

COVID & HEALTH: CAN I IMPROVE MY METABOLIC HEALTH AND LOWER MY RISKS?

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Ballantrae Community Zoom presentation 4 Feb 2021

This presentation concerns metabolic health — a far greater global pandemic than COVID-19. Most of us are concerned over the COVID-19 situation and would like to do everything in our power to stay as healthy as possible, while avoiding this awful virus. I wish to be very clear from the beginning of this presentation. I am not giving anyone medical advice, do not put myself forward as an expert on COVID, however I attempt to provide people with good evidence-based science. I welcome respectful debate surrounding the science topics I will present and often learn from others.

Non-specific symptoms that present in some patients with COVID-19

Symptoms that may be seen in patients with COVID-19
▪ Cough
▪ Fever
▪ Myalgias
▪ Headache
▪ Dyspnea (new or worsening over baseline)
▪ Sore throat
▪ Diarrhea
▪ Nausea/vomiting
▪ Anosmia or other smell abnormalities
▪ Ageusia or other taste abnormalities
▪ Rhinorrhea and/or nasal congestion
▪ Chills/rigors
▪ Fatigue
▪ Confusion
▪ Chest pain or pressure

Centers for Disease Control and Prevention. Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19). Available at: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>. UpToDate COVID-19: Adapted 21 Jan 2021

I will not belabor the public health guidelines we hear about daily regarding COVID-19 presentation - here are the latest CDC listings of SYMPTOMS that **MAY** represent COVID. Most significant illness, that leads to hospital admission involves dry cough, fever and shortness of breath.

Of more interest to us today is what are the risk factors that might increase our likelihood of hospital admission and poor outcomes should we get exposed to the virus? With new variants emerging monthly, like Delta, and science telling us COVID is here to stay, what can we do personally with our lifestyle to keep our health optimum?

Comorbidities the CDC classifies as established or possible risk factors for severe COVID-19^[1,2]

Established risk factors

- Cancer
- Chronic kidney disease
- Chronic obstructive pulmonary disease
- Down syndrome
- Immunocompromised state from solid organ transplant
- Obesity (body mass index $\geq 30 \text{ kg/m}^2$)
- Pregnancy
- Serious cardiovascular disease
 - Heart failure
 - Coronary artery disease
 - Cardiomyopathies
- Sickle cell disease
- Smoking
- Type 2 diabetes mellitus

UpToDate COVID Jan 2021

¹Coronavirus Disease 2019 (COVID-19): Who is at Increased Risk for Severe Illness? - People of Any Age with Underlying Medical Conditions. Centers for Disease Control and Prevention. Available at: <http://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html> ; Accessed 21 Jan 2021

²Coronavirus Disease 2019 (COVID-19): Evidence used to update the list of underlying medical conditions that increase a person's risk of severe illness from COVID-19. Centers for Disease Control and Prevention. Available at: <http://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/evidence-table.html> ; Accessed 21 Jan 2021

Here is the UpToDate Jan 2021 data taken from the CDC website for established or possible risk factors for **SEVERE COVID**

So, we must ask ourselves, what diseases, referred to as comorbidities, jump out as risk factors?

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Cancer, kidney disease, obesity, cardiovascular disease and type 2 diabetes (T2D).

The major risk factors are all related to INSULIN RESISTANCE. We will review what this means shortly.

Catalogue no. 45280001

Canadian Vital Statistics Death Database (CVSD)

StatCan COVID-19: Data to Insights for a Better Canada



COVID-19 death comorbidities in Canada

by Kathy O'Brien, Marylène St-Jean, Patricia Wood, Stephanie Willbond,
Owen Phillips, Duncan Currie and Martin Turcotte

Release date: November 16, 2020



Statistics
Canada

Statistique
Canada

Canada

Statistics Canada: Accessed 30 Jan 2021

[*COVID-19 death comorbidities in Canada \(statcan.gc.ca\)](https://www150.statcan.gc.ca/n1/pub/45280001/article/00001)

In Canada, the Canadian Vital Statistics Death Database (CVSD) is the authoritative source for cause of death data, including COVID-19 deaths.

In addition to identifying the underlying cause of death, the CVSD also includes information on the contributing causes and conditions (or comorbidities). In the context of a death caused by COVID-19, these include other diseases or conditions, such as diabetes or hypertension, that likely put those individuals at higher risk of death from COVID-19.

During the first COVID-19 wave in Canada, NINETY (90)% of deaths were associated with at least 1 comorbidity and 54% of deaths were ≥ 85 years of age.

Dementia or Alzheimer's was the #1 comorbidity – 42% of the women and one-third of the men. The % of women appears higher because, as of July 2020, average life expectancy for men was 80 and women 84. We can't do much about severe Alzheimer's but we do know the second most common cause of death in Canada with COVID.

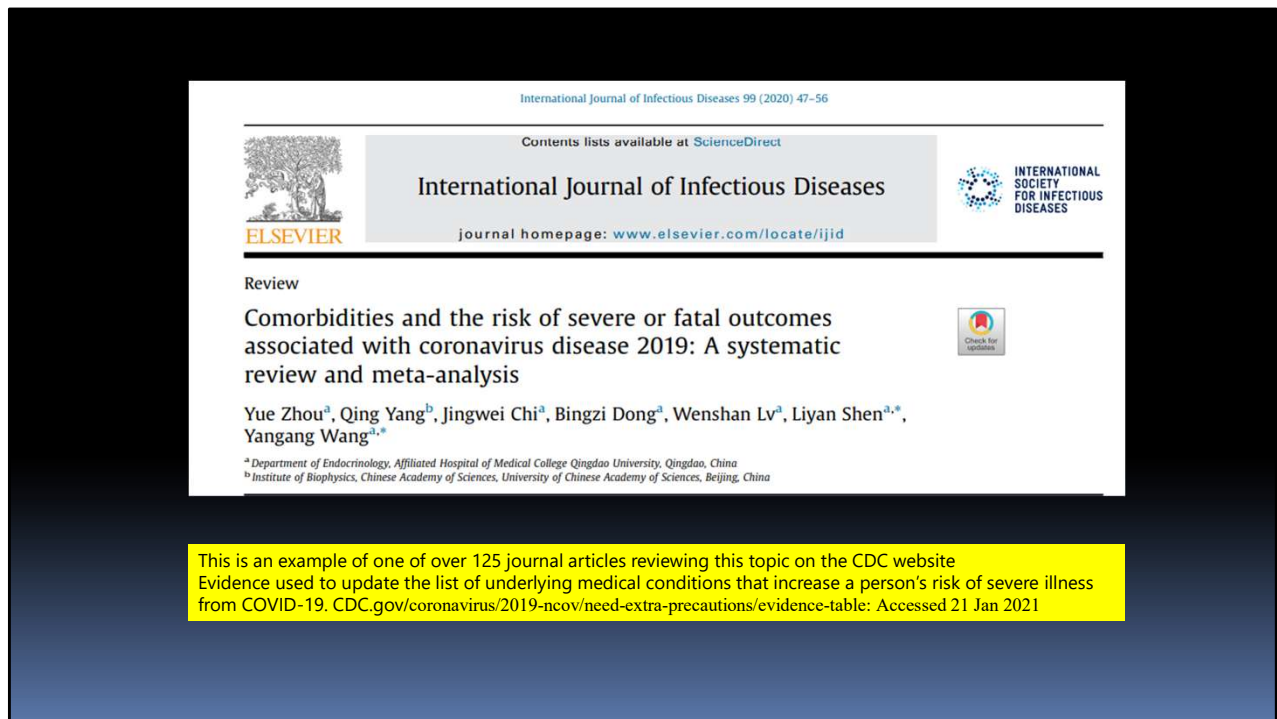
Most of us fear contracting COVID and ending up in an ICU on a ventilator

It is therefore reasonable to appreciate Pneumonia as the 2nd most common comorbidity

Alzheimer's is often referred to as Type 3 diabetes. Could kidney disease, diabetes, cardiovascular diseases, cancer, Parkinson's disease and so many more comorbidities share a common cause?

Let's consider this now

*NEC refers to symptoms, signs and abnormal clinical and laboratory findings,
not elsewhere classified (NEC)*



The following representative study is but one of many regarding comorbidities.

There were over 125 peer-reviewed journal articles on the CDC website as of 21 Jan 2021. Scientists review the quality of evidence and tabulate conditions that increases a person's risk of severe illness from COVID-19

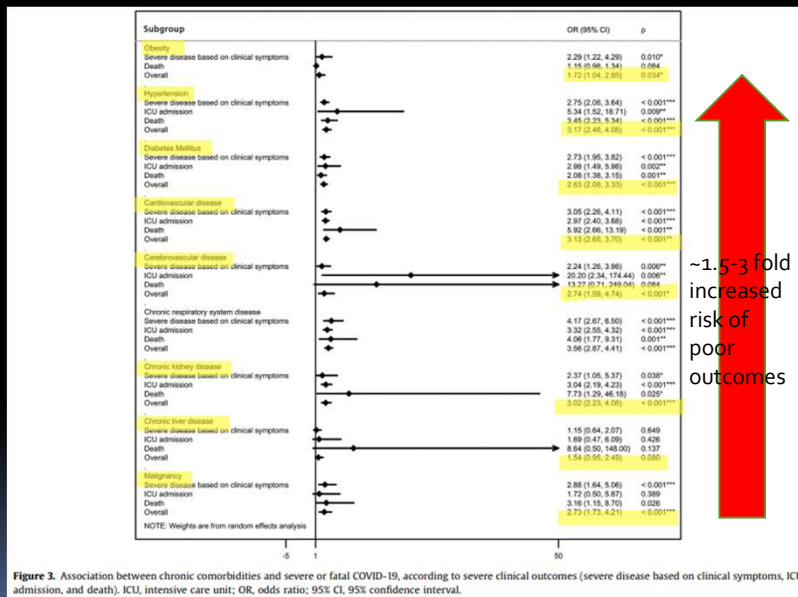


Figure 3. Association between chronic comorbidities and severe or fatal COVID-19, according to severe clinical outcomes (severe disease based on clinical symptoms, ICU admission, and death). ICU, intensive care unit; OR, odds ratio; 95% CI, 95% confidence interval.

Zhou Y et al. Comorbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: A systematic review and meta-analysis. *International Journal of Infectious Diseases*. 2020;99:47–56.

This systematic review and meta-analysis by Zhou et al. demonstrate what many studies highlight. *Click slide x 2*

There is an approximate 1.5-to-3-fold increased risk of poor outcomes with COVID-19 if you have one of these comorbidities. Your risks increase substantially if you have more than 1 disease.

What are we overlooking when discussing public health measures multiple times/day?

What is the elephant in the room?

Diabetes, Hypertension, Cerebrovascular Disease, Obesity, Cancer, Alzheimer's, Cardiovascular disease, Chronic Liver disease, Chronic kidney disease, autoimmune diseases ...

INSULIN RESISTANCE

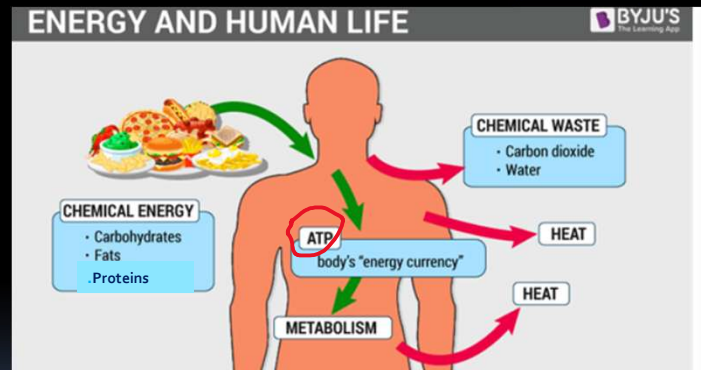
Here is the elephant. So - What is strongly associated with the following: Conditions highlighted in yellow

You might have already guessed the answer but here it is — Yes, you were right it is **INSULIN RESISTANCE**

Table sugar (sucrose) is made up of two 6-carbon molecules attached (fructose + glucose). Biochemistry can be complicated as demonstrated with fructose pathways but we don't need to understand the details to gain an understanding how to improve our chances of gaining better metabolic health.

SO -what is metabolism and metabolic health anyways?

Metabolism: all the chemical processes inside the body allowing us to maintain life. Like money in the bank, what is the “energy currency” of the body?



It's **ATP**
(adenosine
triphosphate)

Adapted from Byju's classes. Metabolism. What is metabolism? Accessed 23 Jan 2021

Metabolism: all the chemical processes inside the body allowing us to maintain life. Like money in the bank, what is the “energy currency” of the body? **It's ATP (Adenosine Triphosphate)**

So, when we eat so-called macros, like fat, carbohydrate and protein, we digest the food, eventually producing ATP through very complex pathways — **ATP is the energy source needed to drive all things in metabolism**

Adapted from Byju's classes. Metabolism. What is metabolism? Accessed 23 Jan 2021

ATP Energy produced allows us to:

- Grow, build new tissue and repair existing structures (Anabolism)
- Eliminate waste
- Move (muscle power)
- Tear things down (Catabolism)
- Fight off disease (Immunity)
- Cellular reproduction (generate new cells or reproduce the species)
- Eliminate sick or diseased cells (Autophagy)

ATP is the energy that allows us to do all things shown in the slide

Now what is this concept of metabolic health people talk about?

Metabolic Health is the absence of metabolic disease

NHANES – What is it?

