF) improved circadian gene expression probably by activating sirtuin-1, which TRF can regulate normal hepatic metabolism by modulating liver enzymes.TRF could be a safe remedy for the prevention of metabolic diseases related to dyslipidemia. Dyslipidemia and inflammation associated with obesity predispose to the pathogenesis of atherosclerosis, which is a clinical manifestation of vascular inflammation in metabolic diseases.

Time-restricted feeding reduced the production of proinflammatory cytokines. Reduced microbiome diversity, altered gut microbial activities, and relative abundance of dispersed microbiomes, especially, Bacteroidetes and Firmicutes, are associated with the development of obesity, TRF modulates gut microbiota, which exhibits genetic pathway regulation. Indeed, Sirt1 expression was positively correlated with gut microbiome richness. Serum HDL level showed a trend towards a positive association, while serum albumin has a significant negative correlation with gut microbiome richness. This indicates that TRF reduces the burden of metabolic risk by regulating Sirt1 expression, serum HDL, and albumin levels induced by modulating the gut microbiome.

www.cambridge.org/core/journals/british-journal-of-nutrition/article/e.. microbiome-in-healthymales/A8C3BF83CBE5BF9CAC65ED783FA0FFD2 (2021)

#### stoneharbor

Yes, intermittent fasting is a key method to help the body daily recovery from any glucose load, even if it hasn't been an excess of glucose. The long period of fasting daily, even of 14-16 hours duration, helps glucose get cleared from circulation, even if you happen to be a bit insulin resistant. It's only once the glucose is cleared from circulation AND the insulin levels have dropped that fat cells become able to release free fatty acids to feed cells your cells. This is part of your parasympathetic nervous system's "recovery" protocol that should take place every night to keep your cells' vitality in order.

As long as there is insulin in circulation it is used to actually put triglycerides into fat cells and when this occurs no fat can be taken out of fat storage. So you have two things to gain by doing intermittent fasting: 1) you reduce glucose circulating because insulin is used up to put the glucose into muscle cells, or the liver, or convert it into triglycerides which are put on LDL and sent to fat storage; but also 2) you are using up high levels of insulin that have been circulating and contributing to insulin resistance. But the fasting period allows a time that your body is no longer plagued by "insulin push" and you can recover somewhat from your muscle/liver/fat cells having to "resist" the insulin.

They all get a rest. How wonderful, and suiting for you body to have this rest time each morning, when fat cells can finally release fats to be consumed by the rest of your cells (except your brain which still need glucose or ketones). Here are the 5 ways intermittent fasting affects glucose levels: www.nutrisense.io/.../intermittent-fasting-glucose-levels Notice that effect #5 is that intermittent fasting actually boosts the circadian effectiveness of insulin also! Intermittent fasting is a win/win for not just glucose control in circulation, but also insulin control.

Brilliant contributions, stoneharbor. Consider that time-restricted fasting (TRF) is advisable but not the trend of fasting until midday (omission or delay in breakfast) that is increasingly common in modern society. This eating pattern triggers discordance between endogenous circadian clock rhythms and the feeding/fasting cycle and is associated with a higher incidence of obesity and T2D. Mounting evidence suggests that fasting until midday, also known as "prolonged postabsorptive state," has the potential to cause a deleterious effect on clock gene expression and disrupt body weight regulation. postprandial and overall blood glucose, skeletal muscle protein synthesis and appetite, and may also lead to lower energy expenditure. Finally, the metabolic advantages of transferring more energy, carbohydrates (CH) and proteins to the first hours of the day are discussed. www.mdpi.com/.../7154 (2023)