National Health and Nutrition Examination Survey 2009–2016¹

This is how NHANES defined metabolic health:

1. Waist Circumference (WC) <102/88 cm for men/women (40"/35")
2. Fasting glucose <5.5 mmol/L (100 mg/dl) and HgA1c < 5.7%
3. Blood Pressure < 120 systolic and <80 diastolic
4. Triglycerides (TG) < 1.7mmol/L (150 mg/dl)
5. High-density Lipoprotein cholesterol (HDL) ≥1.0/1.30 mmol/L (men/women) (40/50 mg/dl)

Prevalence of metabolic health is the proportion of people who have optimal levels of all the risk factor variables without any medication

¹Araújo J. Prevalence of Optimal Metabolic Health in American Adults: National Health and Nutrition Examination Survey 2009–2016. *Metabolic Syndrome and Related Disorders*. 2019;17(1):46–52.

To better understand metabolic health let us examine NHANES – The National Health and Nutrition Examination Survey (NHANES) is a major program of the National Center for Health Statistics (NCHS). NCHS is part of the Centers for Disease Control and Prevention (CDC), responsible for producing vital and health statistics for the US. Since 1999, the survey became a continuous program with reports released every 2 years. Because of the complexities of gathering data, doing follow-ups, and analyzing statistics, reports are often completed and released

with data representative of findings from several years in the past.

An excellent example of this is the 2019 publication for NHANES – with Data collected between 2009-2016

**This is how the survey defined metabolic health –
What measurement we hear about so often is
conspicuously absent?**

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LDL Cholesterol is NOT included.
Why? It has very little relevance to metabolic health except for DENSE SMALL LDL particles which are prone to oxidation. It's the oxidation and small size of these particles that is atherogenic (more likely to cause cardiovascular disease)

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Only 12.2% of Americans exhibited "metabolic health" between 2009-2016¹

Insulin Resistance

¹Araújo J. Prevalence of Optimal Metabolic Health in American Adults: National Health and Nutrition Examination Survey 2009–2016. *Metabolic Syndrome and Related Disorders*. 2019;17(1):46–52.

So, How healthy is the American population?

Shockingly only 12.2% met the criteria of good metabolic health which means 88% of the US population is SICK—and that was between 2009-2016. We know it is worse today because all the indices get worse over time. Again what is the elephant in the room — INSULIN RESISTANCE

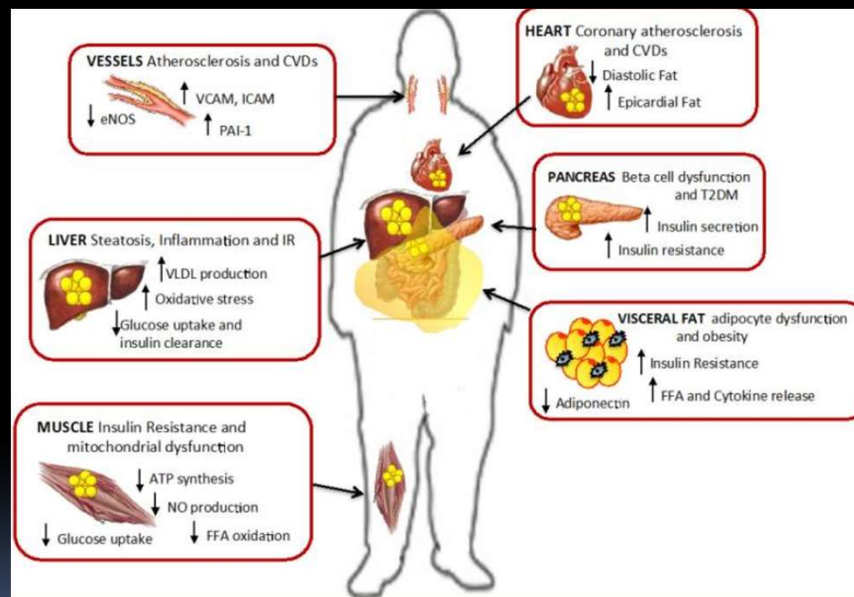


Fig. 6 Ectopic fat accumulation and effect of lipotoxicity. Fat accumulation in non-adipose tissues promotes cell dysfunction, insulin resistance and inflammation in liver, muscle, pancreas and visceral fat. Also, in vessels and heart lipotoxicity leads to increased risk for cardiovascular diseases and atherosclerosis. Saponaro C et al. The subtle balance between Lipolysis and Lipogenesis: A critical Point in Metabolic Homeostasis. *Nutrients* 2015;7(11):9453-9474.

Jiggly **subcutaneous** fat over the hips and thighs is mostly benign. **Ectopic fat** accumulation is **TOXIC**. Fat accumulation in non-adipose tissues promotes cell dysfunction, insulin resistance and inflammation in liver, muscle, pancreas. Also, in vessels and heart, lipotoxicity leads to increased risk for cardiovascular disease and atherosclerosis

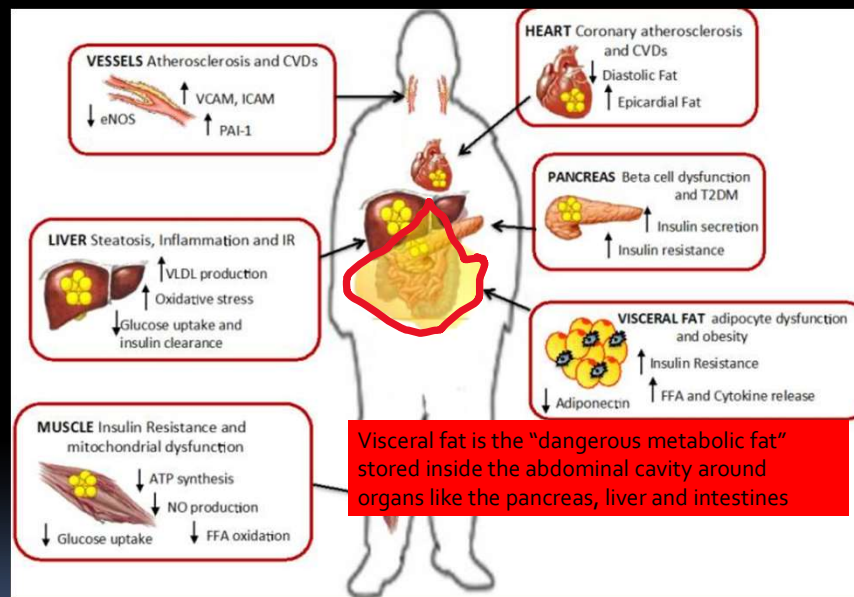
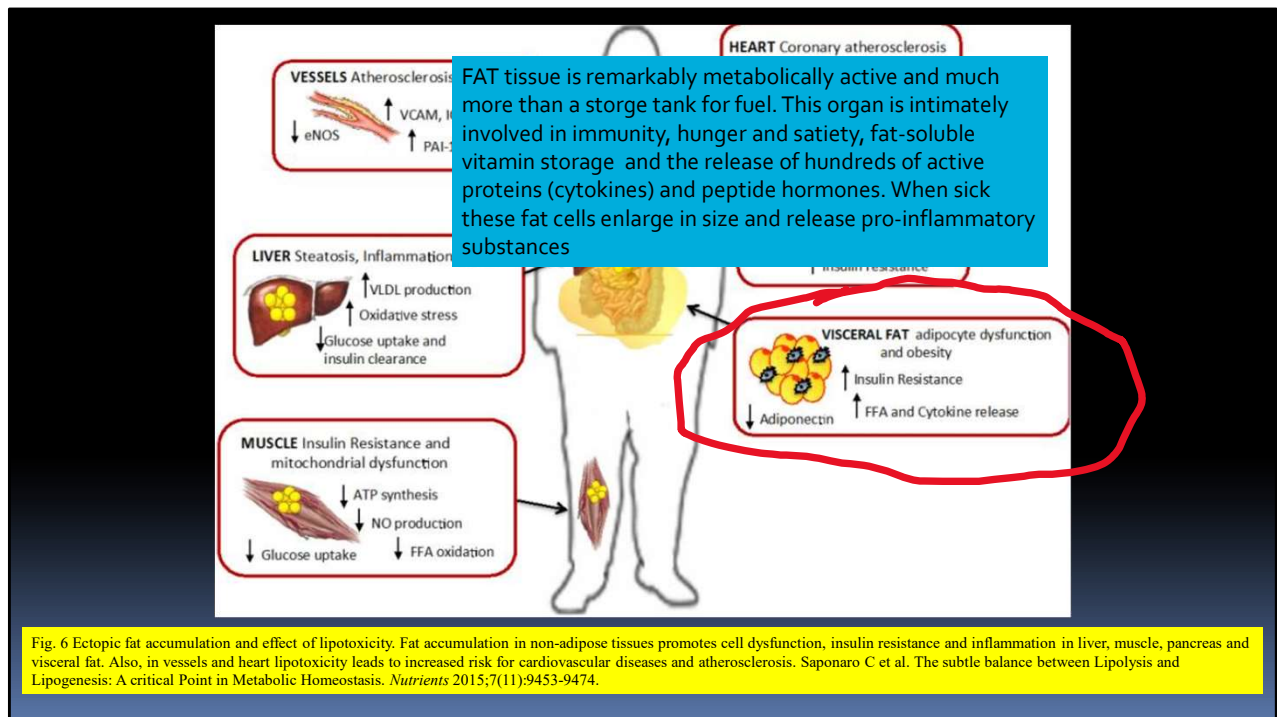


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Visceral fat is the “dangerous metabolic fat” stored inside the abdominal cavity around organs like the pancreas, liver and intestines.



FAT tissue is remarkably metabolically active and much more than a storage tank for fuel. This organ is intimately involved in immunity, hunger and satiety, fat-soluble vitamin storage and the release of hundreds of active proteins (cytokines) and peptide hormones. When sick these fat cells enlarge in size and release pro-inflammatory substances.

Visceral fat in the liver produces “fatty liver” (Non-alcoholic fatty liver disease; NAFLD). Your liver starts producing more fat and exports it to other areas of the body in VLDLs which convert to SMALL DENSE LDLs; strongly associated with cardiovascular disease. The liver is unable to take in glucose normally (Insulin resistance; IR) yet continues to make new glucose. Blood glucose rises, Insulin rises, and IR gets worse. This is a vicious cycle.

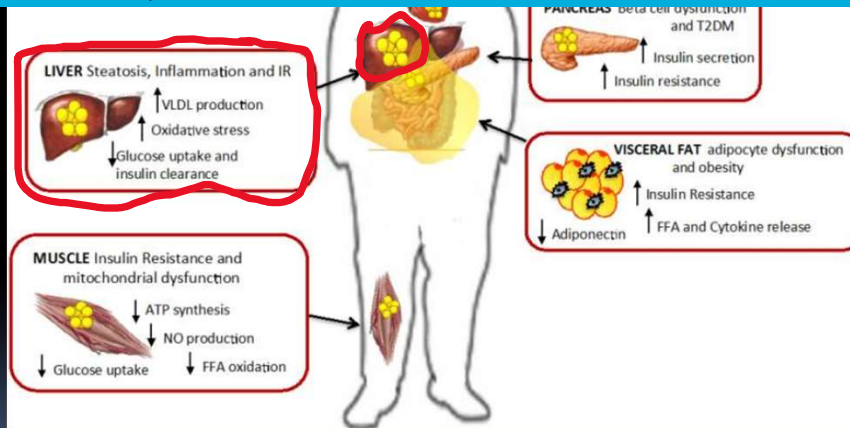


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VLDL (Very-low density lipoproteins); LDL (Low-density lipoproteins)

The pancreas is “stressed out” trying to pump out more insulin to control toxic high blood sugar levels. The higher the insulin rises the greater the insulin resistance becomes in tissues like liver, adipose tissue (fat cells), and muscle. Eventually the motor, or insulin producing pancreatic β -cells burn out; now you have diabetes

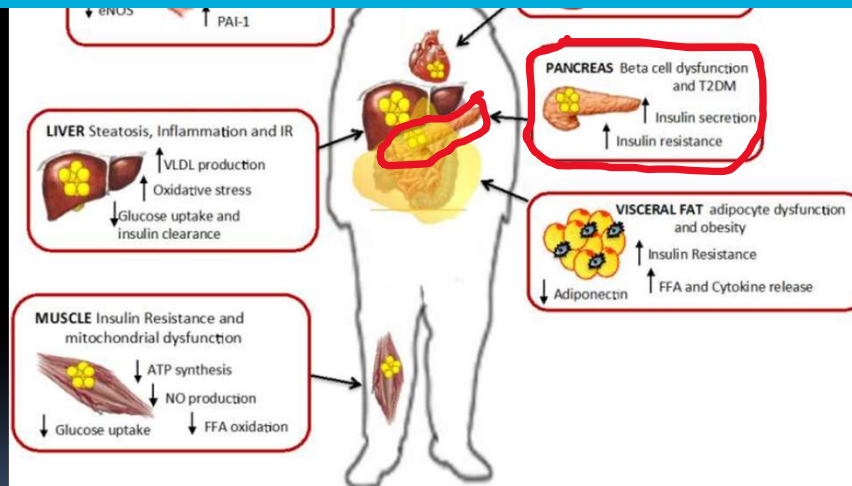
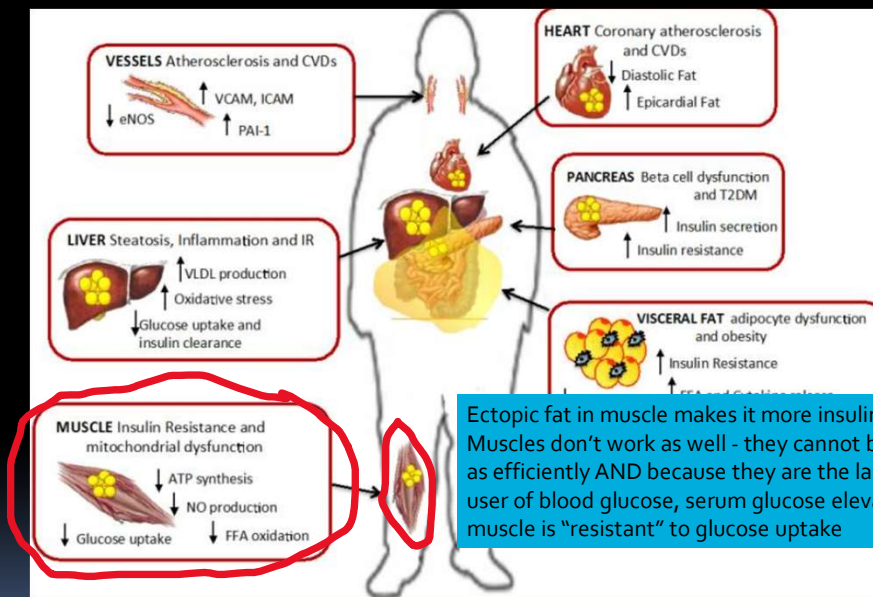
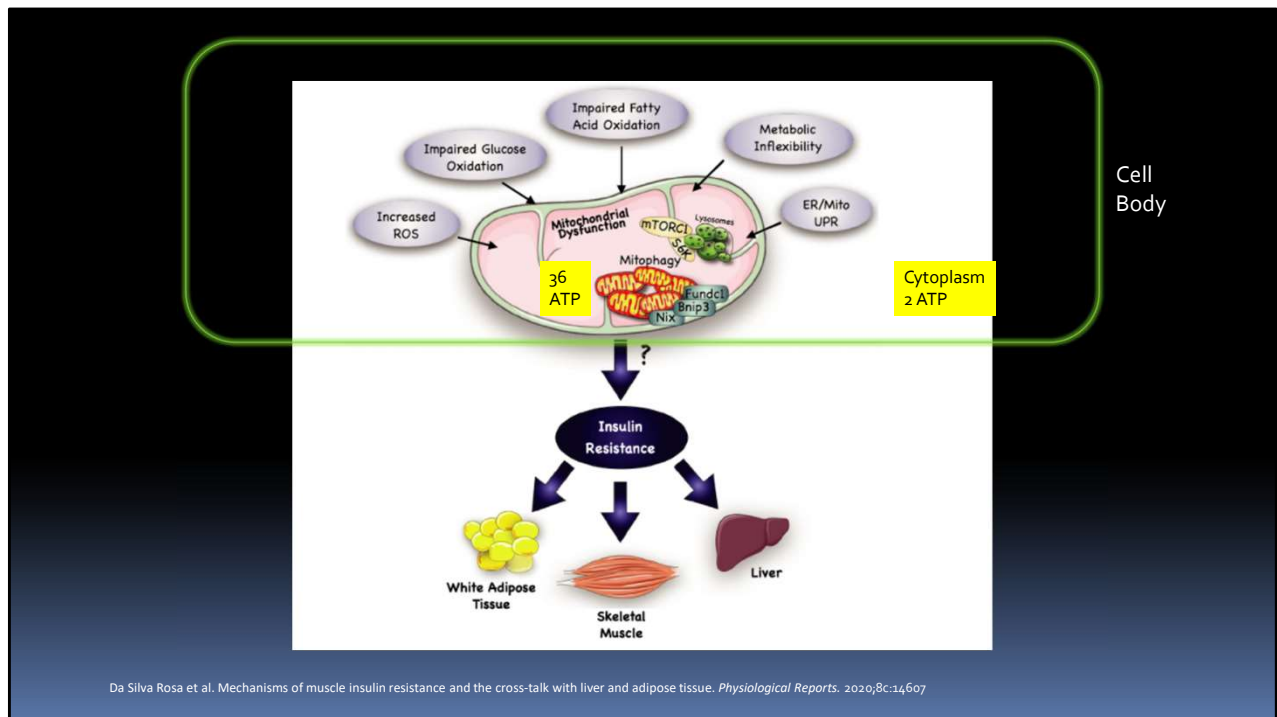


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Ectopic fat in muscle makes it more insulin resistant. Muscles don't work as well - they cannot burn fat for fuel as efficiently AND because they are the largest SINK, or user of blood glucose, serum glucose elevates since the muscle is "resistant" to glucose uptake

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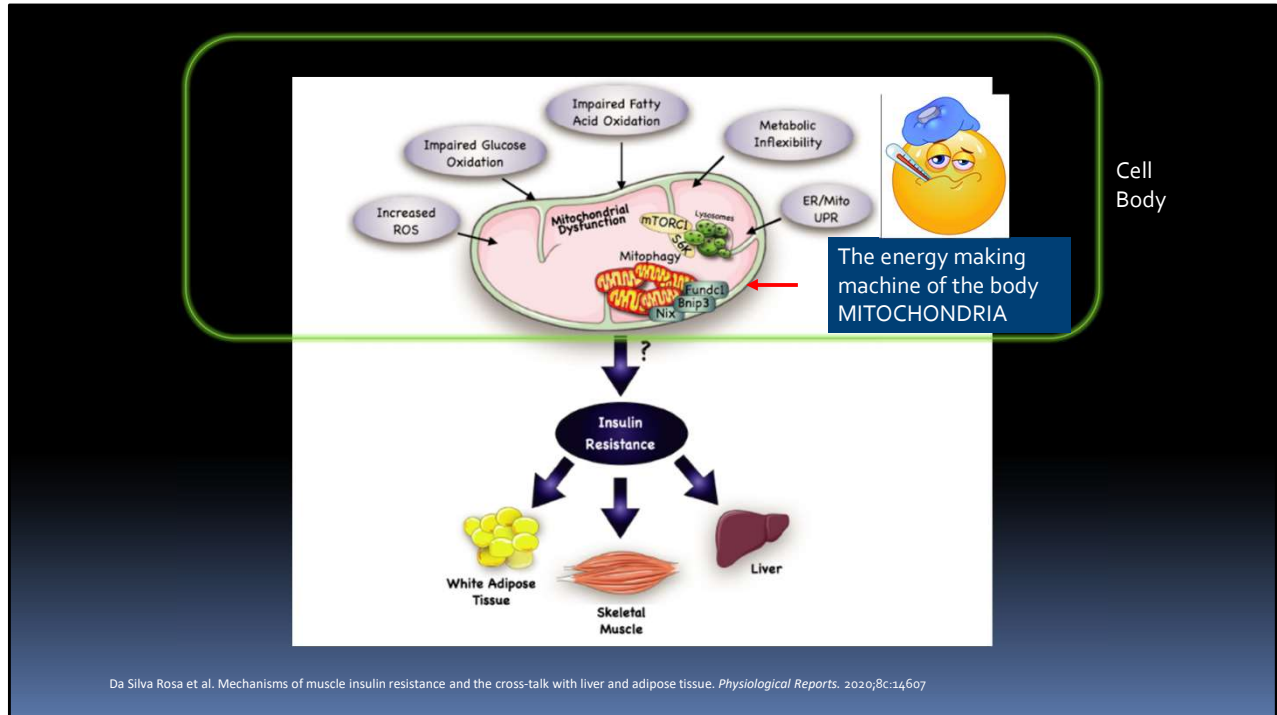
Inside the majority of cells in your body, excluding specialized kidney and red blood cells, are organelles called mitochondria. We can produce our energy currency of the cell, the ATP in 2 ways: without oxygen making 2 packets of energy (ATP) in the fluid within the cell (the cytoplasm) or in the “energy factories” of the cell, the mitochondria, with oxygen required, thereby making 36 ATP – most of the energy we need for metabolism; 95% to be precise.

Fig. 1 Overview of possible mechanisms leading to insulin resistance. Impaired mitochondrial functioning is a suggested mechanism through which insulin resistance develops. Several factors have been implicated in the development of mitochondrial dysfunction. Some of the most reported factors include: (a) an increased production of reactive oxidative species (ROS). ROSs are necessary by-products of mitochondria energy metabolism; however, if their production is not adequately coupled by intracellular antioxidants, then oxidative damage to mitochondrial DNA (mtDNA) can occur. (b) Impaired glucose oxidation and fatty acid oxidation may result from metabolic inflexibility, which is commonly described as an inability to adapt fuel oxidation to fuel availability. Ultimately, these events may lead to both the development of ROS and ectopic lipid accumulation, resulting in mitochondrial damage and removal through mitophagy pathways. Further investigation on

the genes involved in mitophagy (i.e., Bnip3, Nix, Fundc1) may allow the discovery of pathways that explain the correlation between mitochondrial dysfunction and insulin resistance in adipose, hepatic, and skeletal muscle tissue. (c) Endoplasmic Reticulum (ER) stress is also involved in the pathogenesis of mitochondrial dysfunction. Lipotoxicity and glucotoxicity can induce ER stress, which may trigger an adaptive signaling pathway, known as

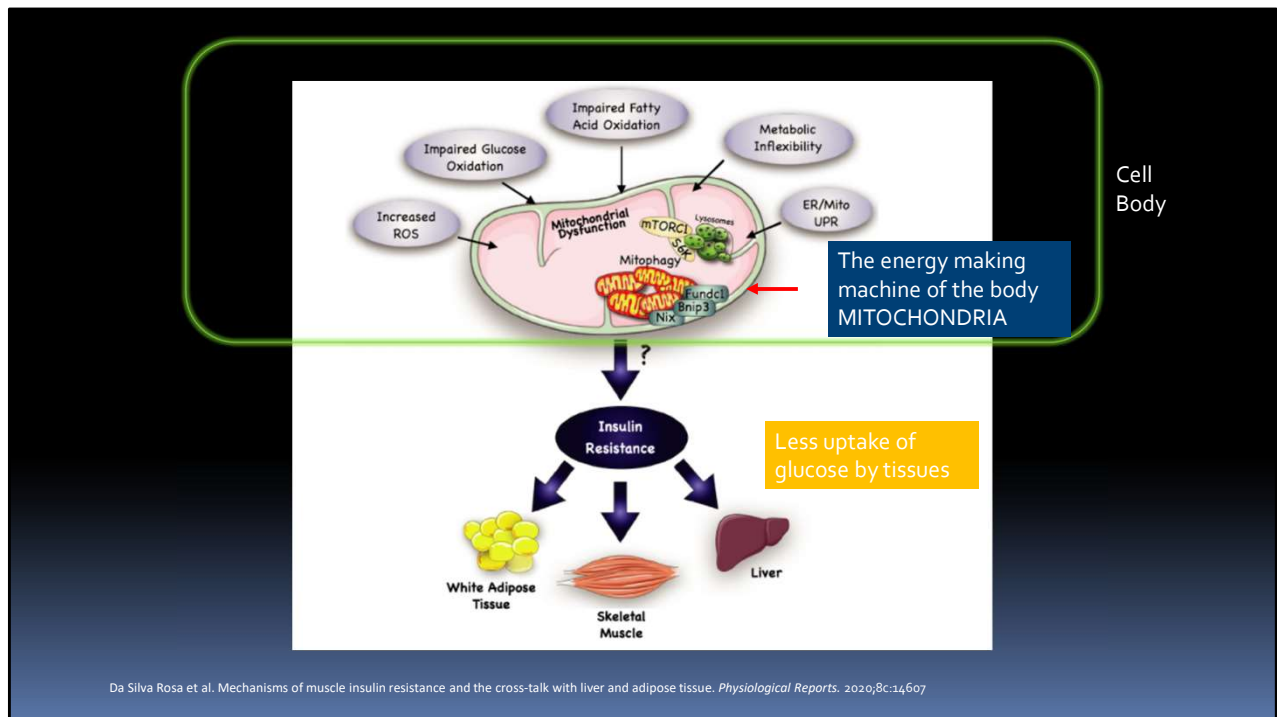
the unfolded protein response (UPR). If ER stress fails to be relieved by this UPR, then this can lead to the provocation of both mitochondrial dependent and independent cell death pathways. Together, the ability of the mitochondria to respond to metabolic disruptions is essential for healthy cellular bioenergetics, and interference with this process may prompt unregulated mitochondrial biogenesis and mitophagy, thus contributing to insulin resistance

Da Silva Rosa et al. Mechanisms of muscle insulin resistance and the cross-talk with liver and adipose tissue. Physiological Reports. 2020;8c:14607

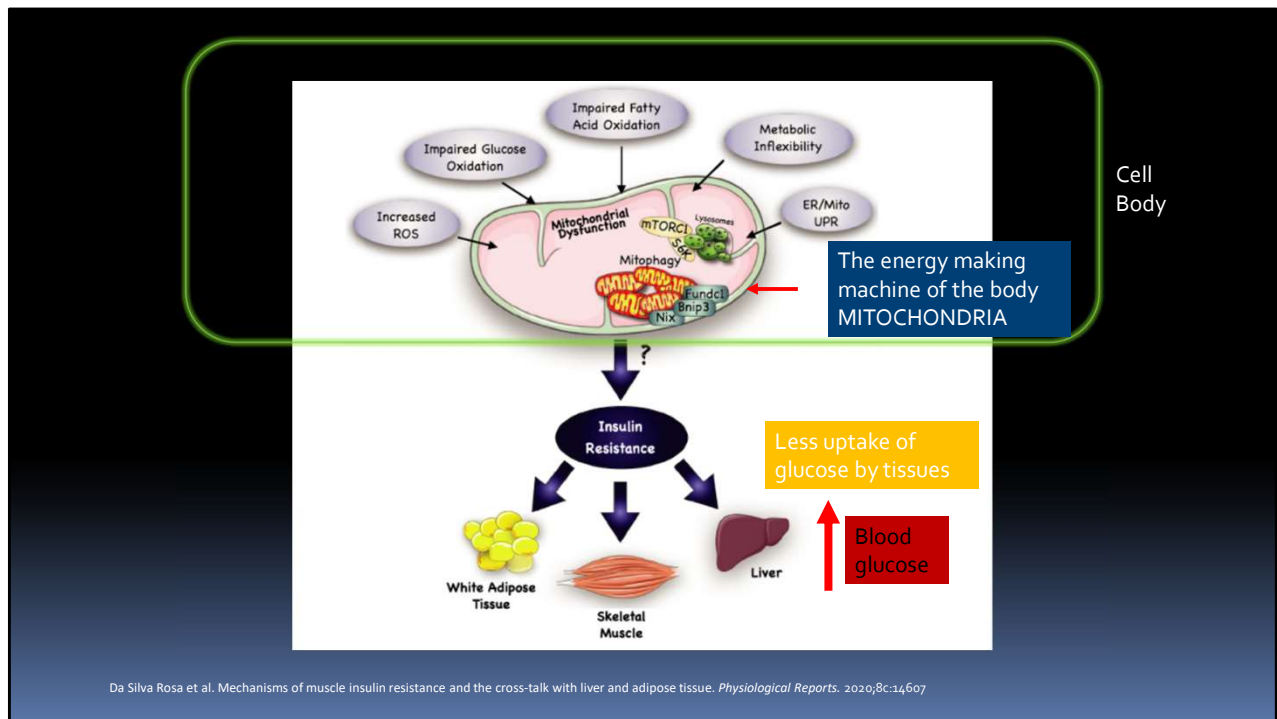


If the mitochondria become sick so do we. Sick mitochondria, regardless of cause, creates insulin resistance.

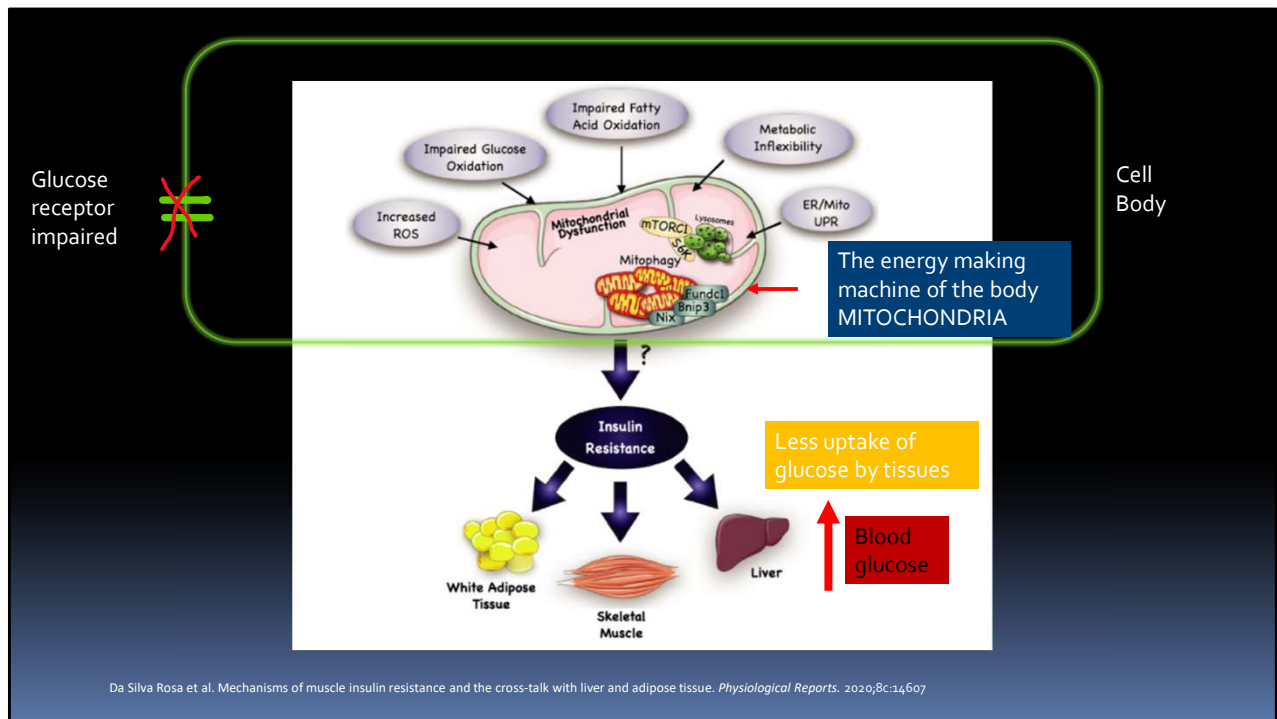
So, what does insulin resistance cause?



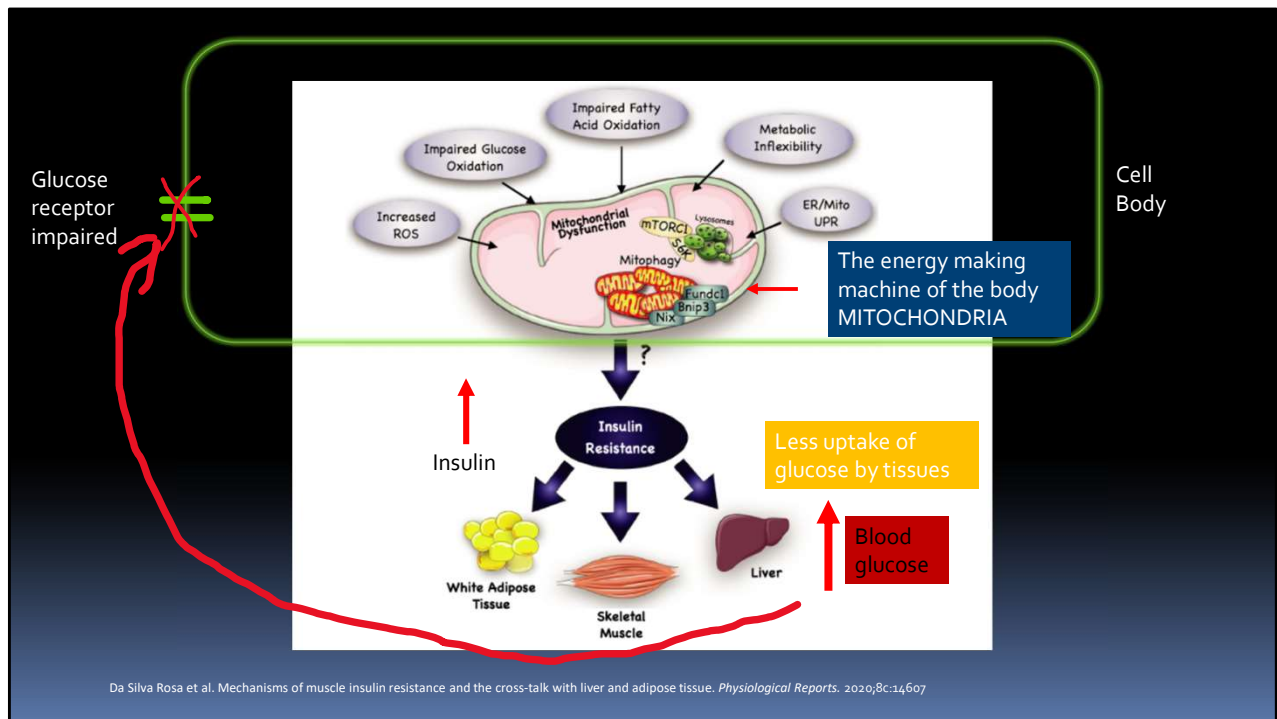
Receptors on cells help glucose enter the cells of your body. Insulin resistance impairs the function of these receptors making it harder for glucose to get into tissues like muscle, adipose tissue and liver



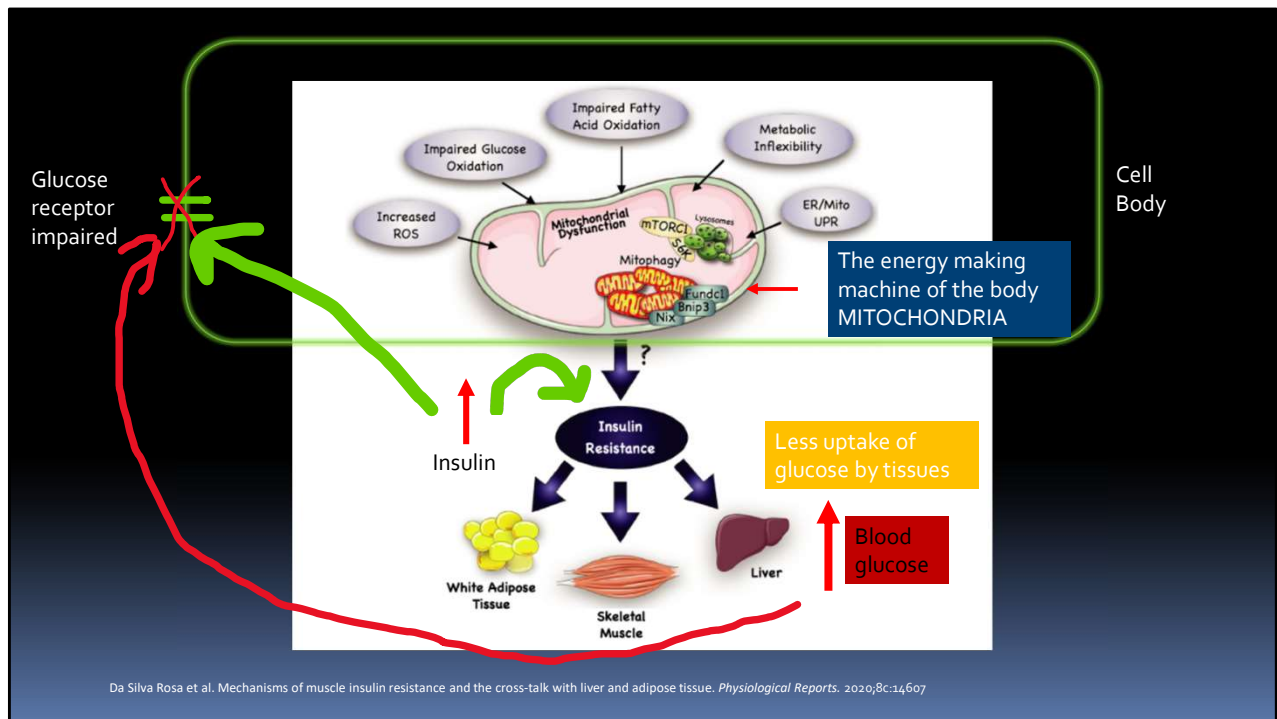
Blood glucose levels begin to rise



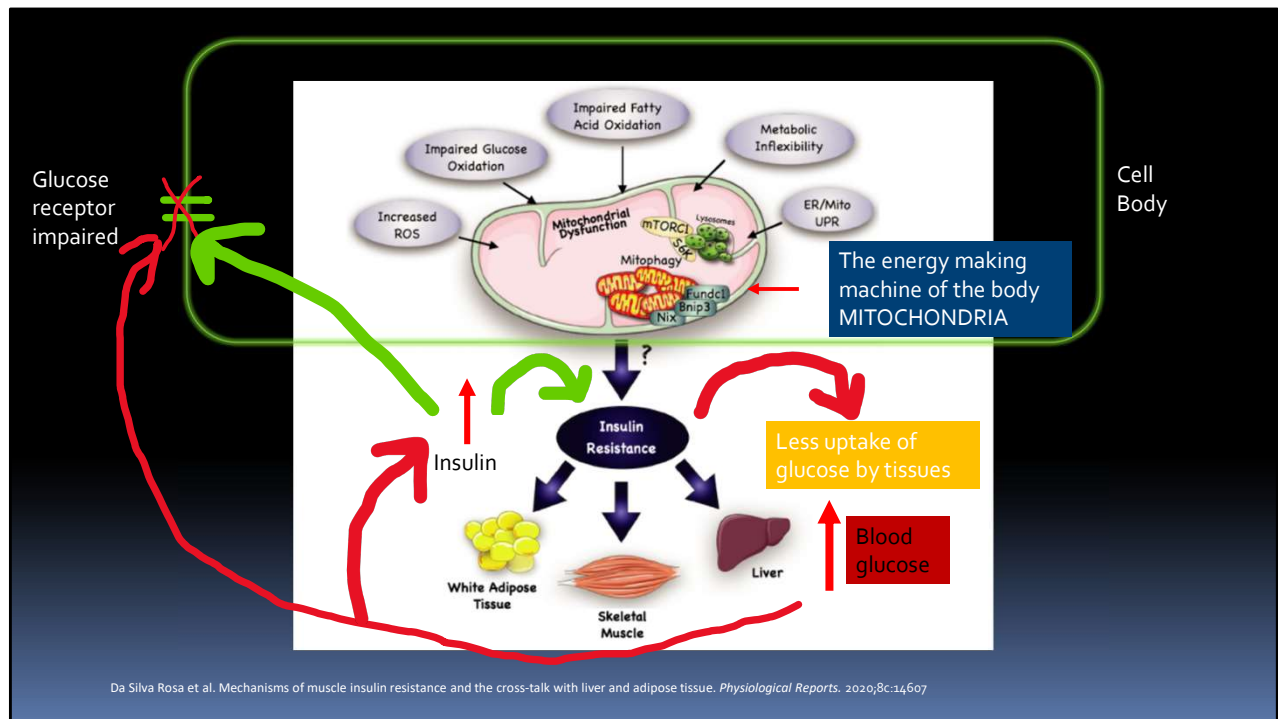
Elevated blood glucose allows a little more glucose to enter the cell through the impaired glucose receptors



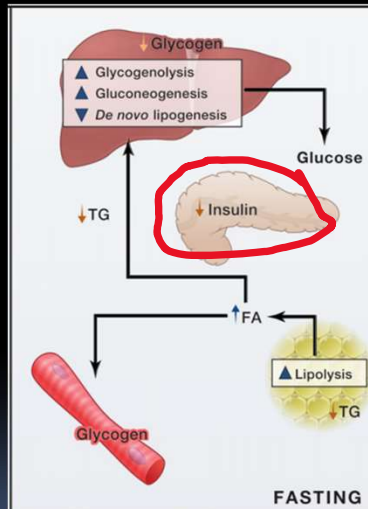
Exposure to higher glucose levels leads to further impairment of the receptor and MORE insulin resistance



A vicious cycle begins – higher glucose = higher insulin levels = greater insulin resistance = high blood glucose = higher insulin resistance etc. etc.



How do we exit this vicious cycle and improve our metabolic health?



Modified from Fig. 1: Samuel V T et al. Mechanisms for Insulin Resistance: Common Threads and Missing Links. *Cell*. 2012;148(5):852-871.

1. Decrease the amount of ingested carbohydrates: refined white flour and added sugars
2. Increase the amount of time spent in the fasting phase: intermittent fasting and time restricted eating

LOWER
INSULIN

Decrease the amount of time your body spends producing insulin

1. **Decrease the amount of ingested carbohydrates: refined white flour and added sugars**
2. **Increase the amount of time spent in the fasting phase: intermittent fasting and time restricted eating**

We reviewed the biochemistry of why insulin resistance is so bad for our metabolic health. This is relevant at all times but particularly so during this time of COVID

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So, why are we even more concerned now during our pandemic?

We reviewed the biochemistry of why insulin resistance is so bad for our metabolic health. This is relevant at all times but particularly so during this time of COVID

Why? Because observational studies have noted greater mortality if you present to the hospital with higher blood glucose levels or higher levels of HgA1c - Regardless of diabetes status

¹Carrasco-Sanchez F J et al. Admission Hyperglycaemia as a predictor of mortality in patients hospitalized with COVID-19 regardless of diabetes status. *Annals of Medicine*. 2020. 53;1:103-116.

²Wang Z et al. Glycosylated hemoglobin is associated with systemic inflammation, hypercoagulability, and prognosis of COVID-19 patients. *Diabetes Res Clin Pract*. 2020. Jun;164:108214.

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COVID doesn't care if you are diabetic or not. Recall that higher blood sugar levels are associated with POOR metabolic health

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Wang Z et al. Glycosylated hemoglobin is associated with systemic inflammation, hypercoagulability, and prognosis of COVID-19 patients. Diabetes Res Clin Pract. 2020. Jun;164:108214.

I hear a lot about vitamin D. What's that all about?



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If you are looking for a science and evidence-based review consider watching this YouTube 10 Dec 2020 video: Vitamin D and COVID 19: The Evidence for Prevention and Treatment of Coronavirus (SARS CoV 2); Prof. Roger Seheult

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So, Let's explore Vitamin D briefly as it is a popular topic. The evidence is mainly **observational** – meaning – just because we observe Vitamin D levels lower in COVID patients, doing poorly, doesn't mean this association **CAUSED** the poor outcome (which would be **CAUSATION**) – other factors could be involved

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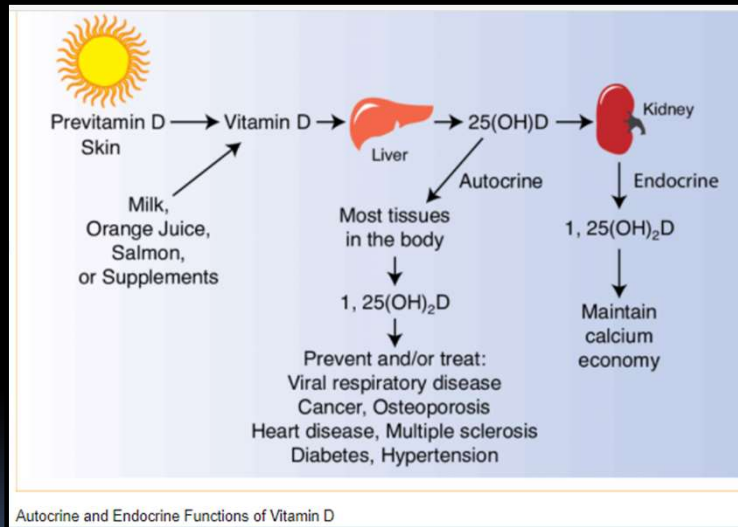
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Association does not = Causation

If you have enough observational studies, showing association, and the results are compelling and scientifically reasonable then we can infer CAUSATION. As an example there was a 20+ fold increase in lung cancer in smokers as compared with non-smokers. Because it was unethical to do an interventional trial (RCT – randomized controlled clinical trial) there was enough evidence of extremely strong association to imply causation. The same holds true for seatbelts and bicycle helmets.

Association does not equal causation **BUT** If you have enough observational studies, showing association, and the results are compelling and scientifically reasonable then we can infer CAUSATION. As an example there was a 20+ fold increase in lung cancer in smokers as compared with non-smokers. Because it was unethical to do an interventional trial (RCT – randomized controlled clinical trial) there was enough evidence of extremely strong association to imply causation. The same holds true for seatbelts and bicycle helmets.

Vitamin D – So much more than just calcium and bone health



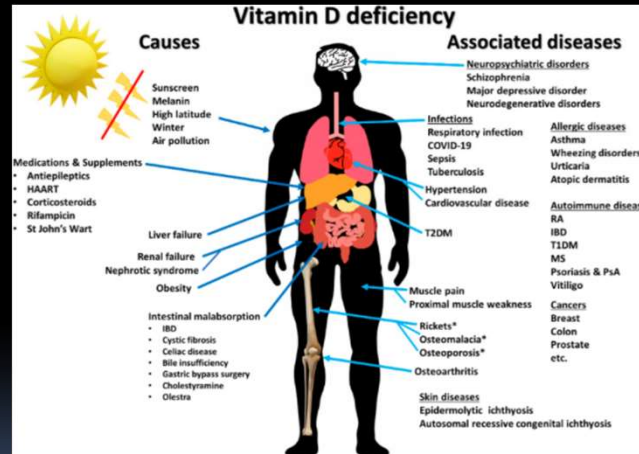
Lockau L et al. In Vitamin D deficiency in bioarchaeology and beyond: The study of rickets and osteomalacia in the past. *International Journal of Paleopathology*. 2018;23:6-14.

Cannell J et al. (2008). Use of vitamin D in clinical practice. *Altern med rev*. 2008;13(1):6-20.

Because we live North of the 35th parallel, about midway between north and south USA mainland states, being outdoors in summertime still produces inadequate Vitamin D levels. Many of us only think about Vitamin D with respect to bone health calcium, and phosphorous. Since we cannot produce enough Vitamin D from sunlight, we need to ingest it from food, like sardines or salmon, or supplements. Vitamin D is converted to the active form of 25(OH)D [hydroxy-vitamin D] by the liver. Researchers previously believed only the kidney converted 25(OH) D into the active form 1,25 (OH)₂. There is now compelling evidence that immune cells convert 25(OH)D to 1,25(OH)₂D in an unregulated manner and are dependent on the circulating levels of 25(OH)D to be at least 30 ng/mL (75 nmol/L).

Lockau L et al. In Vitamin D deficiency in bioarchaeology and beyond: The study of rickets and osteomalacia in the past. International Journal of Paleopathology. 2018;23:6-14.

Cannell J et al. (2008). Use of vitamin D in clinical practice. Altern med rev. 2008;13(1):6-20.



Charoenngam N et al. Immunologic Effects of Vitamin D on Human Health and Disease. *Nutrients*. 2020; 12(7):2097. <https://doi.org/10.3390/nu12072097>
 Griffin G et al. Vitamin D and COVID-19: evidence and recommendations for supplementation. *R. Soc. open sci.* 2020;7:201912

Most of the evidence, to date, suggests that maintenance of a healthy vitamin D status is important for modulating the body's immune function (*both innate and adaptive immunity*).

Association between low levels of serum 25-hydroxyvitamin D and increased risk of developing several immune-related diseases and disorders, including psoriasis, type 1 diabetes, multiple sclerosis, rheumatoid arthritis, tuberculosis, sepsis, respiratory infection, and COVID-19, has been observed.

Some of the causes and associated diseases with Vitamin D deficiency are illustrated on the slide.

Charoenngam N et al. Immunologic Effects of Vitamin D on Human Health and Disease. *Nutrients*. 2020; 12(7):2097. <https://doi.org/10.3390/nu12072097>

Vitamin D is critical to optimal health and involved in our immune system.

Studies across several populations reveal inadequate Vitamin D levels in over ½ to 2/3 of participants, depending on the level of Vitamin D deemed “adequate.”

Some studies use cut-off levels, based on old Vit D levels to prevent rickets in children; (50 nmol/L = 20 ng/ml)¹. Using this LOW old standard, prior to our understanding of immunity, revealed 40% of Canadians in wintertime are BELOW this level. A much higher number of Canadians would be BELOW the lower limit of 30 ng/mL (75 nmol/L) required by immune cells to convert 25(OH)D to 1,25(OH)2D. Below 30 ng/mL (75 nmol/L) the innate and adaptive immune systems are compromised²

¹StatCan Report. Vitamin D blood levels of Canadians. 2011. Statcan.gc.ca: Accessed 1 Feb 2021.

² Charoenngam N et al. Immunologic Effects of Vitamin D on Human Health and Disease. *Nutrients*. 2020. 12; 2097:1-28.

So, what do we can we say about Vitamin D at this point.

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Table 1. The recommended dosage for vitamin D intake in individuals who are at risk for vitamin D deficiency and dosage of vitamin therapy treatment for patients with vitamin D deficiency.

Age Group	For Individuals at Risk for Vitamin D Deficiency		Treatment for Patients with Vitamin D Deficiency
	Daily Requirement	Upper Limit	
0–1 years	400–1000 IU	2000 IU	- 2000 IU/d or 50,000 IU/wk of vitamin D ₂ or D ₃ for at least 6 wk to achieve serum 25(OH)D >30 ng/mL (75 nmol/L) - maintenance therapy of 400–1000 IU/d
1–18 years	600–1000 IU	4000 IU	- 2000 IU/d or 50,000 IU/wk of vitamin D ₂ or D ₃ for at least 6 wk to achieve serum 25(OH)D >30 ng/mL (75 nmol/L) - maintenance therapy of 600–1000 IU/d
>18 years	1500–2000 IU	10,000 IU	- 6000 IU/d or 50,000 IU/wk of vitamin D ₂ or D ₃ for 8 wk to achieve serum 25(OH)D >30 ng/mL (75 nmol/L) - maintenance therapy of 1500–2000 IU/d
Obese and malabsorptive patients	4000–6000 IU	10,000 IU	- Dosage should be increased by 2–3 times

Adapted from Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society Clinical Practice Guidelines [11].

Hollick M F et al. The Hormone Foundation's Patient Guide to Vitamin D Deficiency. *The Journal of clinical endocrinology and metabolism*. 2011;;96 (7):1-29.

Charoenngam N et al. Immunologic Effects of Vitamin D on Human Health and Disease. *Nutrients*. 2020. 12; 2097:1-28.

So, we are all at risk here in Canada, **even more so** in the wintertime. The recommended dose of Vit D – IF YOUR LEVELS ARE ADEQUATE is 1500-2000 IU daily. Yes you can get a blood test for Vit D for ~ 25.00 and it's covered if you have osteopaenia or osteoporosis

If your below the 30 ng/ml (75 nmol/L) the endocrine society recommends 6000 IU/day, or 50,000 IU/week for a couple of months and then return to 1500-2000 IU daily

Charoenngam N et al. *Immunologic Effects of Vitamin D on Human Health and Disease. Nutrients*. 2020. 12; 2097:1-28.

Hollick M F et al. *The Hormone Foundation's Patient Guide to Vitamin D Deficiency. The Journal of clinical endocrinology and metabolism*. 2011;;96 (7):1-2

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What about obesity. Some of us don't absorb Vit D as well, especially if we have inflammatory bowel disease or previous gastric bypass surgery.

Obesity is independently associated with lower Vit D levels, which is a fat soluble Vitamin. Also check with your doctor because some medications interfere with Vit D absorption and/or metabolism in the liver. Therefore the recommended Endocrine Society dose for obese and malabsorptive patients is 4000-6000 IU daily. In cases where your blood test shows you <30 ng/ml (75 nmol/L) the dose is 12,000 – 18,000 IU daily

Meds that can alter Vit D metabolism (AIDS meds, Antifungals, Glucocorticoids, Antiseizure meds and Cholestyramine)

Hollick M F et al. The Hormone Foundation's Patient Guide to Vitamin D Deficiency. The Journal of clinical endocrinology and metabolism. 2011;;96 (7):1-2

Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline

Michael F. Holick, Neil C. Binkley, Heike A. Bischoff-Ferrari, Catherine M. Gordon, David A. Hanley, Robert P. Heaney, M. Hassan Murad, and Connie M. Weaver

Boston University School of Medicine (M.F.H.), Boston, Massachusetts 02118; University of Wisconsin (N.C.B.), Madison, Wisconsin 53706; University Hospital Zurich (H.A.B.-F.), CH-8091 Zurich, Switzerland; Children's Hospital Boston (C.M.G.), Boston, Massachusetts 02115; University of Calgary Faculty of Medicine (D.A.H.), Calgary, Alberta, Canada T2N 1N4; Creighton University (R.P.H.), Omaha, Nebraska 68178; Mayo Clinic (M.H.M.), Rochester, Minnesota 55905; and Purdue University (C.M.W.), West Lafayette, Indiana 47907

Objective: The objective was to provide guidelines to clinicians for the evaluation, treatment, and prevention of vitamin D deficiency with an emphasis on the care of patients who are at risk for deficiency.

Participants: The Task Force was composed of a Chair, six additional experts, and a methodologist. The Task Force received no corporate funding or remuneration.

Consensus Process: Consensus was guided by systematic reviews of evidence and discussions during several conference calls and e-mail communications. The draft prepared by the Task Force was reviewed successively by The Endocrine Society's Clinical Guidelines Subcommittee, Clinical Affairs Core Committee, and cosponsoring associations, and it was posted on The Endocrine Society web site for member review. At each stage of review, the Task Force received written comments and incorporated needed changes.

Conclusions: Considering that vitamin D deficiency is very common in all age groups and that few foods contain vitamin D, the Task Force recommended supplementation at suggested daily intake and tolerable upper limit levels, depending on age and clinical circumstances. The Task Force also suggested the measurement of serum 25-hydroxyvitamin D level by a reliable assay as the initial diagnostic test in patients at risk for deficiency. Treatment with either vitamin D₂ or vitamin D₃ was recommended for deficient patients. At the present time, there is not sufficient evidence to recommend screening individuals who are not at risk for deficiency or to prescribe vitamin D to attain the noncalcemic benefit for cardiovascular protection. (*J Clin Endocrinol Metab* 96: 1911–1930, 2011)

Hollick M F et al. The Hormone Foundation's Patient Guide to Vitamin D Deficiency. *The Journal of clinical endocrinology and metabolism*. 2011;96 (7):1-2

To summarize the endocrine societies guidelines — read the yellow insert; conclusions

Hollick M F et al. The Hormone Foundation's Patient Guide to Vitamin D Deficiency. *The Journal of clinical endocrinology and metabolism*. 2011;96 (7):1-2

No study shows you can PREVENT COVID-19 and an early open-label randomized control trial in Spain showed benefit to those patients treated with high dose Vit D¹. The answer will come as more trials are underway.

I'm worried Vit D might be toxic. That is a reasonable concern.

What is evidence for toxicity? Fortunately we have the answer from a recent study²
"The evidence is clear that Vitamin D toxicity is one of the rarest medical conditions and is typically due to intentional or inadvertent intake of extremely high doses of vitamin D (usually in the range of >50,000 100,000 IU/d for months to years." The only patient found with toxicity was also taking high dose calcium supplements.

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Diabetes, Hypertension, Cerebrovascular Disease, Obesity, Cancer, Alzheimer's, Cardiovascular disease, Chronic Liver disease, Chronic kidney disease, autoimmune diseases ...

INSULIN RESISTANCE



So, Here we are full circle with the elephant in the room. All of these “diseases of civilization are linked to insulin resistance

How did we ever survive as a species

In order to understand where our population is regarding metabolic health, we need to examine the history of our diets in developed countries like North America

Has our diet changed in the previous 2 centuries?

We will briefly examine the US diet because of excellent data

To understand metabolic health we need to understand how we ate previously.

So, have our diets changed over the past 100-200 years?

1. Let's talk about the U.S. Diet – The Big Picture
2. 4 Major Changes have occurred in the U.S., with the world following suit, three of which were introduced between 1880 and 1911.
3. These four things are nutrient-deficient, toxic, processed foods.

*Despite reading several science-based nutrition books over the previous decade, I never fully appreciated the powerful impact of diet regarding health. Everything changed for me in early 2019 after reading the 1939 work of Weston Price – “**Nutrition and Physical Degeneration**”.*

*Subsequent discoveries led me to a book by ophthalmologist Chris Knobbe – “**Ancestral***

***Dietary Strategy to Prevent and Treat Macular Degeneration** published in 2016". Because of my interest in nutritional biochemistry, I quickly went down the **diet causes disease** "rabbit hole" following several conversations with Chris. If any ideas seem valuable, or slides are of interest during this talk, they are 100% attributed to Chris Knobbe's research over the previous 9 years, therefore igniting my interest in preventative medicine.*

I declare NO CONFLICTS OF INTEREST. I have followed dietary and lifestyle changes in order to reverse my insulin resistance over the last 2+ years. (LCHF)

1. White Flour - 1880



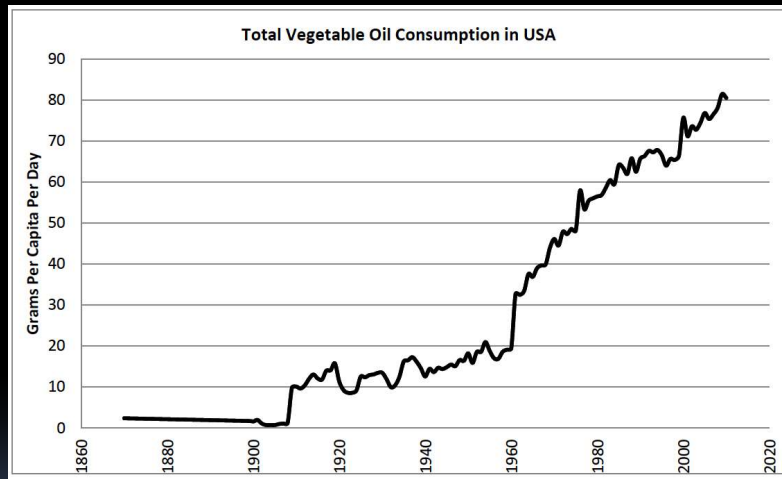
1. White flour – introduced in 1880. Up until 1880, all wheat was ground to whole-grain flour, because wheat was ground on stone mills.
2. In 1880, ROLLER MILL technology replaced stone mill technology.
3. Roller mill technology shears away the bran and the germ, leaving behind only the endosperm.
4. This effectively removes most of the B-vitamins, E-vitamins, fiber, minerals, and omega-3 and omega-6 fats, thereby leaving behind a nutrient-deficient food.
5. **Today, wheat is 20% of the world's diet on a caloric basis.**
6. **85.3%** of wheat consumed is now “**highly processed refined grains.**” – Loren Cordain's group has shown this.

2. Vegetable Oils (PUFAs)



Soybean Oil
Corn Oil (Maize Germ Oil)
Cottonseed Oil
Rape/Rapeseed & Canola Oil
Sunflower Oil
Safflower Oil
Rice Bran Oil
Mustard Oil

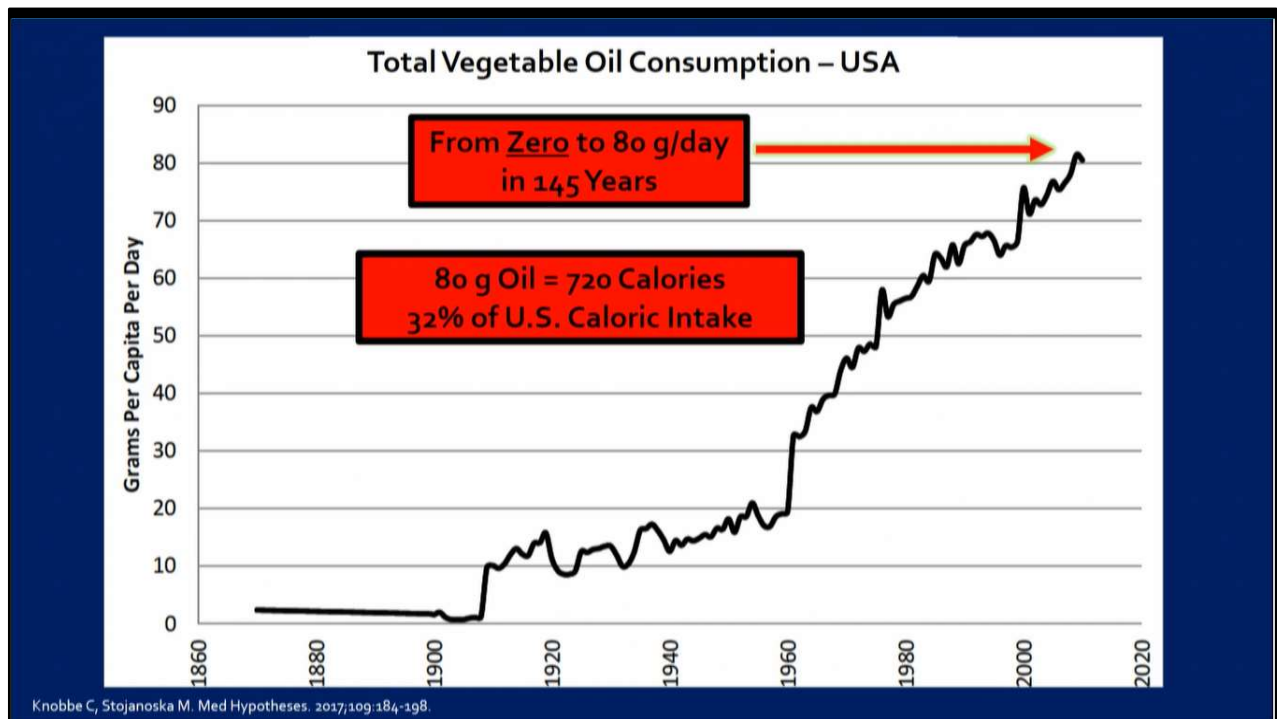
1. Vegetable Oils – Polyunsaturated Fatty Acids -- also known as PUFAs, introduced in 1866 after the American Civil War (cottonseed oil).
2. Manufacturers determined they could take cotton seeds – a waste product – crush them, heat them to HIGH temperatures multiple times,, run them through a hydraulic press – and then take that substance and treat it to a petroleum derived hexane solvent bath, steam it, alkalinize it, bleach it, and finally, deodorize it – chemically – and declare “now we’ve got something they say is safe to eat”.
3. These are extraordinarily dangerous products. They’re highly oxidized by the time they hit the bottle. And then, when we cook with them and metabolize them, they oxidize even further.
4. **I think these are the SINGLE MOST DANGEROUS substances in our food supply – because a poison is all about the dose – and we’re currently consuming 24% of our calories as PUFA vegetable oils.**



Knobbe C et al. The "Displacing Foods of Modern Commerce" Are the Primary and Proximate Cause of Age-Related Macular Degeneration: A Unifying Singular Hypothesis. *Medical Hypotheses* 109 (2017) 184-198

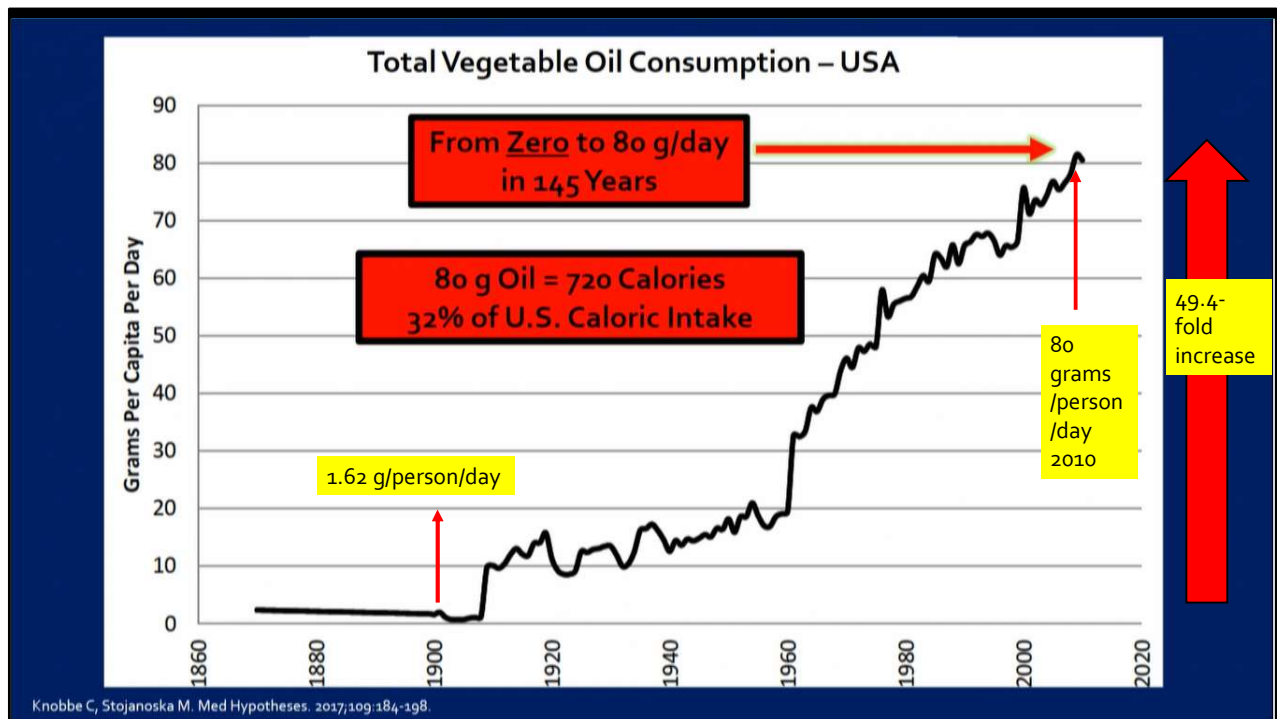
1. Here is total vegetable oil consumption in the U.S. over time

Chris Knobbe's colleague in this research, Marija Stojanoska, produced all these graphs

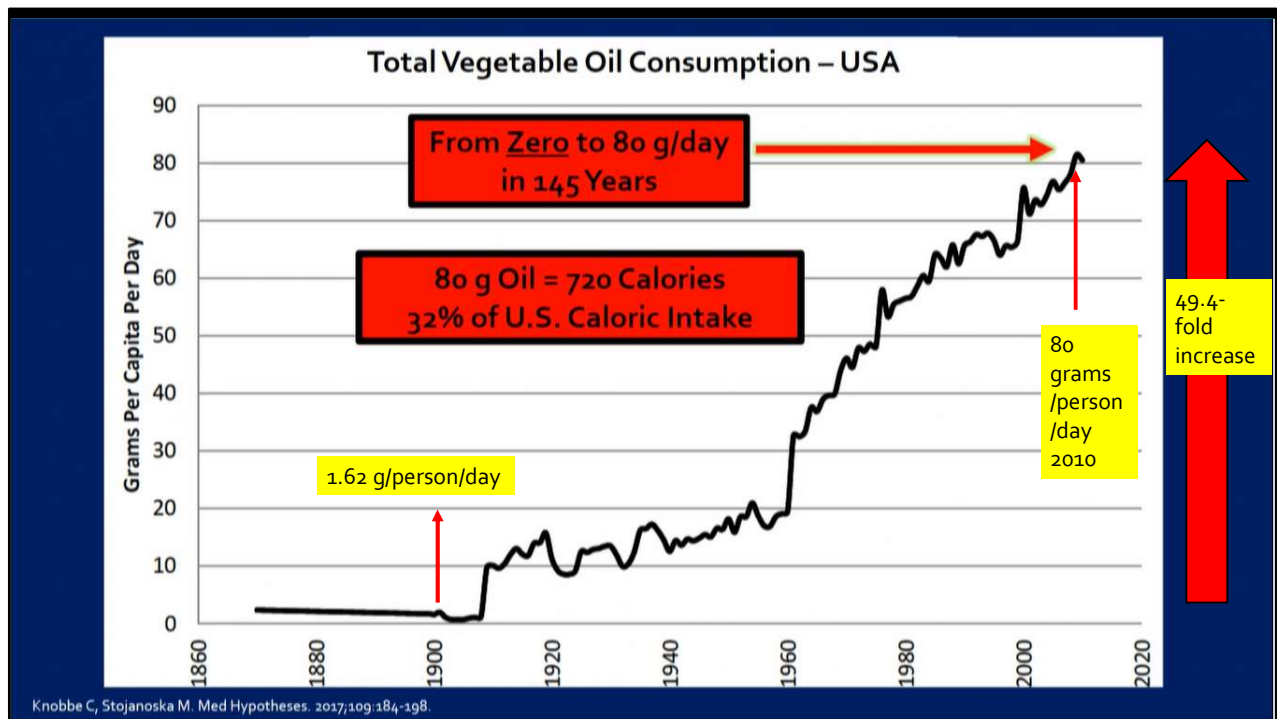


1. So, look at vegetable oil consumption here. You can see we were near **zero grams a day in 1900**, climbing all the way to **80 grams a day by 2010**.
2. This is a staggering amount.

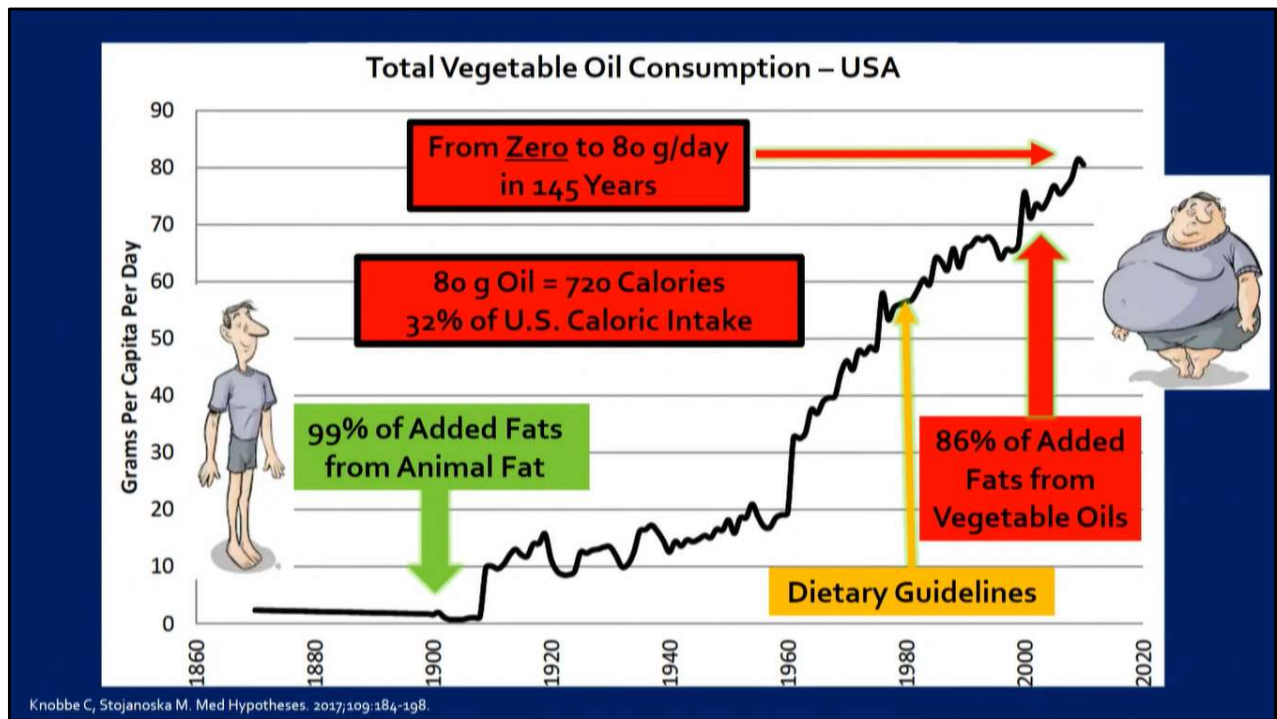
80 grams of oil = 720 calories accounting for 32% of US caloric intake of 2250 Calories/day in 2010 [1999; (NHANES data calorie consumption: 1999-2000)]



This change in Total vegetable oil consumption, 1.62g/person/day in 1900 to 80g/person/day in 2010, is a 49.4-fold increase ($80/1.62=49.4$)



YES – you read it correctly; a 4,940% INCREASE



Consider this: In 1900, 99% of our ADDED FATS came from animal fats – **butter, lard, and beef tallow**. By 2005, 86% of our added fats came from vegetable oils.

Now, let me remind you, that in 1900 cancer, diabetes, heart disease and “other westernized diseases” were rare or virtually absent

Obesity was 1.2% prior to 1900; 13.3% by 1960 and 42.4% in 2017-2018 (CDC National Center for Health Statistics (NCHS) from NHANES data Feb 2020; **the US is on track by 2030 for a 50% obesity rate**. (NHANES) National Health and Nutrition Examination Survey

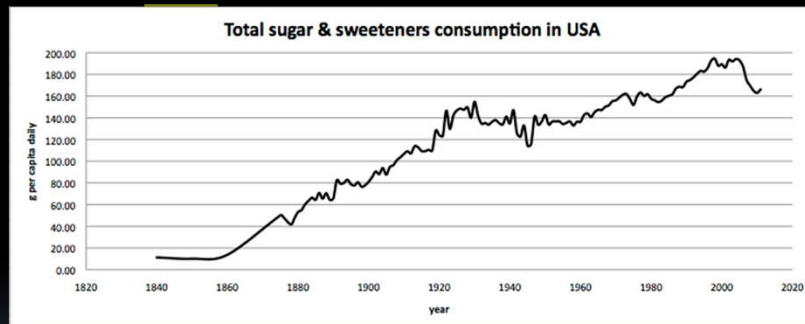
Note: Added oil of 80 grams includes the vegetables oils added AND hidden in processed food (crackers, cakes, ice cream etc.)

3. Trans Fats – 1911

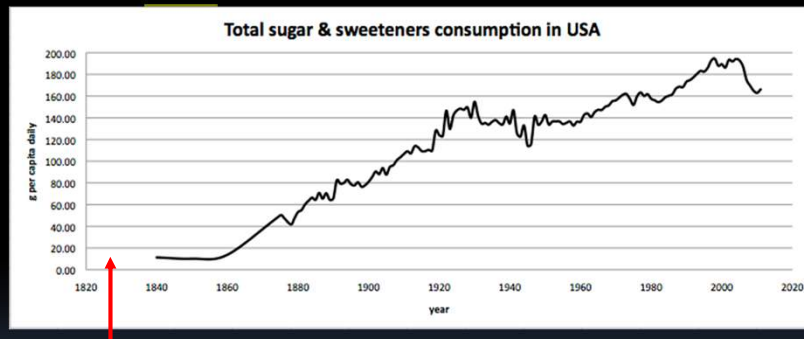


Proctor & Gamble:
When a candle
maker and soap
maker collaborate

1. Our THIRD nutrient-deficient, processed food, is trans fats – Partially hydrogenated and hydrogenated vegetable oils – CRISCO.
2. We all know these are extremely dangerous substances, and we've consumed billions of pounds of these since they were introduced in 1911.
3. The FDA removed these from GRAS (generally regarded as safe) status June 16, 2015, with 3 years for manufacturers to implement the removal, but they're not going away, because they're in vegetable oils.
4. Vegetable oils have up to 4.6% trans fats and average 1.1% trans fats.

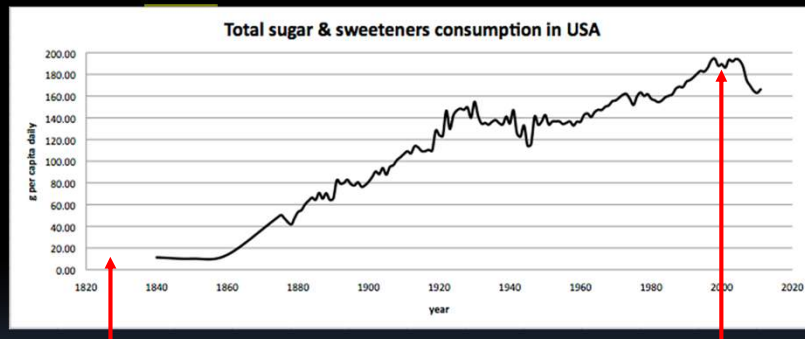


This is from Chris Knobbe's research, showing sugar consumption from 1840 forwards.



1822
1.79 tsp/person/day

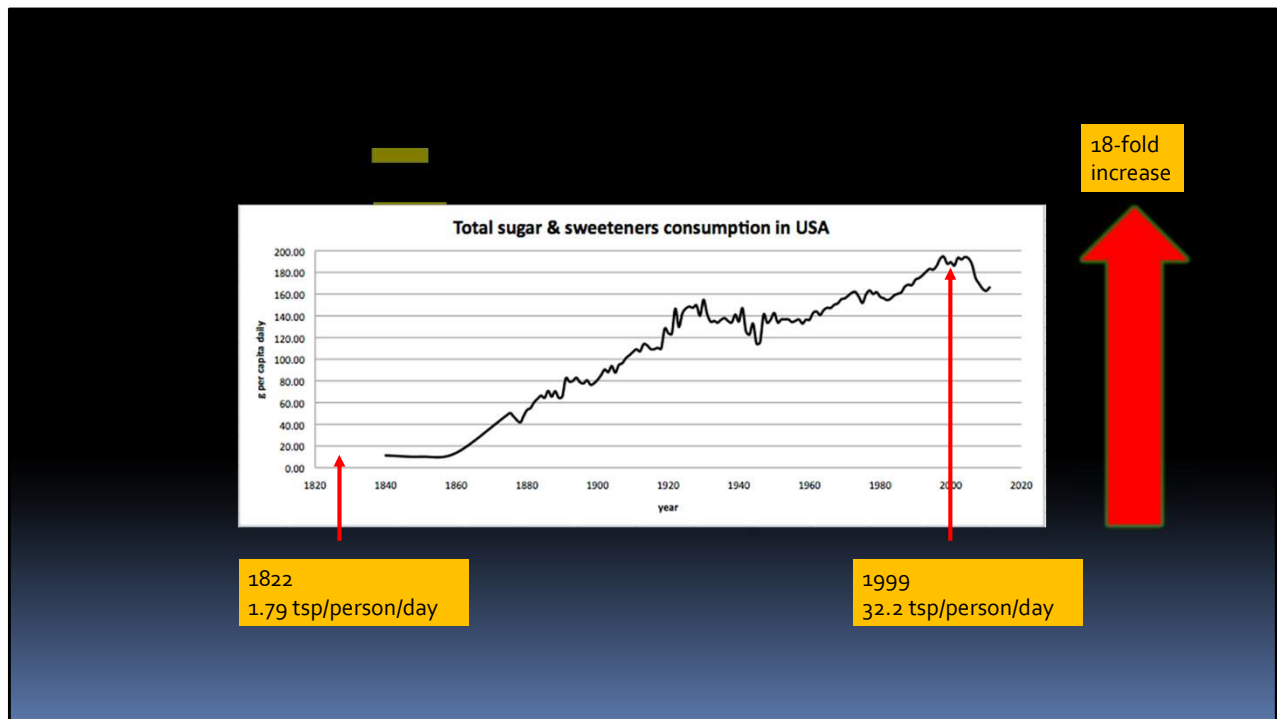
Stephan Guyenet, University of Washington, showed us several years ago that the US consumed 6 pounds of sugar/person/year in 1822, the equivalent of 1.79 teaspoon/person/year



1822
1.79 tsp/person/day

1999
32.2 tsp/person/day

By 1999, we consumed 108 lbs/person/yr., the equivalent of **32.2 teaspoons/person/day**



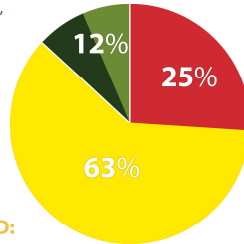
Therefore between 1822 & 1999 there was an $(32.2/1.79)$ 18-fold increase in sugar consumption

Sugar is our 4th Nutrient-Deficient, Processed Food.

U.S. FOOD CONSUMPTION AS A PERCENT OF CALORIES - 2009

PLANT FOOD:
Fruits, Vegetables, Legumes,
Whole Grains, Nuts & Seeds

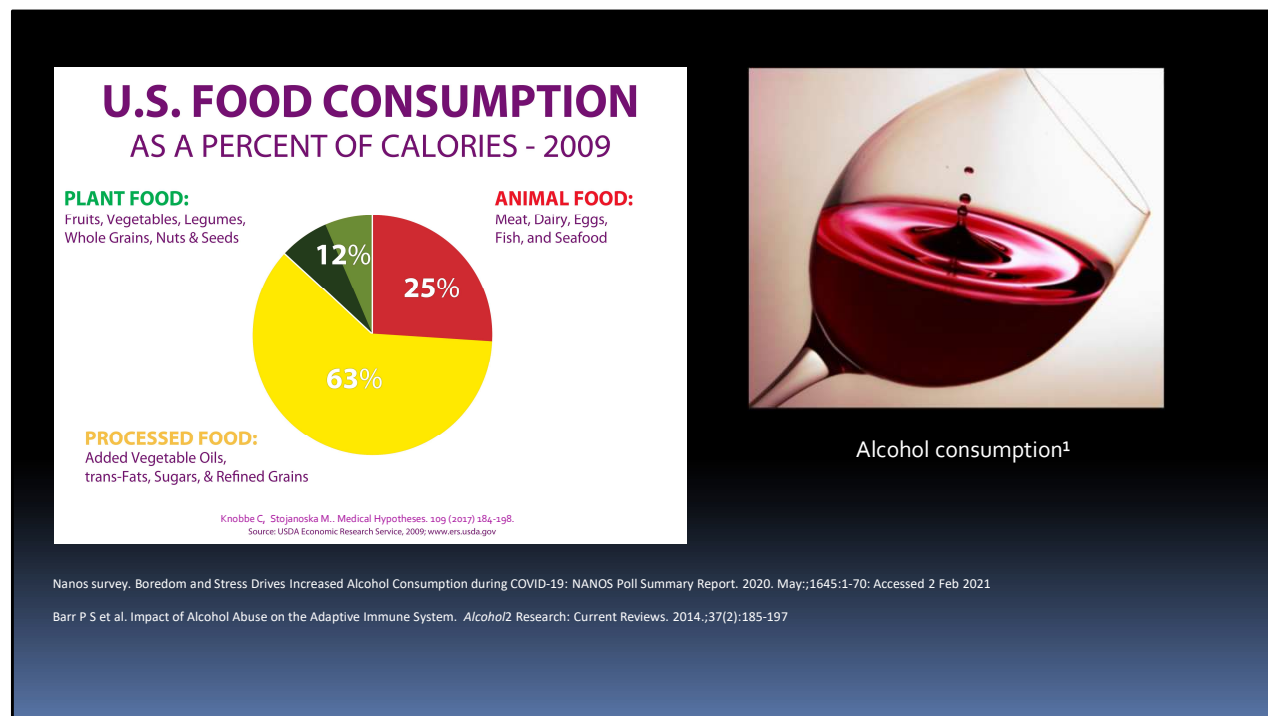
ANIMAL FOOD:
Meat, Dairy, Eggs,
Fish, and Seafood



PROCESSED FOOD:
Added Vegetable Oils,
trans-Fats, Sugars, & Refined Grains

Knobbe C, Stojanaska M. Medical Hypotheses. 209 (2017) 184-198.
Source: USDA Economic Research Service, 2009; www.ers.usda.gov

1. Put those four foods together, and as of 2009, you have 63% of the U.S. diet – made up of white flour, sugar, vegetable oils, and trans fats; slightly more if alcohol is included.
2. Four processed foods – WITH VIRTUALLY NO MICRONUTRIENTS – Vitamins or Minerals -- at all, apart from a small amount of vitamin E in the vegetable oils.
3. This is a recipe for metabolic disaster, and it was successful **with only 12.% of the US population metabolically healthy between 2009-2016**



So, way back in 2009, you have 63% of the U.S. diet – made up of white flour, sugar, vegetable oils, and trans fats;

12 years later, and with COVID, I suspect the % of toxic, nutrient-deficient , processed food is far worse.

Although the Canadian Centre on Substance Use and Addiction Report, May 2020, reported 10% of Canadians surveyed drank less alcohol (because we can't socialize), 20% are consuming more. This trend may be increasing with longer COVID lockdowns.

Now I'll admit I previously enjoyed a glass of red wine once or twice a week with my wife for a treat. Now I gave it up until the pandemic is over. Why?

There are several recent studies revealing suppression of our immune system with alcohol. I'm looking forward to celebrating the end of the pandemic with a nice glass of Merlot but for now I'm trying to give myself every advantage, should I become infected with COVID despite my long list of precautions. (Update: 2 weeks after my second vaccine I enjoyed a glass of red wine)

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Diabetes, Hypertension, Cerebrovascular Disease, Obesity, Cancer, Alzheimer's, Cardiovascular disease, Chronic Liver disease, Chronic kidney disease, autoimmune diseases ...

INSULIN RESISTANCE

Artist unknown

Added sugars and refined white flour makes us INSULIN RESISTANT.

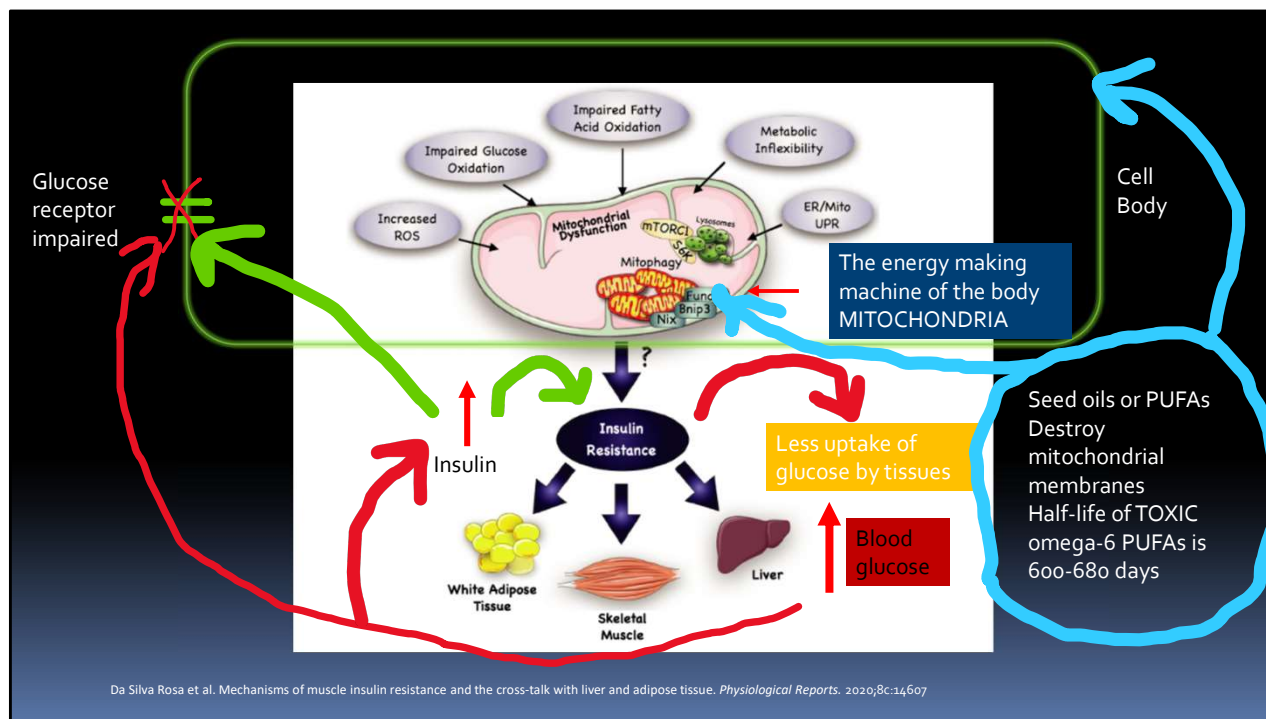


Added sugars and refined white flour makes us INSULIN RESISTANT.

Dr. Gary Fettke and Dr. Robert Lustig have hypothesized that anything greater than 1 teaspoon of glucose in the bloodstream, the equivalent of ~ 4 grams, is TOXIC.

Between 1822 & 1999 our sugar consumption went from 1.79 teaspoons/person/day to 32.2 teaspoons/person/day, an $(32.2/1.79)$ astounding 18-fold increase. This is clearly driving our obesity, diabetes, metabolic syndrome and a multitude of other “diseases of modern civilization”

There are more precisely 4.2 grams of glucose /tsp. (teaspoon) but most articles round this down to 4.0



Seed oils or polyunsaturated fatty acids, most often called PUFAs are one of the most dangerous products we consume. They destroy the energy producing factories of the cell, called mitochondria, responsible for producing 95% of the energy (ATP) we require for our metabolism. The half-life of these toxic omega 6 oils is 600-680 days

Fig. 1 Overview of possible mechanisms leading to insulin resistance. Impaired mitochondrial functioning is a suggested mechanism through which insulin resistance develops. Several factors have been implicated in the development of mitochondrial dysfunction. Some of the most reported factors include: (a) an increased production of reactive oxidative species (ROS). ROSs are necessary by-products of mitochondria energy metabolism; however, if their production is not adequately coupled by intracellular antioxidants, then oxidative damage to mitochondrial DNA (mtDNA) can occur. (b) Impaired glucose oxidation and fatty acid oxidation may result from metabolic inflexibility, which is commonly described as an inability to adapt fuel oxidation to fuel availability. Ultimately, these events may lead to both the development of ROS and ectopic lipid accumulation, resulting in mitochondrial damage and removal through mitophagy pathways. Further investigation on the genes involved in mitophagy (i.e., Bnip3, Nix, Fundc1) may allow the discovery of pathways that explain the correlation between mitochondrial dysfunction and insulin

resistance in adipose, hepatic, and skeletal muscle tissue. (c) Endoplasmic Reticulum (ER) stress is also involved in the pathogenesis of mitochondrial dysfunction. Lipotoxicity and glucotoxicity can induce ER stress, which may trigger an adaptive signaling pathway, known as the unfolded protein response (UPR). If ER stress fails to be relieved by this UPR, then this can lead to the provocation of both mitochondrial dependent and independent cell death pathways. Together, the ability of the mitochondria to respond to metabolic disruptions is essential for healthy cellular bioenergetics, and interference with this process may prompt unregulated mitochondrial biogenesis and mitophagy, thus contributing to insulin resistance

Da Silva Rosa et al. Mechanisms of muscle insulin resistance and the cross-talk with liver and adipose tissue. Physiological Reports. 2020;8c:14607

“Replacing” naturally derived vitamins from whole food with synthetic ones. Good idea or not?

Cochrane Collaboration, 2012:

- 78 Trials confirm higher death rate (1.04-fold) from all causes when consuming synthetic multivitamins.

Bjelakovic G, et al. Cochrane Collaboration. 2012. March 14.

So why not keep eating ultra-processed addictive food and take a multivitamin to cover yourself – just in case

Consider this before you do.

“Replacing” naturally derived vitamins from whole food with synthetic ones. Good idea or not?

Cochrane Collaboration, 2012:

- 78 Trials confirm higher death rate (1.04-fold) from all causes when consuming synthetic multivitamins.

Bjelakovic G, et al. Cochrane Collaboration. 2012. March 14.

78 Trials confirm higher death rate (1.04-fold) from all causes when consuming synthetic multivitamins.

What to eat? I will quote Dr. Gary Fettke who recently gave his definition for “dietary guidelines”

Finally, at the end of this presentation my wife would say to me - just give me the summary. Here it is:

What to eat? I will quote Dr. Gary Fettke who recently gave his definition for “dietary guidelines”

Eat fresh, local, seasonal, whole food according to your cultural and environmental beliefs avoiding added sugar and seed oils

Eat fresh, local, seasonal, whole food according to your cultural and environmental beliefs avoiding added sugar and seed oils (Dr. Gary Fettke)

What to eat? I will quote Dr. Gary Fettke who recently gave his definition for “dietary guidelines”

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Consider stopping or cutting back on alcohol ; this may improve immune health

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You will never “out-supplement” or “out-exercise” a bad diet

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Healthy fats or chemical factory produced "seed oils" — you can make an informed decision

How can we consume only ~1% Om-6 PUFA?

No Seed Oils!



Avoiding everything in the slide will immensely improve your metabolic health

For more information on biochemistry and metabolic health I recommend YouTube presentations by Dr. Gary Fettke, from Tasmania (orthopaedic surgeon)

Diet Doctor website – this is an excellent platform with a lot of free information and good science articles for anyone with more interest. Everyone can reduce their carbohydrate intake regardless of diet preferences and improve health

Look up on the internet Quit Sugar summits from the past. There are often free videos of good speakers

A local nephrologist, Jason Fung, has several good videos on YouTube regarding intermittent fasting, and has authored several books (Diabetes Code, Obesity Code, Cancer Code and the Complete Guide to Fasting) Jason Fung on YouTube

Empower yourself with knowledge. Beware of all things promising “cures” especially if the website is “selling a magic pill, supplement, or ancient remedy”. Above all conflicts of interest should always be declared up front.

For additional information on metabolic health consider visiting the sites mentioned on the slide

Thank you



Thank you so much for the opportunity to discuss the importance of metabolic health and its relationship to COVID.

My beautiful wife also wanted me to point out to the audience that Mount Everest is in the background in this picture with our daughter. Luckily, she may not recall we awoke at 0400 hours and climbed from Ghorepani with headlamps at -5C with windchills of -15-20C, in order to reach Poon Hill lookout for sunrise; elevation 3193m, or 10475 feet.

